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The Defensive Chemistry of Land and Water Beetles[**]

By H. Schildknecht[*]

Wherever life forms have arisen, they have had to defend themselves, even on the lowest levels, against their own kind. Darwin called this the struggle for life. The following discussion shows that this struggle can be carried on chemically with compounds of widely differing classes. Examples of defensive substances found are hot quinones in bombardier beetles, and weak and strong carboxylic acids, phenols, terpenes, steroids, and alkaloids in other Adephaga.

1. Introduction

Beetles require extraordinary means for the acquisition and preservation of their *Lebensraum*, for wherever they live, under stones and in the ground, in soil and dung, or in a pool, there are always various kinds of microorganisms present. They must also defend themselves against other insects, as well as against larger enemies such as birds, mice, and frogs. The fact that beetles nevertheless exist, are practically free from attack by fungi, and always look clean is largely due to a defensive chemistry suited to their living habits.

2. Contents of the Pygidial Defensive Glands of Land Beetles

Like insects, many bacteria are attracted by warmth and humidity; however, the latter prefer neutral or weakly alkaline media. The simplest way for a beetle to protect itself against microbes is therefore to render its immediate surroundings either acid or strongly basic.

For example, those silphids that live in carrion secrete a 4.5% ammonia solution for their protection[1]. In this way the carrion beetles defend themselves not only against attack by putrefactive bacteria but also against larger enemies and against feeding rivals.

Only three species of beetles, *i.e. Oeceoptoma thorica* L., *Silpha obscura* L., and *Phosphuga atrata* L., have been found to use a base as a defensive substance. Carboxylic acids are more common[2]; isobutyric and isovaleric acids, for example, can be detected by electrophoresis and gas chromatography in six groups of carabids. These lower fatty acids are not very effective, and do not provide sure protection in a frequently changing environment, particularly since the action of any antiseptic is concentration-dependent[3]; it is also inconceivable that these carboxylic acids could ensure lasting repulsion of predatory insects. A better repellent is strong formic acid, which can be effective as a cytotoxin even when dilute, particularly if its penetration into the hostile organism is assisted by lipophilic aliphatic hydrocarbons[4]. In 25 species of beetles we found that, with only one exception (*Lebia chlorocephala*), formic acid was accompanied mainly by *n*-undecane, and in some cases by *n*-decane and *n*-tridecane. Beetles of the genus Pseudophonus (9–16 mm) can spray 70–75% formic acid over a distance of 20 cm in fine droplets from their 1.5–2 mm paired pygidial defensive glands (see Fig. 1)[5].

When a stone is turned by the wayside during a search for insects an aromatic odor often becomes percepti-

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[**] Based on a plenary lecture to the 105th meeting of the Gesellschaft Deutscher Naturforscher und Ärzte on October 8 1968, in Heidelberg. Arthropod Protective Substances, Part 40.– Part 39: *H. Schildknecht* and *R. Bühner*, Z. Naturforsch. *24b*, 532 (1969).

[1] *H. Schildknecht* and *K. H. Weis*, Z. Naturforsch. *17b*, 452 (1962).

[2] *H. Schildknecht*, *H. Winkler*, and *U. Maschwitz*, Z. Naturforsch. *23b*, 637 (1968).

[3] *W. B. Hugo*, J. appl. Bacteriol. *30*, 17 (1967).

[4] *H. Remold*, Z. vergleich. Physiol. *45*, 636 (1962).

[5] *H. Schildknecht* and *K. H. Weis*, Z. Naturforsch. *16b*, 361 (1961).

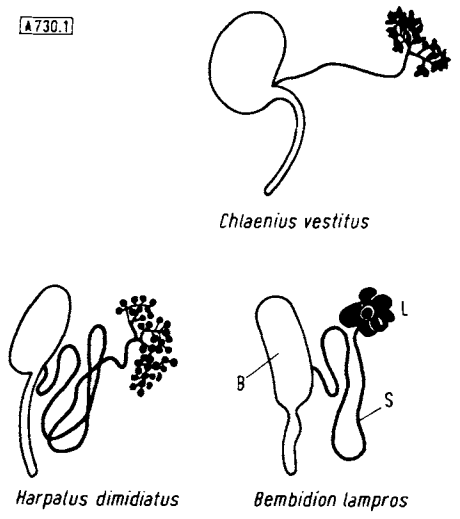


Fig. 1. Schematic diagram of the defense organs of carabids. The defensive substances produced in the lobes L and led through the collecting tubes S into the storage bladders B are listed in Table 1.

ble before any creature is observed. On closer examination, a shiny ground beetle, *e.g. Carabus auratus*, will be seen which emits clouds of aromatic vapor when touched, even in captivity. This vapor is almost pure methacrylic acid, which the beetle secretes, contaminated with about 5% of the homologous tiglic acid (*trans*-2-methylbutenoic acid) (see Table 1). These acids are also cytotoxins, and though they are more lipophilic than formic acid, the C_{10}, C_{11}, and C_{13} paraffins have also been detected in half of the 16 species examined.

Table 1. Carabids with the defensive substances methacrylic acid, tiglic acid, *n*-undecane, *n*-decane, and *n*-tridecane [2, 7].

Genus Species	Methacrylic and tiglic acid	*n*-Undecane alongside *n*-decane and *n*-tridecane
Carabini		
Carabus auratus	+	
C. granulatus	+	
C. auronitens		
C. problematicus	+	
C. convexus	+	
C. cansellatus	+	
Nebriini		
Leistus ferrugineus	+	
Nebria livida	+	
Pterostichini		
Poecilus cupreus	+	+
Pterostichus niger	+	+
Pt. macer	+	+
Pt. vulgaris	+	+
Pt. melas	+	+
Pt. metallicus	+	+
Abax parallelus	+	
Ab. ovalis	+	
Ab. ater	+	
Molops elatus	+	
Amarini		
Amara similata	+	+
Am. familiaris	+	+

As a hypothesis regarding the evolution of the compounds that occur in the defensive secretions, it may be assumed that in the origin of species of beetles, selection of a chemical characteristic can also be advantageous for a particular species [6]. In this light the saturated fatty acids may be regarded as original and the unsaturated acids as derived. The antibiotically active unsaturated carbonyl group can become effective only if adequate lipophilicity is assured, either by an aliphatic residue in the molecule itself or by admixture with an aliphatic solubilizing agent. We have observed both principles, and they will undoubtedly be encountered even more often during the elucidation of chemical defense mechanisms.

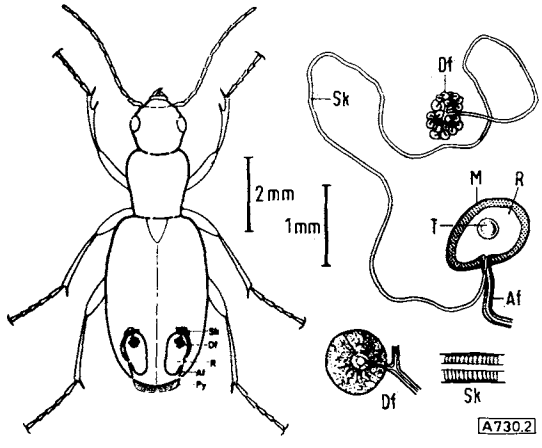


Fig. 2. *Idiochroma dorsalis* and its pygidial defensive gland system; Sk = collecting tube, Df = glandular follicle, Af = excretory tube, Py = pygidium, R = reservoir, M = musculature, T = "oily" droplet.

The pygidial defensive glands of *Asaphidion flavipes* and of *Bembidion quatriguttatum*, for example, contain *n*-valeric acid mixed with paraffins, as well as salicylaldehyde; from *Idiochroma dorsalis* (Fig. 2) we isolated not only the more lipophilic methyl salicylate but also *n*-undecane as the main component, together with 12% of formic acid and a little *n*-decane [8].

The phenolic active group, which is present in salicylaldehyde and in salicylic acid, occurs particularly widely in water beetles. Use of the particularly effective disinfectant *m*-cresol very probably also represented an advance for the three species of Chlaenius *Ch. tristis*, *Ch. crysocephalus*, and *Ch. bipunctatus* [2,9]. The hydroquinones are less effective than *m*-cresol, since they lack the alkyl group. We therefore find them only as precursors of the bactericidal and fungicidal *p*-benzoquinones [10], which are so characteristic as defensive substances in beetles that we referred to an entire group of these insects, in an earlier publication [11], as "quinone beetles".

[6] *H. Schildknecht, U. Maschwitz*, and *H. Winkler*, Naturwissenschaften *55*, 112 (1968).

[7] *H. Schildknecht* and *K. H. Weis*, Z. Naturforsch. *17b*, 439 (1962).

[8] *H. Schildknecht, H. Winkler, D. Krauss*, and *U. Maschwitz*, Z. Naturforsch. *23b*, 46 (1968).

[9] *T. Eisner*, Ann. Entomol. Soc. Am. *57*, 44 (1964).

[10] *H. Schildknecht* and *H. Krämer*, Z. Naturforsch. *17b*, 701 (1962).

[11] *H. Schildknecht et al.*, Angew. Chem. *75*, 762 (1963); Angew. Chem. internat. Edit. *3*, 73 (1964).

Nevertheless, neither the tenebrionid family [12–14] nor the carabid genera Scaritini and Chlaeniini, with their defensive substances *p*-benzoquinone, toluquinone, ethylquinone, and 2-methyl-3-methoxy-*p*-benzoquinone (in *Clivina fossor*) can match the brachynids (bombardier beetles) in the effectiveness and elegance of their protection.

3. The Defensive Chemistry of the Bombardier Beetle

The brachynids have bladders weighing 1 mg in which they store, not the unstable quinones, which react with protein, but aromatically stabilized hydroquinones in a hydrogen peroxide solution whose concentration is frequently as high as 28% [15]. A hot toxic gas consisting of benzoquinone, toluquinone, and unreacted hydroquinone and hydrogen peroxide is emitted with an audible report by oxygen under pressure (Fig. 3).

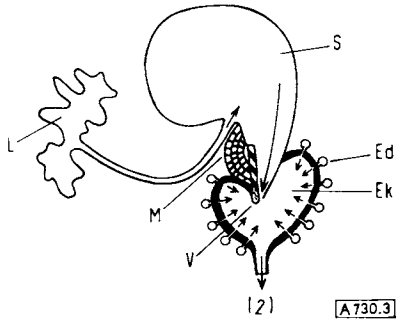


Fig. 3. Pygidial defensive gland system of the bombardier beetle; L = lobes, S = collecting bladder, M = sphincter muscle, V = valve, Ed = enzyme glands, Ek = explosion chamber. The collecting bladder S contains *(1)* and H_2O_2.

These were our first observations [15,16] on this defense mechanism, which is unique in the entire animal kingdom. The further results reported here arise from experiments on the nature of the catalysts that bring about the explosive reaction of the pygidial gland secretion in the combustion chambers [17]. These chambers are chitin capsules 200 to 300 μm long with very spiny interiors, into which emerge, from raised sieve plates, bundles of excretory tubes of numerous unicellular annex glands, whose enzyme secretion can be pipeted off with glass capillaries as a deep brown liquid. Indigenous bombardier beetles such as *Br. explodens* yield 0.01 to 0.03 μl, and the rather larger *Br. crepitans* yield 0.02 to 0.1 μl of a 40 to 60% protein solution that decomposes hydroquinone/hydrogen peroxide solution explosively, even in a test tube, to

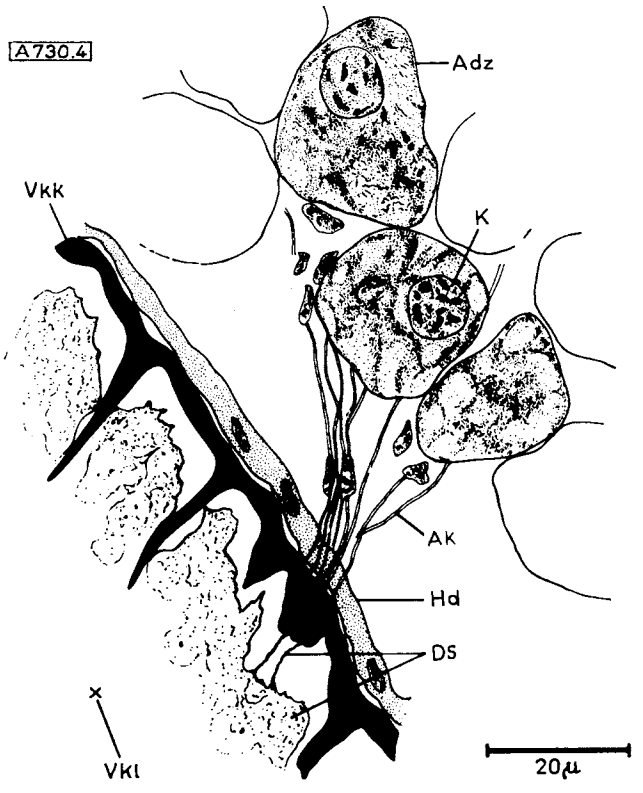
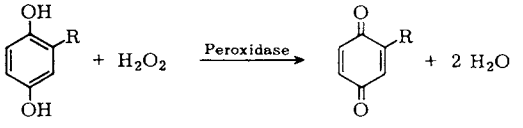


Fig. 4. Cross section through the pygidial defensive gland vestibule and the annex glands (Adz) of the bombardier beetle (portion). Ak = excretory tube, K = nucleus, Hd = hypodermis, Vkk = vestibular cuticle, Ds = glandular secretion, VkL = vestibular lumen.

give benzoquinone and oxygen. This double reaction of the pygidial gland secretion requires two enzymes, *i.e.* catalase for the decomposition of the hydrogen peroxide into water and oxygen, and peroxidase for the oxidation of hydroquinone, if one disregards the slight peroxidase activity of catalases.

$$2\ H_2O_2 \xrightarrow{\text{Catalase}} 2\ H_2O + O_2$$



(1) R = H, CH_3 *(2)*

After micro zone electrophoresis of the combustion chamber liquid, we detected both enzymes on the cellulose acetate film by spraying with a synthetic pygidial gland secretion. For seven species of Brachynus (*Br. crepitans, explodens, immaculicornis, plagiatus, sclopeta, ganglbaueri, exhalans*), we observed one spot giving strong liberation of gas and another that merely turned brown. Only for *Br. ganglbaueri* was the catalase transported farther than the peroxidase. The enzyme pattern obtained in this way is reproducible and characteristic of the species, both in the rates of migration of the proteins and in the intensity of the spots.

The micropreparative isolation and subsequent characterization [18] of these insect catalases and peroxidases was facili-

[12] *H. Schildknecht* and *K. H. Weis*, Z. Naturforsch. *15b*, 757 (1960).

[13] *J. D. Laconti* and *L. M. Roth*, Ann. Entomol. Soc. Am. *46*, 281 (1953).

[14] *T. Eisner*, J. Insect. Physiol. *8*, 175 (1962).

[15] *H. Schildknecht*, Angew. Chem. *69*, 62 (1957).

[16] *H. Schildknecht* and *K. Holoubek*, Angew. Chem. *73*, 1 (1961).

[17] *H. Schildknecht, E. Maschwitz*, and *U. Maschwitz*, Z. Naturforsch. *23b*, 1213 (1968).

[18] *H. Schildknecht, E. Maschwitz*, and *U. Maschwitz*, J. Insect. Physiol., in press.

tated by the unusually high concentrations in which these enzymes are present in the brachynids, which are up to 10000 times the concentrations in the livers of mammals.

The annex gland secretion was separated into three fractions by gel filtration on Sephadex G-200 (see Fig. 5). The first fraction, which had a high molecular weight, exhibited peroxidase and catalase activity, the

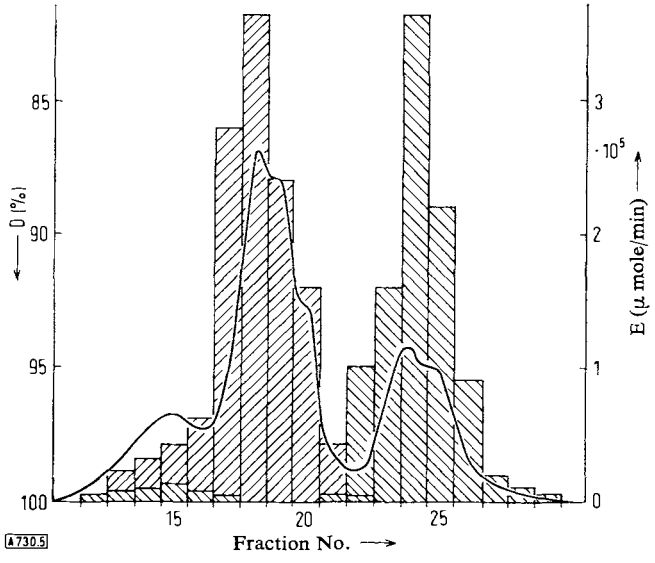


Fig. 5. Fractionation of the combustion chamber proteins from *B. crepitans* by gel filtration; D = transmission at 280 nm (%)[continuous curve], E = enzyme activity (µmole of H_2O_2 transformed/min). Hatching: /// = catalase; \\\ = peroxidase.

second exhibited only catalase activity, and the third only peroxidase activity. A combination of micro zone electrophoresis and gel filtration allowed the isolation, from the three beetle peroxidases, of one peroxidase that was uniform on disk electrophoresis. Of two catalase fractions, one was almost uniform, while the other consisted of three protein components exhibiting catalase activity. The molecular weight of the uniform crepitans catalase (225000) is very similar to that of plant and animal catalases; the molecular weight of the one beetle peroxidase corresponds to that of the ox thyroid, cytochrome c, and lacto-peroxidases. The typical prosthetic group of the known catalases and peroxidases, protohematin IX, was also found in the beetle enzymes.

An unusual feature of the Brachynus catalase, however, is the fact that it has its optimum activity between 70 and 80 °C, and even exhibits considerable activity after being boiled for a short time. The ox liver

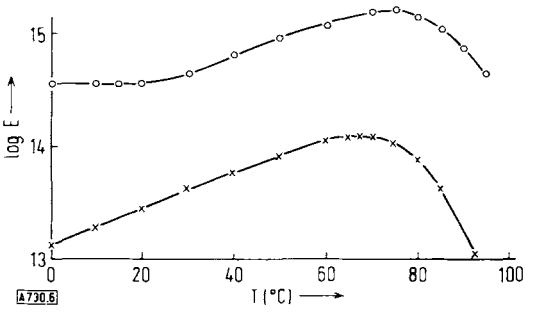


Fig. 6. Temperature-activity diagram of Branchynus catalase (-o-o-o-) and of Brachynus peroxidase (-x-x-x-); E = enzyme activity (µmole of H_2O_2 transformed/min · mole porphyrin).

catalase with which it was compared has its activity optimum at 52 °C and is completely inactivated at 62 °C. The optimum temperature range for the Brachynus peroxidase is between 65 and 75 °C; there is nothing unusual about this, since the peroxidases include some of the thermally most stable enzymes known. What is unusual is its substrate stability and donor specificity. It is appreciably more stable to hydrogen peroxide than other peroxidases, and, unlike most, it does not react with benzidine or *p*-phenylenediamine, but prefers hydroquinone or pyrocatechol as its hydrogen donor.

This is practically the only system that can be used by an organism to produce an explosive reaction using endogenous substances, since it is particularly characteristic of catalases that their activity increases without limit with the concentration of the substrate [19]. The nature of the enzyme, the high hydrogen peroxide concentration, and the reaction temperature in the chitin capsule, which is unusually high for a biochemical process, allow such rapid evolution of gas that an explosion occurs, and the denaturing action of hydrogen peroxide on the enzymes hardly becomes effective.

The secretion of the annex glands, which is retained in the explosion chamber by many chitin bristles (see Fig. 4), thus remains so active after each defensive reaction by a hot detonation [*] that it can still ignite the last of a dozen propellant charges.

4. Defensive Substances of Water Beetles (Dytiscidae)

4.1. Active Substances of the Pygidial Defensive Glands

The dytiscids are among the best swimmers of all fresh-water invertebrates. The boat-shaped beetles can slide through the water with the minimum of friction, unimpeded by spines or projections of any kind. Only when they are forced to remain in the water for a long time do their wing covers become coated with a microbial slime and the surface of the insect loses its water repellency. Since a hydrophilic body does not pass through the water so easily, the beetles remove these parasites from time to time by coating themselves with a disinfectant paste, which they force out of their pygidial defensive glands while sitting on a blade of grass. The principal components of the paste, apart from benzoic acid, are phenols, all of which have an antiseptic action [20]. It can be seen from Table 2 that

[19] *B. Chance*: Technique of Organic Chemistry. Vol. VIII, Part II, pp. 1314–1360, Interscience, New York 1963.

[*] The manuscript of this publication of the lecture of October 8, 1968, was already complete when our assumption that the development of heat is also part of the defensive reaction was confirmed by accurate measurement of the temperature of the "spray vapor" by *D. J. Aneshansley et al.*, cf. [17] and Science (Washington) *165*, 61 (1969).

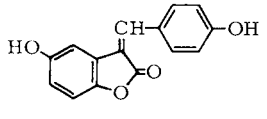
[20] *H. Schildknecht, D. Hotz, H. Neumaier, W. Körnig, H. Birringer, H. Tacheci, S. K. Sharma*, and *U. Maschwitz*, to be published.

Table 2. Contents of the pygidial defensive glands of the water beetles Dytiscinae and Colymbetinae.

	Benzoic acid	*p*-Hydroxy-benzoic acid	Methyl *p*-hydroxy-benzoate	*p*-Hydroxy-benzaldehyde	Methyl 3,4-dihydro-benzoate	Ethyl 3,4-dihydroxy-benzoate	Hydro-quinone	Methyl 1,4-dihydroxy-phenyl-acetate
Dytiscinae								
Dytiscus marginalis	+		+	+				+
Cybister lateralimarginalis	+		+	+	+	+		
Cybister tripunctatus?	+		+	+				
Acilius sulcatus	+		+	+				
Graphoderus cinereus	+	+	+	+	+			
Colymbetinae								
Rhantus exoletus	+	+	+	+			+	
Colymbetes fuscus	+	+	+	+	+		+	
Copelatus ruficollis			+	+				
Agabus sturmi	+		+	+				
Agabus bipustulatus			+	+	+			
Ilybius fenestratus	+	+	+	+			+	

methyl *p*-hydroxybenzoate (PHB) is particularly common as an antiseptic in water beetles. This may be related to the observation, by *Beveridge* and *Hugo* [21], that none of the nine strains of bacteria that they examined could decompose methyl *p*-hydroxybenzoate, though they could decompose other aromatic compounds studied, and that despite the use of this ester by water beetles for millions of years, the microorganisms have evidently never built up a resistance to it.

The great diving beetle (*Dytiscus marginalis*) uses a disinfectant paste that is formed in its defensive glands from methyl *p*-hydroxybenzoate, benzoic acid, and a glycoprotein, which is pre-crosslinked by *p*-hydroxybenzaldehyde (also present in a high concentration) and the ε-amino groups of lysine. During the act of cleaning [22] in air, compact, often film-like deposits are formed on the wing covers, the antiseptics being embedded in the coating. Evidence concerning the nature of the coating is provided by an electron micrograph, by its extreme insolubility, and by the high cysteine/cystine content (17.25%) of the high molecular weight glycoprotein [23]. Owing to its hydrophilic sugar component the film is removed spontaneously when the insect returns to the water, the beetle thus regaining its hydrophobic surface. It is not yet known whether the marginalin [3-(*p*-hydroxyphenylmethylene)-5-hydroxybenzo[*b*]furan-2-one] *(3)* [24] that also occurs in the



(3)

pygidial defensive glands of *Dytiscus marginalis* also possesses properties that are of use to the beetle, since this lactone, like all other derivatives of benzylideneisocoumaranone, had not previously been found in nature and no relation is known between structure and antibacterial action in unsaturated lactones [25].

4.2. Active Substances of the Prothoracic Defensive Glands

If a great diving beetle is taken from the aquarium for the investigations described above, it may be found to spray the fetid contents of its rectal ampoule in a thick jet from its anus. At the same time it often emits, from the collecting bladders situated in its prothorax, a milky liquid, which is reported by *Frisch* [26] to poison fish and amphibians. *Blunck* [27] assumed that this is a specific means by which the beetle protects itself against large enemies among the vertebrates, *i.e.* a nerve poison that affects heart beat and breathing. The pure crystalline active substance was identified on the basis of spectroscopic data as 11-deoxycorticosterone (Cortexone) [28].

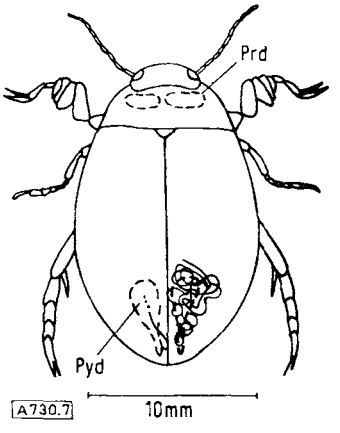


Fig. 7. *Acilius sulcatus* with prothoracic (Prd) and pygidial (Pyd) defensive glands.

[21] *E. G. Beveridge* and *W. B. Hugo*, J. appl. Bacteriol. *27*, 304 (1954).

[22] *U. Maschwitz*, Naturwissenschaften *54*, 649 (1967).

[23] *H. Schildknecht* and *R. Bühner*, Z. Naturforsch. *23b*, 1209 (1968).

[24] *H. Schildknecht, W. Körnig, R. Siewerdt*, and *D. Krauss*, Liebigs Ann. Chem. 1970, in press.

[25] *W. A. Sexton*: Chemische Konstitution und biologische Wirkung. Verlag Chemie, Weinheim 1958, p. 217.

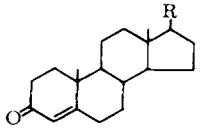
[26] *J. L. Frisch*: Beschreibung von allerley Insecten in Teutschland, nebst nützlichen Anmerkungen und nöthigen Abbildungen von diesem kriechenden und fliegenden inländischen Gewürme, zur Bestätigung und Fortsetzung der gründlichen Entdeckung, so einige von der Natur dieser Creaturen herausgegeben, und zur Ergänzung und Verbesserung der andern. 4th Edit., Part 2, Nicolai, Berlin 1721.

[27] *H. Blunck*, Z. wiss. Zool. *117*, 205 (1917).

[28] *H. Schildknecht, R. Siewerdt*, and *U. Maschwitz*, Angew. Chem. *78*, 392 (1966); Angew. Chem. internat. Edit. *5*, 421 (1966)

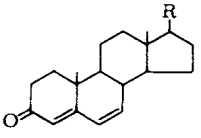
When administered per os to pike or trout, this steroid has the same stunning effect as the natural secretion. Cortexone (as a foreign hormone) has no effect on the beetle itself. It is also found in the prothoracic defensive glands of other water beetles (see Fig. 7) such as *Agabus bipustulatus* and *Acilius sulcatus* (19 μg/beetle)[29], which are in fact a treasure trove of α,β-unsaturated and α,β-γ,δ-diunsaturated C_{21} keto-steroids. 6,7-Dehydrocortexone, which is the principal component (56 μg) in the vesicles of Acilius, had not previously been known as a natural product; other components detected are 1 μg of 20α-hydroxy-4-pregnen-3-one, 6 μg of 4,6-pregnadiene-3,20-dione, and 7 μg of cybisterone (20α-hydroxy-4,6-pregnadien-3-one), which was first discovered in *Cybister*

Table 3. α,β-Unsaturated C_{21} keto steroids from the prothoracic defensive glands of water beetles.



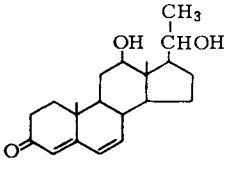
R	Steroid	Beetle
$-\overset{\overset{O}{\|}}{C}-CH_2OH$	21-Hydroxy-4-pregnen-3,20-dione (Cortexone)	*Dytiscus marginalis* *Acilius sulcatus* *Agabus bipustulatus*
$-CHOH-CH_3$	20α-Hydroxy-4-pregnen-3-one	*D. marginalis* *Ac. sulcatus*
$-CHOH-CH_3$	20β-Hydroxy-4-pregnen-3-one	*Ilybius fenestratus*

Table 4. α,β-γ,δ-Diunsaturated C_{21} keto steroids from the prothoracic defensive glands of water beetles.

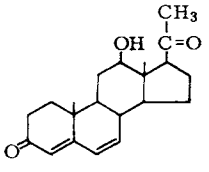


R	Steroid	Beetle
$-\overset{\overset{O}{\|}}{C}-CH_2OH$	21-Hydroxy-4,6-pregnadien-3,20-dione	*Ac. sulcatus* *Cybister lateralimarginalis*
$-CHOH-CH_3$	20α-Hydroxy-4,6-pregnadien-3-one (Cybisterone)	*C. lateralimarginalis* *D. marginalis* *Ac. sulcatus*
$-\overset{\overset{O}{\|}}{C}-CH_3$	4,6-Pregnadien-3,20-dione	*Ac. sulcatus*

lateralimarginalis[30]. An interesting subsidiary steroid found in this Cybister species is 12β,20β-dihydroxy-4,6-pregnadien-3-one *(4)*, dehydration of which on C-20



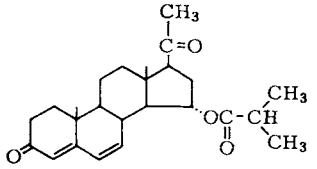
(4)



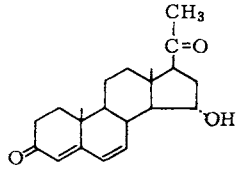
(5)

gives 12-hydroxy-4,6-pregnadiene-3,20-dione *(5)*, the principal steroid in a Mexican Cybister species (*C. tripunctatus?*). The Mexican Cybister, which I caught in an ideal biotope for water beetles, *i.e.* the ditches of the floating gardens at Xochimilco (Mexico City), keeps more than 1 mg of this steroid available for its protection[32].

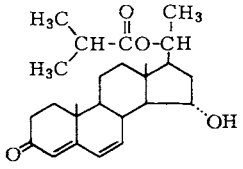
The steroids *(6)*, *(7)*, and *(8)* of *Agabus sturmi* are further modified by a change in the position of the OH groups; these are hydroxylated pregnadienones (which



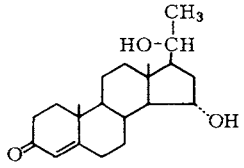
(6)



(7)



(8)



(9)

are typical of dytiscids) only one of which had previously been known[33], and which can also occur here as esters of isobutyric acid[31]. The steroid *(9)* of *Platambus maculatus* (7–8 mm long) is also hydroxylated on C-15; 0.7 mg of *(9)* have been isolated from the milky secretion of 100 beetles[34].

Of the insect steroids mentioned, some that can be prepared in good yields have been tested for their action on cold-blooded animals. At a concentration of 2 mg of steroid/1 l of water, for example, the test fish showed appreciable changes in behavior after 15 to 30 minutes. They could be turned on their side, and righted themselves only with difficulty. At a steroid concentration of 10 mg/l, the fish were lying motionless at the bottom of the tank after half an hour, but recovered completely when placed in fresh water. Experiments in which *Ilybius fenestratus* (Fig. 8) were fed to toads and frogs were particularly informative.



Fig. 8. *Ilybius fenestratus* (12 mm).

[29] *H. Schildknecht*, *D. Hotz*, and *U. Maschwitz*, Z. Naturforsch. *22b*, 938 (1967).

[30] *H. Schildknecht*, *R. Siewerdt*, and *U. Maschwitz*, Liebigs Ann. Chem. *703*, 182 (1967).

[31] *H. Schildknecht* and *D. Hotz*, unpublished.

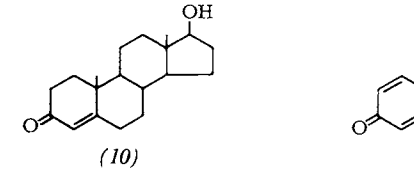
[32] *H. Schildknecht* and *W. Körnig*, Angew. Chem. *80*, 45 (1968); Angew. Chem. internat. Edit. *7*, 62 (1968).

[33] *P. Potier*, *C. Kan*, and *J. Lemen*, Tetrahedron Letters *1964*, 1673.

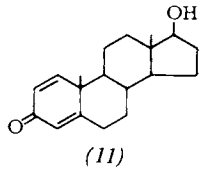
[34] *H. Schildknecht*, *H. Tacheci*, and *U. Maschwitz*, Naturwissenschaften *56*, 37 (1969).

After only 20 minutes, one common toad vomited out the four beetles that it had eaten within five minutes. The beetles are often still alive when they are disgorged. If they are dead, they have sacrificed themselves for the continued existence of their entire race, since after they have been fed once or twice with *Ilybius*, the toads will no longer eat beetles, even when they are very hungry.

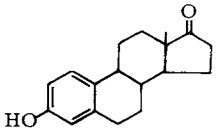
In addition to a very small quantity of a C_{21} steroid (cf. Table 3) the secretion contains the C_{19} and C_{18} steroids *(10)* (28 μg)[35], 1,2-dehydrotestosterone *(11)* (16 μg), estrone *(12)* (2 μg), and 17β-estradiol *(13)* (19 μg)[36], and, to our great surprise, methyl 8-hydroxyquinoline-2-carboxylate *(14)* as the principal component (350 μg)[37].



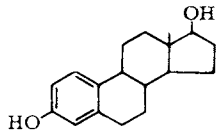
(10)



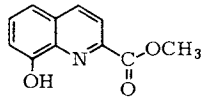
(11)



(12)



(13)



(14)

It is possible that the insect uses this strong antiseptic to prevent the penetration of microorganisms into its large defensive organs, which would result in total infection of its body, while it again has the pygidial defensive substances *p*-hydroxybenzaldehyde, *p*-hydroxybenzoic acid, and the methyl ester of the latter for external disinfection of its body.

The biosynthesis of insect steroids can be studied with ^{14}C-labeled precursors. Beetles are excellent subjects for such studies, since the steroids produced are not metabolized further, but collect as described in readily isolable glands. Moreover, the regenerating power, as in the case of *Acilius sulcatus*, is very high, even in insects kept in the laboratory.

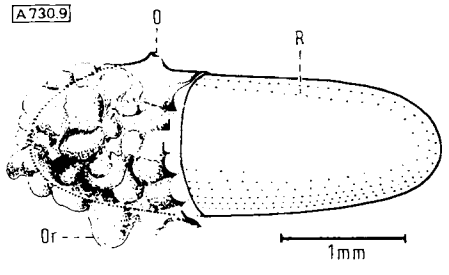


Fig. 9. Prothoracic defensive gland of *Dytiscus marginalis* with secretion cells above; R = reservoir, Dr = glands, and O = opening.

Insects require cholesterol, sitosterol, or similar starting materials for the formation of steroids[38]. The greater the similarity of a sterol to cholesterol, the more efficiently it can be used; cholesterol is often degraded by removal of the entire side chain at C-17 or of part of it at C-20, with formation of pregnenolone, from which progesterone is then formed.

In our experiments[39] we injected 25 to 30 water beetles with [2-^{14}C]-mevalonolactone, [4-^{14}C]-cholesterol, or [4-^{14}C]-progesterone; after a regeneration time of six weeks, the concentration and activities of the Acilius steroids were determined. The steroids of the insects treated with mevalonolactone, as expected, exhibited no activity; cholesterol and progesterone, on the other hand, were incorporated. The water beetles must therefore absorb cholesterol or steroids of similar structure with their food.

Table 5. Specific incorporation and specific activities after injection of [4-^{14}C]-cholesterol and [4-^{14}C]-progesterone.

	Cholesterol		Progesterone	
	(%)	(μCi/mmole)	(%)	(μCi/mmole)
6,7-Dehydrocortexone	0.73	[310]	0.01	[3.4]
Cortexone	0.51	[230]	0.14	[50]
Cybisterone	1.13	[480]	0.03	[10]
6,7-Dihydrocybisterone	1.20	[510]	2.46	[881]
6,7-Dehydroprogesterone	0.85	[360]	0.007	[2.4]

In our biosynthesis experiments, which are described only briefly here, we were able to show that after injection of [4-^{14}C]-cholesterol, the rates of incorporation for the enones and dienones are of the same order of magnitude, whereas after injection of [4-^{14}C]-progesterone the dienones were labeled to a much smaller extent than the enones (see Table 5).

We assume that the biosynthetic path for these groups of steroids branches before the progesterone stage. This hypothesis is supported, in our opinion, by the fact that with [^{14}C]-4,6-cholestadien-3-one as a precursor, the rates of incorporation were higher for the dienones than for the enones. No activity was found in the dehydroprogesterone, which thus appears to be formed by an entirely different path from the other dienones. It can be provisionally concluded that progesterone, which has not so far been found in the defensive glands of water beetles, is metabolized in the lobes into cortexone and dihydrocybisterone, but dehydroprogesterone is not converted into dehydrocortexone and cybisterone.

5. *Stenus bipunctatus*

Stenus bipunctatus is a small black staphylinid. As a land beetle, it lives in the region of river banks, but can also move well on the water. If the beetle, which on average weighs 1.5 mg and is about 5 mm long, is chased by a bird while on the water, it streaks toward the bank and safety with the speed of an arrow and without using its legs[40]. To produce this elegant

[35] *H. Schildknecht, H. Birringer*, and *U. Maschwitz*, Angew. Chem. *79*, 579 (1967); Angew. Chem. internat. Edit. *6*, 558 (1967).

[36] *H. Schildknecht* and *H. Birringer*, Z. Naturforsch. *24b*, 1529 (1969).

[37] *H. Schildknecht, H. Birringer*, and *D. Krauss*, Z. Naturforsch. *24b*, 38 (1969).

[38] *F. J. Ritter* and *W. H. J. M. Wientjens*: Steroid Metabolism of Insects. Centraal Laboratorium TNO, Delft, P 67/14 (1967).

[39] *D. Hotz*, Dissertation, Universität Heidelberg (1968).

[40] *V. B. Wigglesworth*: The Life of Insects. Weidenfeld and Nicolson, London 1964, p. 35–36.

movement, the beetle immerses the tip of its abdomen into the water and emits, from two protruding sacs corresponding to the pygidial defensive glands of other land beetles, substances that propel it in the same way as a toy boat is propelled by camphor. The reaction necessary for driving the beetle forwards is most probably provided by the spreading pressure that is set up when the surface-active secretion is transferred to the surface of the water.

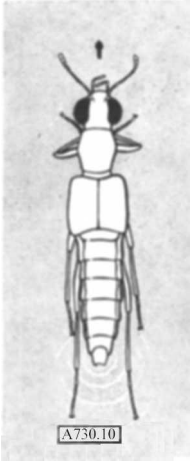
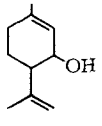


Fig. 10. *Stenus bipunctatus* in motion. Drawing by *T. Hölldobler*.

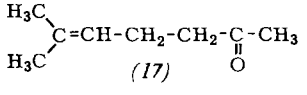
In agreement with preliminary tests, which pointed to a complex secretion [41], *Maschwitz* found two pairs of pygidial defensive glands on dissection of *Stenus bipunctatus*, the larger smelling of amine when crushed and the smaller having a peppermint-like odor. To isolate the pygidial gland secretion in large quantities, we heated 1000 insects under vacuum, extracted the distillate with benzene, and concentrated the extract by ice zone melting. The concentrate was divided into three fractions by gas chromatography. The principal component was 1,8-cineole [*] *(15)*, while isopiperitenol [**] *(16)* and methylheptenone [*] *(17)* were also



(15)



(16)



(17)

present. All these terpenes are surface active, and propel a "paper beetle" through water in the manner described. Whether the nitrogen heterocycles of the large glands reinforce this effect or have some other function cannot be decided until the compounds have been synthesized.

[41] *D. Berger*, Dissertation, Universität Heidelberg, 1968.

[*] We are grateful to Dr. *Klein*, Holzminden, for kindly supplying samples of these compounds.

[**] It could not be established whether the compound was *cis*- or *trans*- isopiperitenol.

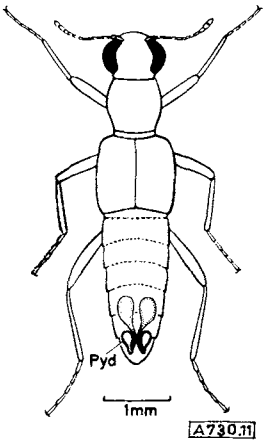


Fig. 11. *Stenus bipunctatus* with pygidial defensive glands.

6. Outlook

The functional assignment of the pygidial defensive glands of the Adephaga on the basis of the chemical findings is indisputable. However, one can think of enemies, other than microorganisms, that must also be fought with the substances mentioned. This is supported *e.g.* by the work of *Eisner* [42,43].

The antimicrobial activity must be regarded from the viewpoint of a homology between the epidermal glands and the complex defensive glands of the beetle. The toxins stored in the latter may originally have been intended for protection of the entire body against attack by microorganisms; *i.e.* the pygidial defensive glands formed by combination of the epidermal glands also secrete antiseptic substances, but the spectrum of action of these substances is extended. Could this not have been so even at the epidermal gland stage? It is through the skin that the principal contact with the hostile environment occurs. Primitive poison equipment intended for use against enemies of other species is found mainly in the skin and have developed from the skin.

The chemistry of the epidermal glands is important. The function of the pygidial glands of the true water beetles could not be correctly demonstrated until the contents of the appropriate storage organs had been identified. The substances in the epidermal glands of the dytiscids were then seen to be insufficient by themselves for the bodily hygiene of the insects.

The question of the action of the as yet unknown contents of the known pygidial defensive glands was thus reversed in the case of the water beetles. It was known that the water beetles periodically coat themselves with the secretion from their pygidial glands [44]. The question why was answered by chemistry. On the other hand, at least the toxic action was known for the prothoracic glands of some species of Dytiscinae [27],

[42] *T. Eisner*, J. Insect. Physiol. *2*, 215 (1958).

[43] *T. Eisner* and *J. Meinwald*, Science (Washington) *153*, 1341 (1966).

[44] *H. Naumann*: Der Gelbrandkäfer. A. Ziemsen Verlag, Wittenberg Lutherstadt 1955, p. 21.

whereas the elucidation of the natural products was not easy.

In the case of the Colymbetes species, neither the function of the prothoracic glands nor the nature and action of their chemical products has been fully explained, and this is also true of the pygidial glands of the whirligig beetles.

Colymbetes fuscus leads an amphibious existence. It requires no special protection in or on the water against predaceous fish and frogs, since it is nimble and readily takes to the air. On land, however, it finds great difficulty in moving around, and could easily be attacked by small mammals. It is therefore not surprising that the substances in its prothoracic glands are very toxic to rats. One fraction obtained on fractionation of the crude secretion on Sephadex caused a decrease of up to 30% in blood pressure [45]. A relationship can be seen here with the toxic action of the principal component of the toxin from the prothoracic defense glands of *Ilybius fenestratus*, which causes clonic spasms in mice [46]. The toxic substance is methyl 8-hydroxyquinoline-2-carboxylate *(14)*.

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Translated by Express Translation Service, London

[45] *H. Tacheci*, Dissertation, Universität Heidelberg, scheduled for 1970. We thank Prof. *Bieckert*, Dr. *Steiole*, and Dr. *Zimmermann*, Ludwigshafen, for their assistance in the physiological tests.

[46] We thank Dr. *Schraufstätter* and Dr. *Weichhöfer*, Wuppertal-Elberfeld, for carrying out the tests.

Organic Dyes in Laser Technology

By F. P. Schäfer [*]

Laser technology has been developed to a very high level since 1960. Significant advances have been made possible only by the use of organic dyes as optical shutters for the production of giant pulses. Ultrashort pulses in the picosecond range were first produced in 1966; their measurement was greatly facilitated by the use of organic dyes. Probably the most important recent advance in the laser field is the dye laser, which was first described in 1966, and in which the active medium is a solution of an organic dye.

1. Organic Dyes as Optical Shutters

To facilitate the explanation of the use of organic dyes as optical shutters, let us first consider the laser principle, taking a simple ruby laser as an example. A ruby rod situated between two mirrors is pumped [**] with a flash lamp. Photons starting out *e.g.* from the point X travel to the left along the optical axis of the resonator, are reflected at the mirror Sp_2, travel back along the ruby rod, are reflected again by the mirror Sp_1, and finally return to the point X; in the course of this journey, the photons are both amplified and attenuated by the resonator. Let the amplification resulting from one passage through the ruby rod be V; let the attenuations due to incomplete reflection by the mirrors Sp_1 and Sp_2 be given by the reflection factors R_1 and R_2 respectively, and other losses, due *e.g.* to scattering, diffraction, and absorption, by an attenuation factor A. The effective amplification for one cycle is therefore $V^2 \times R_1R_2 \times A^2$.

If the effective amplification is less than 1, the number of photons will decrease. If it is equal to 1, the photon flux will remain constant; if it is greater than 1, however, the number of quanta will increase, and the intensity of the light beam will steadily build up, *i.e.* a laser emission occurs. For high values of the loss factor A, this is possible only if the amplification V is sufficiently great, whereas with small losses even a small amplification is sufficient to start the oscillation if the reflection factors are close to unity as a result of complete silvering.

A particularly interesting case is that of time-dependent losses $A(t)$ [1]. This case can be produced *e.g.* by insertion of a Kerr cell and a polarizer in the laser re-

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Physikalisch-Chemisches Institut der Universität
355 Marburg, Biegenstrasse 12 (Germany)

[**] The excitation of the laser material is generally referred to as "pumping".

[1] *R. W. Hellwarth*: Control of Fluorescent Pulsations. Advances in Quantum Electronics. Columbia University Press, New York 1961, p. 334.

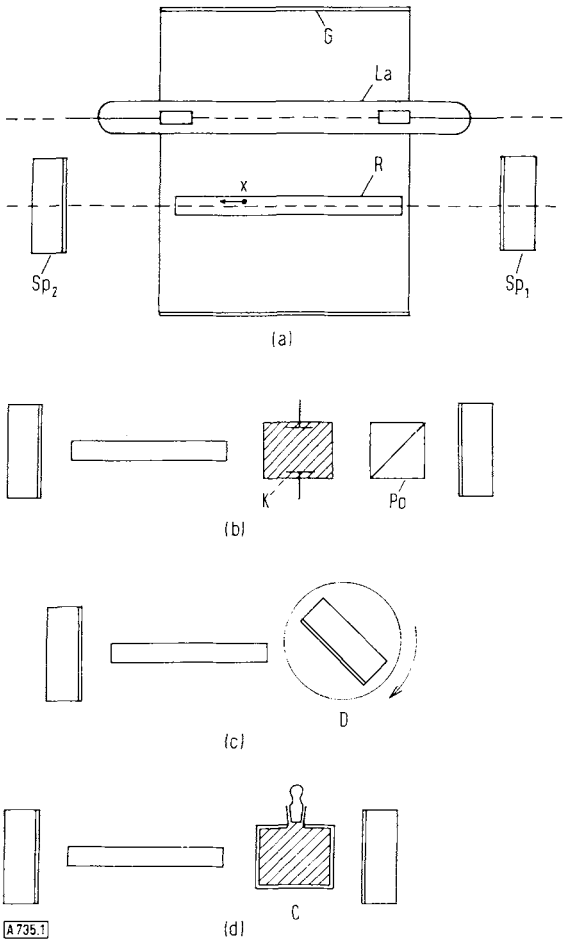


Fig. 1. Construction of normal-pulse and giant-pulse lasers. $Sp_{1,2}$: laser mirrors, R: ruby rod, La: flash lamp, G: reflector for the pumping light, K: Kerr cell, Po: polarizer, D: rotating mirror, C: cell containing dye. The flash lamp and the reflector for the pumping light have been omitted in Figs. 1b–1d.

sonator, as illustrated in Figure 1b [2]. The blocked Kerr cell corresponds to high losses in the resonator, and the open Kerr cell to low losses. In "giant-pulse operation", the ruby rod is first brought to a state of high amplification by a particularly powerful pumping flash, while the Kerr cell is blocked so that no laser oscillation can occur, since the losses in the resonator cannot be overcome even at very high amplification. The ruby rod reaches its highest amplification shortly after the pumping flash reaches its maximum intensity, and the Kerr cell is now opened by a sudden increase in voltage. The resulting sudden decrease in the losses allows the effective amplification to increase to far beyond unity, so that laser oscillation can occur. Because of the high effective amplification, this oscillation can build up to a high intensity within a few cycles in the resonator, so that a very intense, short laser flash, *i.e.* a "giant pulse", is emitted. The main difficulty of this process is the accurate synchronization of the pumping flash and the jump in the voltage across the Kerr cell.

Another method of producing giant pulses is to mount one of the mirrors of the laser resonator on the shaft of a high-speed motor (Fig. 1c) [3,4]. While the rotating mirror is not exactly parallel to the fixed mirror, the losses in the resonator are large, since part of the beam is cut out for each cycle. The pumping flash and the rotation of the mirror can be accurately synchronized so that the parallel position of the mirrors exactly coincides with the maximum amplification in the ruby. In addition to the synchronization difficulties in this case, the high motor speeds required present mechanical and optical problems, so that this method is now used only in special cases.

The synchronization dfficulties in both of these methods result from the fact that the losses in the resonator must be actively eliminated at the exact instant of maximum amplification in the ruby rod. A better method would be one in which the losses are eliminated automatically and passively at the correct instant. A passive optical shutter of this nature can be produced in the form of a cell containing a suitable dye in an appropriate concentration (Fig. 1d) [5–8].

The operation of this optical shutter can be qualitatively explained as follows. The laser emission begins when the amplification reaches a certain value fixed by the absorption in the cell. The initially weak laser beam passing through the cell at first raises only a small proportion of the dye molecules into the excited state. Since the absorption is proportional to the concentration of the molecules in the ground state, it is reduced slightly by the action of the laser light. The effective amplification and the light intensity in the laser beam are accordingly increased and this in turn leads to a further decrease in the absorption of the dye. The absorption of the dye is thus ultimately almost totally eliminated by the increasing intensity of the light in a fast feedback process, and so the optical shutter is opened. As in the cases described above, the effective amplification now has a value much greater than 1, and a giant pulse is produced.

Let us now estimate the order of magnitude of the radiation intensity required to eliminate the absorption for a simplified example. Let photons of frequency ν_L fall on a solution of m dye molecules per unit volume in a cell of length L at a rate of n per cm^2 per second. The molecules are assumed to be either in the ground state or in the first excited singlet state, which is separated from the ground state by an energy $h\,\nu_L$ (h = Planck's constant). Let the effective cross section of the molecules for absorption and stimulated emission be σ (with parallel orientation of the transition moment and the electric vector of the stimulating light). The relation between σ and the molar decadic extinction coefficient ε is given by

$$\sigma\ (\text{in cm}^2) = 0.385 \times 10^{-20}\ \varepsilon\ (\text{in cm}^2/\text{mmole})$$

[2] *F. J. McClung* and *R. W. Hellwarth*, J. appl. Physics *33*, 828 (1962).

[3] *R. C. Benson* and *M. R. Mirarchi*, IEEE Trans. MIL *8*, 13 (1964).

[4] *F. T. Arecchi, G. Potenza*, and *A. Sona*, Nuovo Cimento *34*, 1458 (1964).

[5] *F. P. Schäfer* and *W. Schmidt*, Z. Naturforsch. *19a*, 1019 (1964).

[6] *P. Kafalas, J. I. Masters*, and *E. M. E. Murray*, J. appl. Physics *35*, 2349 (1964).

[7] *B. H. Soffer*, J. appl. Physics *35*, 2551 (1964).

[8] *P. P. Sorokin, J. J. Luzzi, J. R. Lankard*, and *G. D. Pettit*, IBM-J. Res. Developm. *8*, 182 (1964).

Let the occupancies of the ground and excited states be m_0 and m_1, and let the average life of the excited state be τ. The change in the occupancy of the ground state due to absorption is

$$dm_0/dt = -n\,\sigma\,m_0$$

while the change in the occupancy of the excited state due to spontaneous emission is

$$dm_1/dt = -m_1/\tau$$

and that due to stimulated emission is

$$dm_1/dt = -n\,\sigma\,m_1$$

For the steady state, therefore, we have

$$-dm_1/dt = dm_0/dt = -n\,\sigma\,(m_0-m_1) + m_1/\tau = 0 \qquad (1)$$

Substitution of $m = m_0 + m_1$ in eq. (1) gives

$$m_0-m_1 = m/(2\,n\,\sigma\,\tau + 1) \qquad (2)$$

The photon flux n in a thin layer of thickness dl is reduced under these conditions by

$$dn = -(m_0-m_1)\,n\,\sigma\,dl \qquad (3)$$

Insertion of eq. (2) in eq. (3) and integration over the length of the cell gives the absorption law

$$\ln(n_0/n) = m\,\sigma\,L - 2\,\sigma\,\tau\,(n_0-n) \qquad (4)$$

In this equation, n_0 is the incident photon flux, and n is the photon flux emerging from a cell of length L. For small τ or small n_0, eq. (4) becomes the well known Beer-Lambert law.

If the molecules pass very rapidly from the state reached on absorption of a photon into another energy level from which they can fall back to the ground state after an average life τ (by spontaneous emission or radiationless deactivation), appreciable stimulated emission cannot occur at the same frequency ν_L. Thus

$$m_0 = m/(n\,\sigma\,\tau + 1) \qquad (2a)$$

Integration of

$$dn = -m_0\,n\,\sigma\,dl$$

gives the absorption law

$$\ln(n_0/n) = m\,\sigma\,L - \sigma\,\tau\,(n_0-n) \qquad (4a)$$

Figure 2 shows the absorption $1-n/n_0$ found from equations (4) and (4a) for a typical example[9] as a function of the irradiation intensity $S_0 = h\,\nu_L\,n_0$. In the example in question, the absorption is practically eliminated at an irradiation intensity of the order of 10 MW/cm².

[9] *W. Schmidt*, Dissertation, Universität Marburg 1966.

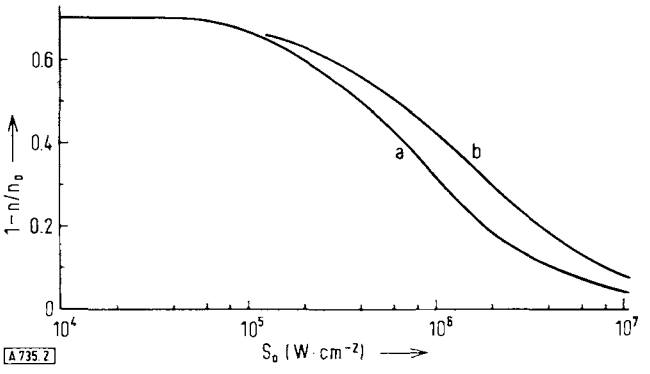


Fig. 2. Absorption $1-n/n_0$ as a function of the irradiation intensity S_0 in a dye solution of concentration $m = 3.2 \times 10^{15}$ cm^{-3} (corresponding to 5.3×10^{-6} mole/l), effective cross section of the molecules $\sigma = 0.39 \times 10^{-15}$ cm² (corresponding to $\varepsilon = 10^5$ lmole^{-1} cm^{-1}), life of the excited state $\tau = 1$ ns, cell length $L = 1$ cm. Curve a) calculated according to eq. (4), curve b) according to eq. (4a) (after [9]).

The quantitative treatment of the production of giant pulses with dye solutions as optical shutters is described by three coupled differential equations, of which one describes the time variation of the occupancies of the ground and excited states of the dye molecules, another gives the time variation of the occupancies of the ground and excited states of the chromium ions in the ruby rod, and the third gives the time

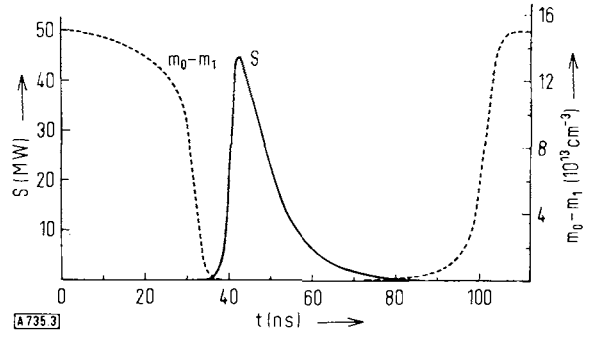


Fig. 3. Radiation output S and occupancy difference m_0-m_1 between the excited state and the ground state as functions of time for a typical example (after [9]).

variation of the photon flux in the laser resonator. The solution obtained for these three coupled differential equations by numerical integration is shown in Figure 3 for a typical example. The diagram shows the rapid increase in the photon flux in the resonator (the quantity plotted is the radiation output $S(t)$, which is proportional to the photon flux) and the simultaneous rapid decrease in the difference in occupancy between the excited and the ground states ($\Delta m(t) = m_0-m_1$) of the dye molecules during the giant pulse. Similar calculations can be found in[10–13].

Good agreement is found for the calculated and experimental values of the maximum intensity and half-width of the giant pulse emitted in the case of the cyanine dye *(1a)* (see Table 1). The quantitative treatment of the effect shows that the ratio of the effective cross sections of the dye molecules and active centers in the laser material at the laser wavelength should be as high as possible. This is satisfactorily fulfilled by the combination *(1a)*/ruby, since the effective cross

[10] *M. Hercher*, Appl. Optics *6*, 947 (1967).

[11] *A. Szabo* and *R. A. Stein*, J. appl. Physics *36*, 1562 (1965).

[12] *V. V. Korobkin, A. M. Leontovich, M. N. Popova*, and *M. Ya. Shchelev*, JETP Letters *3*, 194 (1966).

[13] *B. L. Borovich, V. S. Znev*, and *V. A. Shcheglov*, Soviet Physics JETP *22*, 717 (1966).

section of the dye *(1a)* at the ruby wavelength, σ_F (694 nm), is 0.46×10^{-16} cm^2, while that of the chromium ions in ruby, σ_R (694 nm), is 1.8×10^{-20} cm^2, *i.e.* the ratio $\sigma_F/\sigma_R = 2.5 \times 10^3$.

This means that each photon absorbed in the dye solution, which decreases the absorption of this solution, was formed by stimulated emission in the laser material with passage of an active center into the ground state, *i.e.* its formation was associated with an increase in the absorption of the laser material. In the extreme case, if the effective cross sections in the dye solution and in the laser material are equal, the two effects balance each other, and no shutter effect occurs. It is also clearly advantageous to use dyes whose lives in the excited state are not too short.

This is also readily understandable if one considers that the radiation intensity required to keep a considerable proportion of the dye molecules in the excited state against the deactivation process is of the order of $h\,\nu_L n_{1/2} = h\,\nu_L/(\sigma\tau)$, and the fraction of the photons in the resonator that are consumed for this purpose is lost from the laser output. This is practically equivalent to saying that the fluorescence quantum yield η of these dyes should not be appreciably smaller than 10^{-3}, since η and the lifetime τ of the molecules in the excited state are related by $\tau = \eta\,\tau_0$; τ_0 is the natural lifetime, which can be found from the absorption spectrum of the dye by means of the relation

$$1/\tau_0 = 2.89 \times 10^{-9} \times n_B^2\,\tilde{\nu}_{max}^2 \int \varepsilon(\tilde{\nu})\,d\tilde{\nu}$$

(integral: longest-wave electronic absorption band)

$\tilde{\nu}_{max}$ is the wavenumber of the maximum of the band, and n_B is the refractive index of the dye solution. For the typical value of $\tau_0 = 5$ ns and a fluorescence quantum yield $\eta = 10^{-3}$, therefore, we obtain the very high value of about 10^9 W/cm^2 for the irradiation intensity required to bring half of the molecules into the excited state according to eq. (2a) (at the wavelength of the ruby laser, a photon flux 3.48×10^{18} photon/s corresponds to a power of 1 W). However, all solid laser materials are destroyed at these irradiation intensities, and new disturbance effects occur, such as the two-quantum absorption discussed later.

The number of suitable dyes is extremely large in the case of the ruby laser. The first dyes to be used as optical shutters were phthalocyanines[8] and cyanines[5–7]. The absorption and fluorescence spectra, together with a simplified term diagram, are given in Figure 4 for a phthalocyanine [dye *(5a)*] and in Figure 5 for a cyanine [dye *(1a)*].

The wavelength of the ruby laser practically coincides with the maximum of the long-wave absorption band of the phthalocyanine. The absorption occurs in this case into higher levels of the first excited singlet state, from which a fast relaxation to the ground level of the state occurs in about 10^{-12} s. Stimulated emission at the wavelength of the ruby laser is not possible from this level; the ground state is instead deactivated either

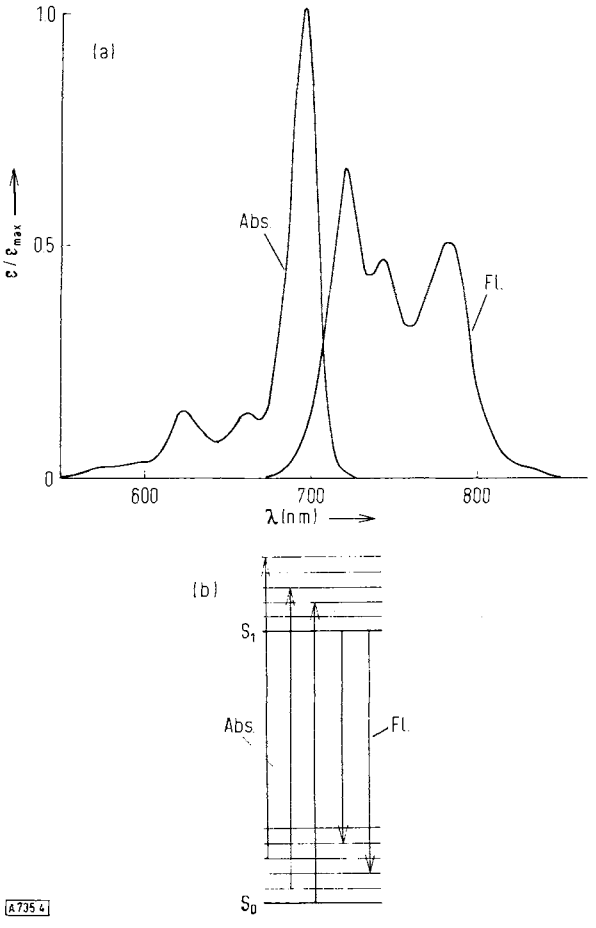


Fig. 4. a) Absorption and fluorescence spectra of the phthalocyanine derivative *(5a)* in α-chloronaphthalene (after [8, 50]).
b) Corresponding term diagram. The length of the absorption arrows corresponds to the energy of a ruby photon.

radiationlessly, by spontaneous emission of fluorescence, or by stimulated emission at a wavelength other than that of the ruby laser. This is therefore a case that fits well into the three-level diagram of Figure 4b.

For the dye *(1a)*, on the other hand, the wavelength of the ruby laser practically coincides with the maximum of the fluorescence band. The absorption takes place in the long-wave tail of the absorption band, mainly from thermally excited levels of the ground state to the ground level of the first excited singlet state, from which the molecule can return to the ground state by stimulated emission at the wavelength of the ruby laser as well as radiationlessly or by spontaneous emission of fluorescence. A suitable model in this case, therefore, is the two-level diagram of Figure 5b.

Under otherwise identical conditions, "two-level dyes" of this type are more effective optical shutters than the "three-level dyes", since a higher radiation intensity is required for the three-level diagram than for the two-level diagram to reduce the absorption to a given value, as can be seen from Figure 5b. The losses in the laser resonator are thus correspondingly reduced; this is particularly important for high-output lasers, in which the radiation intensity is increased to the destruction limit of the ruby crystal to obtain the highest possible outputs.

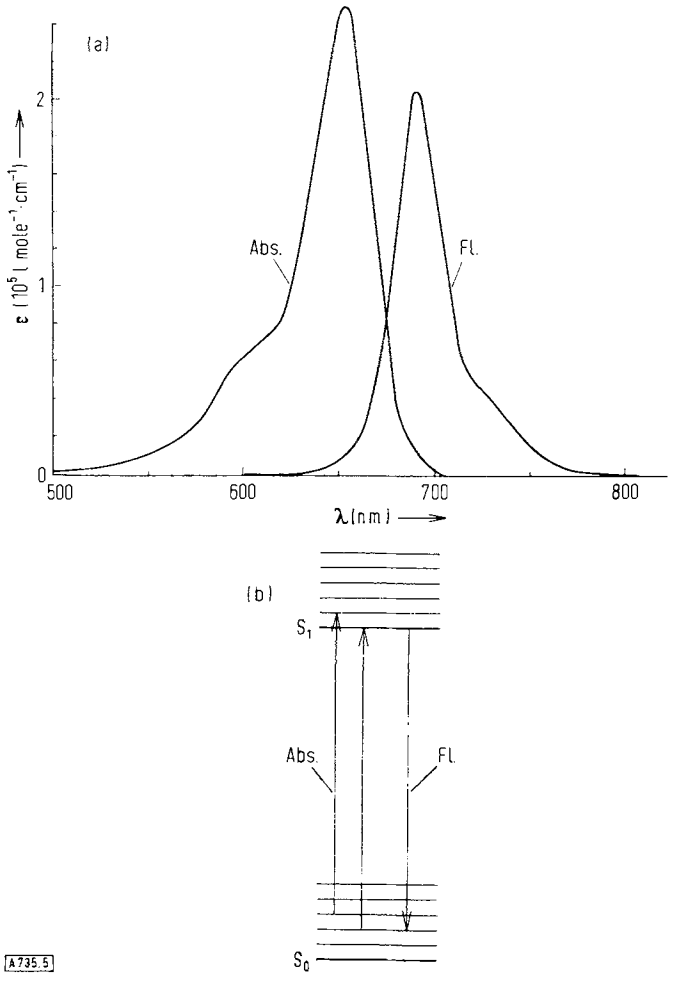


Fig. 5. a) Absorption and fluorescence spectra of cyanine dye *(1a)* in methanol.
b) Corresponding term diagram. The length of the absorption arrows corresponds to the energy of a ruby photon.

Pronounced deviations from the behavior expected on the basis of these models are found with some dyes, in which the absorption decreases only slightly, if at all, at high radiation intensities [9], or in some cases even increases [14], though a shutter effect is to be expected from their absorption spectra and lives. To explain these deviations, it must be remembered that absorption of light quanta at the laser wavelength is possible by transition from the first excited singlet state to higher singlet states, and that for many molecules, particularly with halogen substituents, the radiationless transition from the first excited singlet state to the lowest triplet state (intersystem crossing) is sufficiently fast to bring a considerable fraction of the dye molecules into the triplet state within a few nanoseconds. Additional absorption can also occur in this case by transitions to higher triplet levels.

The transitions from the first to the second excited singlet state that were deduced earlier from deviations of the shutter dyes from the theoretically expected behavior have now been detected directly. An anomalous fluorescence emission from the second excited singlet state to the ground state, such as had previously been found only for azulene, was observed [15]. Moreover, the absorption spectra of the first excited singlet states have recently been measured directly for several dyes [16, 17].

Some shutter dyes are listed in Table 1. As an indication of the effectiveness of the dye, the table contains the ratio (where known) of the intensity (S_R) of the giant pulse produced with this dye to the intensity (S_N) of the normal pulse produced under otherwise identical conditions. No investigations have been carried out as yet to determine which of the above factors is responsible for the difference in the individual activities as shutter dyes.

The effectiveness of the shutter dye is influenced by the solvent as a result of solvatochromism effects, this influence being strong *e.g.* for the dye *(3b)*, as well as by differences in the life of the excited state. The solvent also has a strong influence on the photochemical stability. Thus a 10^{-4} M solution of the dye *(1a)* in methanol can generally be used only for a few days if reproducible giant pulses are to be produced. A similar solution in dimethyl sulfoxide, on the other hand, can be kept for several weeks, provided that the cell containing the dye solution is protected from the UV light of the pumping flash lamp, so that only the laser radiation passes through it.

Figure 6 shows the results of transmission measurements on a cell containing dye solutions as a function of the irradiation intensity. The dyes *(6)* and *(7)* are

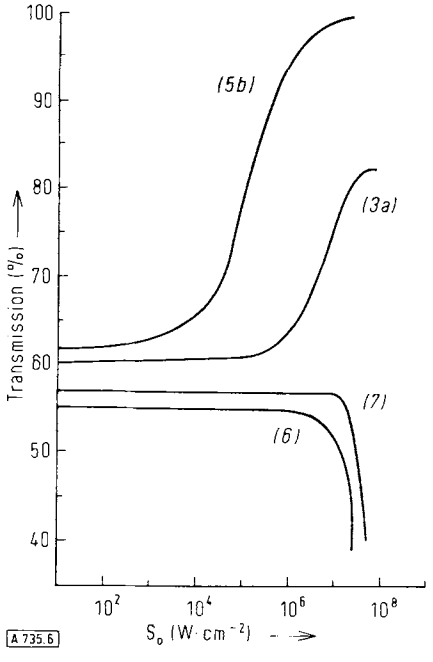


Fig. 6. Transmission of a cell containing dye as a function of the irradiation intensity. The figures by the curves are the numbers of the dyes in Table 1 (after [14]).

examples of dyes whose absorptions are greater in the excited state than in the ground state. These dyes are naturally unsuitable for use as shutter dyes.

Whereas many cyanine dyes and a number of other dyes with favorable switching properties are known

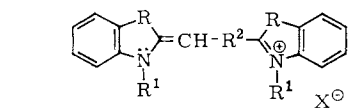
[14] *C. R. Giuliano* and *L. D. Hess*, IEEE J. Quant. Electr. *QE-3*, 358 (1967).

[14a] *M. L. Spaeth* and *W. R. Sooy*, J. chem. Physics *48*, 2315 (1968).

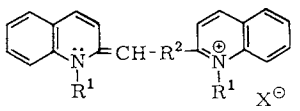
[15] *W. E. K. Gibbs*, Appl. Physics Letters *11*, 113 (1967).

[16] *A. Müller*, Z. Naturforsch. *23a*, 946 (1968).

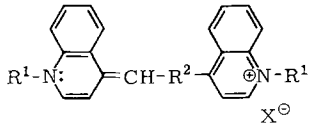
[17] *A. Müller* and *E. Pflüger*, Chem. Physics Letters *2*, 155 (1968).



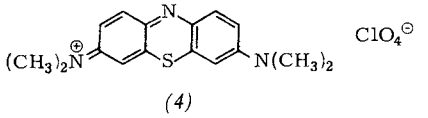
(1)



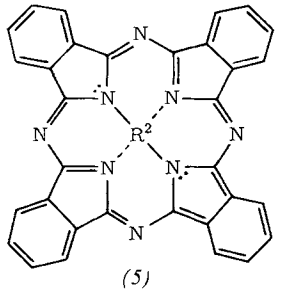
(2)



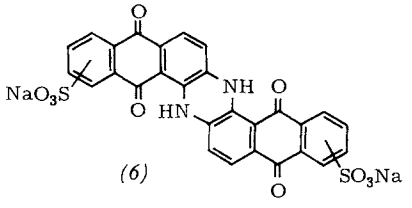
(3)



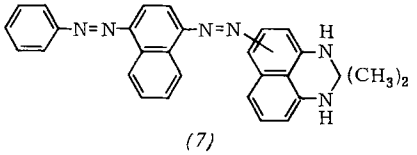
(4)



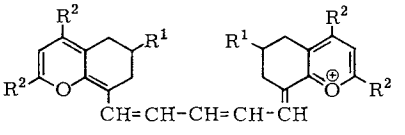
(5)



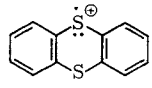
(6)



(7)



(8)



(9)

Table 1. Organic dyes as optical shutters for lasers. *(1)—(3)* are cyanine dyes, *(4)* is methylene blue, *(5)* are phthalocyanines, *(6)* is sulfonated indanthrone, *(7)* is Sudan black B, and *(9)* is the thianthrene radical-ion. S_R/S_N = height of the giant pulse/height of the normal pulse.

Compound	R	R^1	R^2	X	Solvent	λ_{max} (nm)	S_R/S_N	Ref.
(1a)	S	C_2H_5	$-(CH=CH)_2-$	I	CH_3OH	652	100	[9]
(1b)	O	C_2H_5	$-(CH=CH)_3-$	I	CH_3OH	682	100	[9]
(1c)	S	C_2H_5	$-CH=CCl-CH=CH-$	I	CH_3OH	645	100	[9]
(1d)	S	C_2H_5	$-(CH=CH)_3-$	Br	CH_3OH	760	30	[9]
(1e)	$(CH_3)_2C$	CH_3	$-(CH=CH)_2-$	ClO_4	CH_3OH	637	30	[9]
(1f)	Se	C_2H_5	$-(CH=CH)_3-$	I	CH_3OH	770	10	[9]
(1g)	S	C_2H_5	1,3; 7,9-Bis(neopentenylene)decapentaenylene	I	CH_3OH	980		[9, 19]
(1h)	S	C_2H_5	1,3; 9,11-Bis(neopentenylene)dodecahexaenylene	Br	CH_3OH			[9]
(2a)		C_2H_5	$-CH=CBr-CH=CH-$	BF_4	CH_3OH	695	100	[9]
(2b)		C_2H_5	$-CH=C(4\text{-Pyridinyl})-CH=CH-$	BF_4	CH_3OH	696	100	[9]
(2c)		C_2H_5	$-CH=CCl-CH=CH-$	BF_4	CH_3OH	700	100	[9]
(2d)		C_2H_5	$-CH=C(Benzeneazo)CH=CH-$	BF_4	CH_3OH	688	10	[9]
(2e)		C_2H_5	$-(CH=CH)_2-$	I	CH_3OH	706		[27]
(3a)		C_2H_5	$-CH=CH-$	I	CH_3OH	702	100	[6, 7, 9]
(3b)		C_2H_5	$-CH=C(NO_2)-CH=CH-$	BF_4	C_5H_5N	698	30	[9]
(3c)		C_2H_5	$-CH=CH-CH-C(CH_3COO)-(CH=CH)_2-$	I	Acetone	680	10	[9]
					$C_{10}H_7N$	1090		[20]
(4)					H_2O	653	10	[9]
(5a)			$-Al(Cl)-$		α-$C_{10}H_7Cl$	694		[8]
(5b)			$-H \quad H-$		α-$C_{10}H_7Cl$			[8, 14, 14a]
(5c)			$-V-$		$C_6H_5NO_2$	696		[8, 14, 14a]
(6)					H_2O			[14]
(7)					CH_3COOH			[14, 18]
(8a)		H	C_6H_5	ClO_4	CH_3CN	1026		[21]
(8b)		CH_3	C_6H_5	ClO_4	CH_3CN	1026		[21]
(8c)		H	p-$C_5H_{11}OC_6H_4$	ClO_4	CH_3CN	1062		[21]
(9)					CF_3COOH	1060		[32]

for the wavelength of the ruby laser (694 nm), only a few suitable dyes are known for the wavelength of the neodymium glass laser (1064 nm), since only a few substances have electronic bands in this wavelength range. The dyes that do satisfy the requirements are again mainly cyanine dyes [9, 19, 20], as well as pyrylium salts [21].

The structure of the dye in the most widely used commercial shutter solutions (Kodak No. 9860 and Kodak No. 9740) is not revealed by the manufacturers. All these substances have a short storage life even in the dark, and are photochemically

[18] *D. Röss*, Z. Naturforsch. *20a*, 696 (1965).

[19] *B. H. Soffer* and *R. H. Hoskins*, Nature (London) *204*, 276 (1964).

[20] *O. L. Lebedev*, *V. N. Gavrilov*, *Yu. M. Gryaznov*, and *A. A. Chastov*, JETP Letters *1*, 47 (1965).

[21] *J. L. R. Williams* and *G. A. Reynolds*, J. appl. Physics *39*, 5327 (1968).

very unstable. They give reproducible results for a few days only in cells made of red filter glass.

As a possible solution to the problem, it has been suggested that the triplet-triplet absorption of suitable dye solutions be used to produce the shutter effect by subjecting the dye solution to flash irradiation together with the neodymium glass rod in order to bring a large fraction of the molecules into the triplet state [22,23]. Apart from the technical difficulties, this method is not very effective because of the short lives of the higher triplet states and the low steady-state occupancy of the lowest triplet level in liquid solutions (due to the relatively short relaxation time of the lowest triplet level to the ground state). This is confirmed by the existing experimental results [22,23].

A certain improvement could possibly be obtained by the use of solid solutions, *e.g.* dyes polymerized into polymethyl methacrylate. A better solution, in principle, should be the use of stable radical-ions that exist in equilibrium with the oxidized and reduced forms [24,25]. If some of the radicals are destroyed photochemically, they are replaced, provided that sufficient of the reduced and oxidized forms is still available. If the radical-ion content of the solution is relatively low, the absorption can be kept practically constant for long periods in this way. This is illustrated by the case of the radical-ion of thianthrene [dye *(9)*], which is a good shutter for neodymium glasses as a solution in trifluoroacetic acid, and which remains practically unchanged over a period of several weeks [32]. Another well-established method of obtaining reproducible results is the use of a circulating system with a continuous flow cell, a pump, and a large reservoir containing dye solution; the cell may be thermostated to avoid schlieren.

2. Production of Ultrashort Laser Pulses

A particularly interesting development of the method described above leads to a method of producing ultrashort pulses, *i.e.* pulses with half-widths of the order of a few picoseconds, the peak powers of which may be several gigawatts. This method can be readily explained with the aid of an electric analog (Fig. 7) [26].

The signal at the input of a wide-band amplifier is amplified and passed through a delay line with a transit time T_L, through a nonlinear attenuator and a spectral filter, and back to the input of the wide-band amplifier. The spectral filter has a band-pass width of $\Delta\nu$, and the nonlinear attenuator attenuates strong signals to a smaller extent than weak signals.

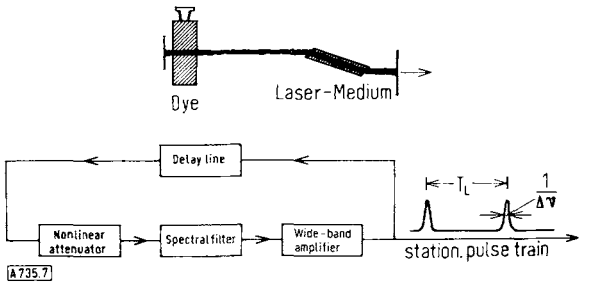


Fig. 7. Construction of a laser for the production of ultrashort pulses and block circuit diagram of an electrical analog. T_L is the transit time of the pulse, and $\Delta\nu$ is the spectral half-width of the spectral filter.

It is clear that this arrangement is a pulse generator, if one considers that even when no external signal is applied to the input of the wide-band amplifier, there is always noise present, and a randomly occurring high noise peak is more strongly amplified than a low noise peak. If the effective amplification of this high noise peak is greater than 1, it undergoes continuous further amplification. Pulses having a half-width $1/\Delta\nu$ in the steady state that depends on the half-width of the spectral filter appear at the output of the wide-band amplifier with a period equal to the transit time T_L.

All these elements can in effect be found in a giant-pulse laser. A dye solution acts as the nonlinear attenuator, the active laser material as the amplifier, the laser material also as the spectral filter (since it amplifies only in the region of its fluorescence band, with consequent restriction of the band width of the laser light), and the time taken by the light to make one round trip in the laser resonator as the delay line. To obtain a uniform train of pulses, the transit time must be uniform, *i.e.* apart from the laser resonator mirrors, there must be no other reflecting surfaces, such as glass-air interfaces of the cell wall. The laser material and the dye cell are therefore either arranged at the Brewster angle or provided with an antireflection coating. The cell containing the dye solution must also be placed as near as possible to one of the mirrors since several concurrent trains of pulses will otherwise be produced.

Pulses having a minimum half-width of 2 to 4 ps and a peak output of 5 GW have been produced in an arrangement of this type with the dye *(2e)* in ruby lasers [27]. To give some idea of what these quantities mean, let us recall that light travels a distance of only 0.3 mm in a picosecond, and that the world electricity production is about 700 GW. Somewhat lower outputs were obtained with dyes *(3a)* [27,28] and *(1a)* [29]. Pulses with half-widths of down to 0.4 ps [30] and outputs of several hundred MW [31] have been produced with the commercial shutter dye solutions Kodak 9740 and 9860 in neodymium glass lasers.

[22] *L. A. Cross* and *C. K. King*, J. appl. Physics *38*, 2290 (1967).

[23] *E. G. Berzing*, *S. V. Lopina*, *Yu. V. Naboikin*, and *Yu. A. Tinnov*, Optics and Spectroscopy *25*, 227 (1968).

[24] *S. Hünig* in *W. Foerst*: Optische Anregung organischer Systeme. Verlag Chemie, Weinheim/Bergstr. 1966.

[25] *S. Hünig*, Chem. Engng. News *44*, No. 41, p. 102 (1966).

[26] *A. J. de Maria*, *D. A. Stetser*, and *H. Heynau*, Appl. Physics Letters *8*, 174 (1966).

[27] *M. E. Mack*, IEEE-J. Quant. Electr. *QE-4*, 1015 (1968).

[28] *H. W. Mocker* and *R. J. Collins*, Appl. Physics Letters *7*, 270 (1965).

[29] *H. J. Cirkel*, unpublished results.

[30] *E. B. Treacy*, Physics Letters *28 A*, 34 (1968).

[31] *A. J. de Maria*, *H. A. Heynau*, *A. W. Penney jr.*, and *G. Wisner*, IEEE-J. Quant. Electr. *3*, 247 (1967).

[32] *F. P. Schäfer* and *L. Ringwelski*, unpublished results.

These low half-widths cannot be measured even with the fastest photoelectric cells and oscillographs available at present. Methods based on the use of nonlinear optical effects in certain crystals have therefore been suggested, and in some cases successfully tried out [33–36]. All these methods demand an advanced experimental technique. It was therefore an important step forward when it was found possible to convert the time information very easily into space information by means of the two-quantum absorption in organic dyes and so to make the time half-width of the pulses directly measurable as a space half-width [37]. A model will now be presented for the two-quantum absorption in organic dyes.

3. Two-Quantum Absorption in Organic Dyes

A general quantum-mechanical theory of multiquantum processes has existed since 1931 [38]. There seems however to be little prospect of applying this theory to organic dyes in the light of the present stage of development of quantum chemistry; at best, the order of magnitude of the absorption can be found by a rough estimation [39]. The absorption can however be calculated [40] with results that agree well with those obtained by experiment, if one starts with the postulate that two photons of wavelength λ_0 striking the molecule simultaneously are absorbed by it, as well as one photon of wavelength $\lambda_0/2$. It must be specified what is meant here by "simultaneously". The transit time of the photons (which are regarded as corpuscular) when they travel with the velocity of light c through the π-electron cloud of the molecule with thickness w and maximum cross section σ_{max} is $T = w/c$. If two photons fall within this time on the area covered by the π-electron cloud of the molecule, this may be described as simultaneous incidence. If n photons/cm^2 s (wavelength λ_0) fall on a thin layer of dye solution having thickness dl, the steady number of molecules m^* through whose π-electron clouds a photon is just passing is given by

$$m^* = (m/3)\,\sigma_{max}\,n\,w\,/\,c \qquad (5)$$

where the factor 1/3 arises from the averaging of the random orientation of the molecules. As was mentioned earlier, σ_{max} can be found from the absorption spectrum of the dye: $\sigma_{max} = 3\sigma$.

According to the postulate mentioned above, the effective cross section σ_1 of any one of these m^* molecules for a second photon of wavelength λ_0 is the same as the effective cross section of the molecule for the absorption of a single photon of wavelength $\lambda_0/2$. The attenuation of the laser light in this layer is therefore

$$-\mathrm{d}n = 2\,\sigma_1\,m^*\,n\,\mathrm{d}l$$

The factor of 2 takes into account the fact that two photons disappear in each act of absorption. Integration over the length L of the cell gives the absorption law for the two-quantum absorption:

$$\frac{1}{n_1} - \frac{1}{n} = \frac{2}{3}\,m\,\frac{w}{c}\,\sigma_{max}\,\sigma_1\,L$$

where n_1 is the photon flux at the rear end of the cell. Even at very high irradiation intensities, the absorption is so weak that we can write $nn_1 \approx n^2$. Introduction of the cross section F of the beam gives, to a good approximation, the number m_{abs} of molecules excited per unit time, and multiplication of m_{abs} by the fluorescence quantum yield η gives the number n_{fl} of fluorescence photons emitted per unit time:

$$n_{fl} = \eta\,m_{abs} = (2/3)\,\eta\,m\,(w/c)\,\sigma_{max}\,\sigma_1 FLn^2 \qquad (6)$$

As can be seen from eq. (6), n_{fl} is proportional to the square of the photon flux n. It should also be proportional to the product of the maximum absorption cross section σ_{max} and the cross section σ_1 at wavelength λ_0. This relation has been checked with the apparatus shown in Figure 8.

The giant pulses emerging from the rotating-prism neodymium glass laser were passed through a reversed Galilean telescope to reduce the cross section of the beam and so increase the intensity; the giant pulses then passed through a frequency doubler crystal, in which part of the neodymium laser light was converted into light of half the original wavelength (532 nm). Either the neodymium laser light or the light of half the original wavelength could be filtered out, as desired, in the succeeding filters. Part of the remaining light was reflected by a glass plate and directed to the monitor photoelectric cell, which recorded the pulse behavior of the light. The major part of the light was then focused by a lens on a cell containing a dye solution that absorbed at half the original wavelength. A photomultiplier recorded the emerging fluorescence light, which was excited either by the neodymium laser light at 1064 by two-quantum absorption or by normal absorption in excitation by light of wavelength 532 nm. This excitation with light of half the original wavelength can be accurately calculated from the intensity measured by the monitor photoelectric cell and the known absorption spectrum of the dye, and can thus be used for the calibration of the fluorescence excited by two-quantum absorption. Owing to the high excitation intensity and the low fluorescence intensity, care was necessary to avoid scattered light and dust.

The relation found between the fluorescence output n_{fl} and the excitation power n for an aqueous solution of Rhodamine B [dye *(10b)*] is shown in Figure 9. The slope of the straight line for two-quantum excitation is 2.05 ± 0.1, while that for one-quantum absorption is 0.98 ± 0.03 (double-logarithmic plot).

A check on the dependence of n_{fl} on $\sigma_{max}\sigma_1$ gives agreement in the order of magnitude, with a relatively

[33] *J. A. Armstrong*, Appl. Physics Letters *10*, 16 (1967).

[34] *M. Maier, W. Kaiser*, and *J. A. Giordmaine*, Physics Rev. Letters *17*, 1275 (1966).

[35] *W. H. Glenn* and *M. J. Brienza*, Appl. Physics Letters *10*, 221 (1967).

[36] *H. P. Weber*, J. Appl. Physics *38*, 2231 (1967).

[37] *J. A. Giordmaine, P. M. Rentzepis, S. L. Shapiro*, and *K. A. Wecht*, Appl. Physics Letters *11*, 216 (1967).

[38] *M. Göppert-Mayer*, Ann. Physik *9*, 273 (1931).

[39] *D. A. Kleinmann*, Physic. Rev. *125*, 87 (1962).

[40] *F. P. Schäfer* and *W. Schmidt*, IEEE-J. Quant. Electr. *QE-2*, 357 (1966).

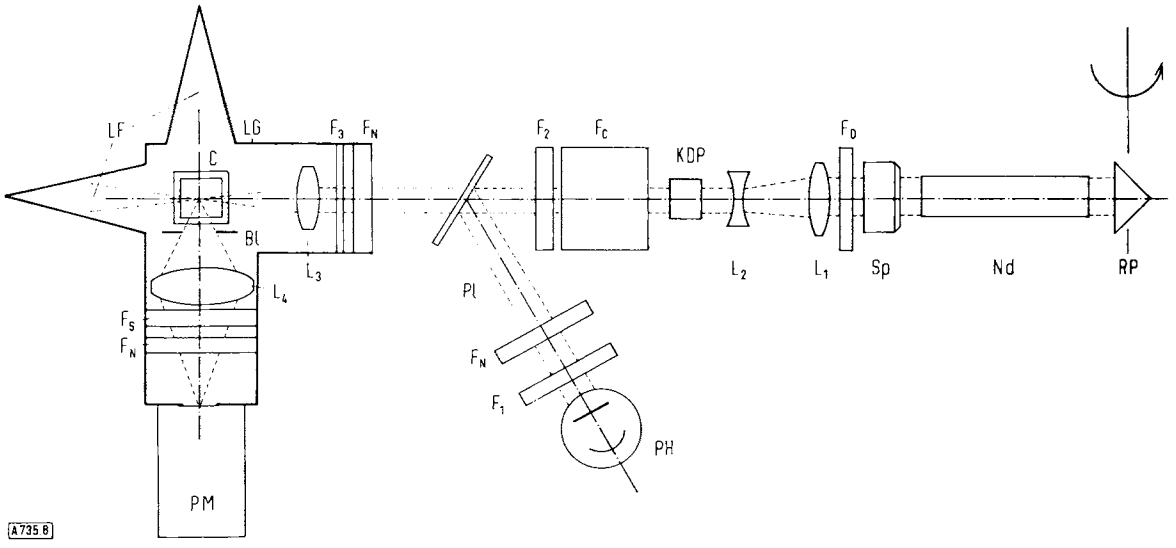


Fig. 8. Arrangement for the measurement of two-quantum absorption in dye solutions. RP: rotating prism, Nd: neodymium glass laser rod, Sp: laser mirror, $F_{0,1,2,3}$: colored glass filters, F_C: filter containing copper sulfate solution, F_N: neutral density filter, F_S: interference filter, Pl: glass plate, KDP: frequency-doubler crystal, $L_{1,2,3,4}$: lenses, PH: monitor photoelectric cell, PM: photomultiplier, C: cell containing dye solution, LG: light-tight housing, LF: light traps, Bl: aperture diaphragm (after [40]).

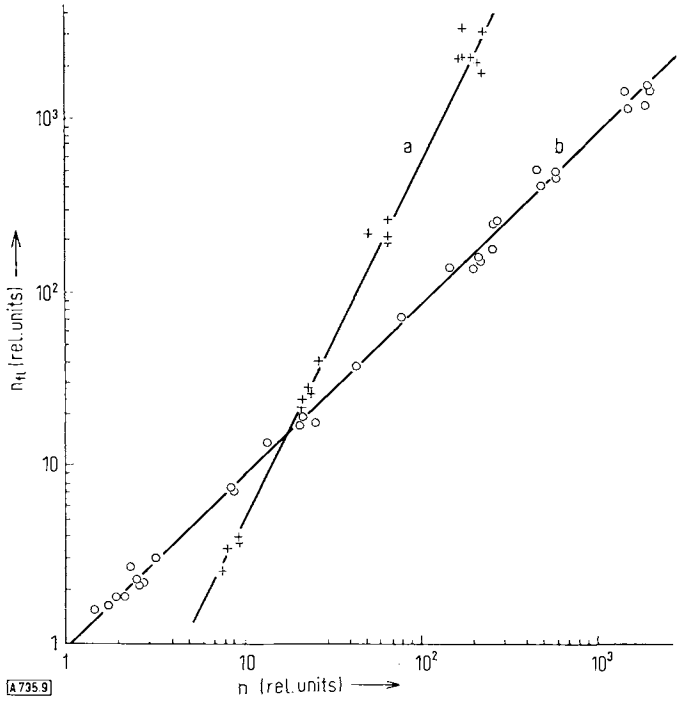


Fig. 9. Fluorescence output n_{fl} as a function of the excitation output n for an aqueous solution of Rhodamine B *(10b)*,
a) with two-quantum excitation (106 nm), b) with excitation by one-quantum absorption (532 nm) (after [40]).

large scatter. Examination of these values suggested that fw/c should be used for the transit time instead of w/c, where f is the oscillator strength of the absorption band in question for one-quantum absorption. The oscillator strength of a band is generally a measure of the resonance of the electrons in the field of the stimulating light wave. Improvement of eq. (6) to eq. (6a)

$$n_{fl} = (2/3)\,\eta\, m f (w/c)\, \sigma_{max}\, \sigma_1\, FLn^2 \qquad (6a)$$

and comparison of the experimental results with those given by eq. (6a) shows not only the required linear dependence of fluorescence intensity n_{fl} on $f\sigma_{max}\sigma_1$ (Fig. 10), but also an excellent agreement with the absolute calculated values if the only remaining free

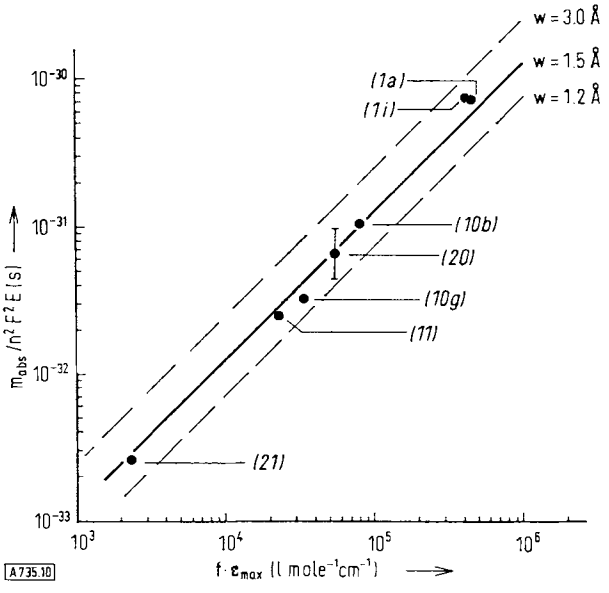
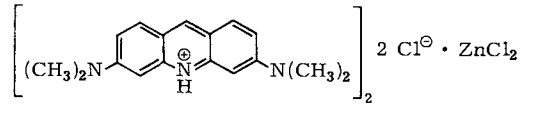


Fig. 10. Dependence of the two-quantum absorption component m_{abs} on $f\varepsilon_{max}$ for a given overall excitation photon flux nF and for a given extinction E of the solution according to the equation

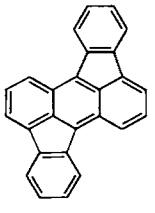
$$m_{abs}/n^2F^2E = 2.68 \times 10^{-38}\, f\, \varepsilon_{max}/F$$

The maximum measuring error is indicated for the acridine orange dimer *(20)* by a vertical line (after [9]).

(20)



(21)



parameter w is taken to have a value of 1.5 Å. This value approximately corresponds to the thickness of the π-electron cloud normal to the molecular plane.

To use the fluorescence stimulated by two-quantum absorption for the measurement of the half-width of ultrashort pulses, the train of pulses is passed through a cell C, the far end of which is silvered (Sp), so that the beam is turned back on itself (Fig. 11). The fluorescence produced by each incoming pulse having a peak

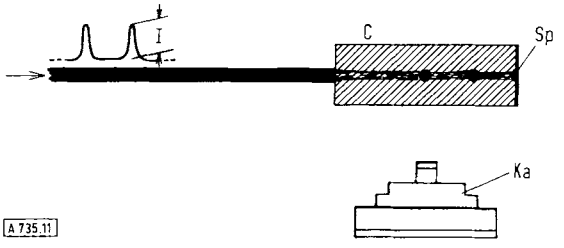


Fig. 11. Arrangement for the measurement of the time half-width of ultrashort pulses with the aid of the two-quantum absorption. Explanation in text.

intensity I (which is proportional to the photon flux n) is $F_{\rightarrow} = \text{const.}\ I^2$, and that of each returning pulse is $F_{\leftarrow} = \text{const.}\ I^2$, *i.e.* the total fluorescence recorded by the camera Ka is

$$F_{\rightarrow} + F_{\leftarrow} = 2 \times \text{const.}\ I^2$$

Only at the points where an incoming and returning pulse meet is the fluorescence intensity $F = \text{const.}\ (2I)^2$, *i.e.* it is twice as high here as at neighboring points. The width of these bright areas divided by the velocity of light then gives the time half-width of the pulses.

In the selection of the dye, it need only be remembered that it should, as far as possible, be free from absorption at the laser wavelength, have a strong absorption band at half the wavelength, and have the highest possible fluorescence quantum yield η. Thus a solution of Rhodamine 6G [dye (10c)] is generally used for neodymium glass laser pulses[41] and *e.g.* 9,10-diphenylanthracene in benzene[42] or 6-acetylaminopyrene-1,3,8-trisulfonic acid in water[29] for ruby lasers (for more detailed discussion, see[43]).

4. Dye Lasers

As was explained in Section 1, a considerable proportion of the molecules of a dye can be raised to the first excited singlet state by irradiation with a giant-pulse ruby laser. Spontaneous fluorescence occurs first from the vibrationless level of the first excited singlet state into higher levels of the electronic ground state, corresponding to a wavelength greater than that of the stimulating laser (cf. Fig. 4b). If one of these fluorescence photons strikes excited molecules on its way out of the cell, it will induce the emission of further fluorescence quanta from these molecules, and is correspondingly amplified when it leaves the cell. If the cell is placed in a laser resonator whose mirrors always reflect part of the light emerging from the cell back into the cell, where it is further amplified, this process can build up into laser emission provided that the effective amplification is greater than 1.

The "threshold condition" for this is found directly if one considers that the substantial attenuation due to incomplete reflection by the mirrors of the resonator (reflection coefficients R) and due to reabsorption of the fluorescence light of wavelength λ in the long-wave tail of the absorption band of the dye takes place by a factor $e^{-\sigma_{abs}(\lambda)m_0L}$, while the amplification factor is $e^{+\sigma_{fl}(\lambda)m_1L}$.

In these expressions L is the length of the cell and σ_{abs} is the effective cross section, which is obtained (see above) from the absorption spectrum at wavelength λ, while the effective cross section σ_{fl} of the stimulated fluorescence emission is obtained from the intensity of the spontaneous fluorescence by means of the relation

$$\sigma_{fl} = \text{const.}\ \lambda^5 \times dI_{fl}/d\lambda$$

with the subsidiary condition $\sigma_{fl,max} = \sigma_{abs,max}$. $dI_{fl}/d\lambda$ is the spectral intensity distribution of the spontaneous fluorescence, such as is usually recorded in fluorescence spectrophotometers. The threshold condition is thus

$$e^{-\sigma_{abs}m_0L}\ R\ e^{+\sigma_{fl}m_1L} \geqslant 1 \qquad (7)$$

Taking logarithms, rearranging, and inserting $m = m_0 + m_1$, we obtain the simpler expression[44]

$$(\sigma_{fl} + \sigma_{abs})\ (m_1/m) - \sigma_{abs} = S_L/m \qquad (8)$$

where

$$S_L = \frac{1}{L} \ln \frac{1}{R}$$

In this form, the left-hand side of the threshold condition contains only spectroscopic data for the dye, with the fraction m_1/m of excited molecules as a parameter, while the right-hand side contains the data for the laser resonator and the concentration of the dye solution. By insertion of the dye and resonator data for a particular case it is possible to calculate the fraction m_1/m of molecules that must be excited (and hence the pump power required) for each wavelength so that the laser emission can begin. The emission will then start first at the wavelength that requires the lowest value of m_1/m, and hence the lowest pumping power. This wavelength also depends on the concentration. Eq. (8) shows that an increase in the concentration has exactly the same effect as *e.g.* an increase in the length of the cell.

[41] *A. J. De Maria, W. H. Glenn,* and *M. J. Brienza* (unpublished), cited in *A. J. De Maria,* Electronics *1968,* 112.

[42] *M. A. Duguay, S. L. Shapiro,* and *P. M. Rentzepis,* Physic. Rev. Letters *19,* 1014 (1967).

[43] *A. J. De Maria, W. H. Glenn jr., M. J. Brienza,* and *M. E. Mack,* Proc. IEEE, *57,* 2 (1969).

[44] *F. P. Schäfer,* invited paper International Quantum Electronics Conference, Miami 1968.

The concentration dependence of the emission wavelength has been calculated for the cyanine dye *(1d)* from its spectroscopic data and plotted in Figure 12

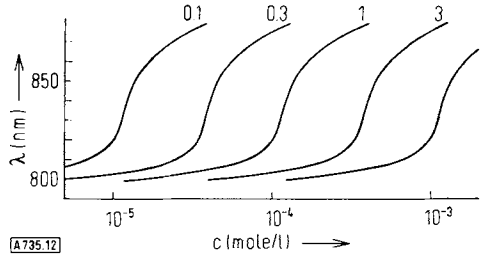


Fig. 12. Concentration dependence of the laser wavelength for *(1d)* according to eq. (8), calculated from the absorption and fluorescence spectra. The figures by the curves show the value of $S_L = \frac{1}{L} \ln \frac{1}{R}$.

with the parameter S_L (see above). It can be seen that *e.g.* 10^{-4} M solutions of this dye in a cell having length $L = 1$ cm and silvered by vapor deposition of silver (one of the deposits being so thin that a transmission of a few percent allows the output of the emission from the laser resonator) corresponding to a value of $S_L \approx 0.3$ cm^{-1} should emit at $\lambda = 875$ nm, whereas in an unsilvered cell corresponding to $S_L \approx 3$ cm^{-1} they should emit at $\lambda = 820$ nm.

The apparatus shown in Figure 13 was used to check this [45]. The solution in the cell is stimulated by the ruby laser. The excitation intensity can be reduced by a fixed factor by means of neutral density filters. Part of the stimulating ruby laser

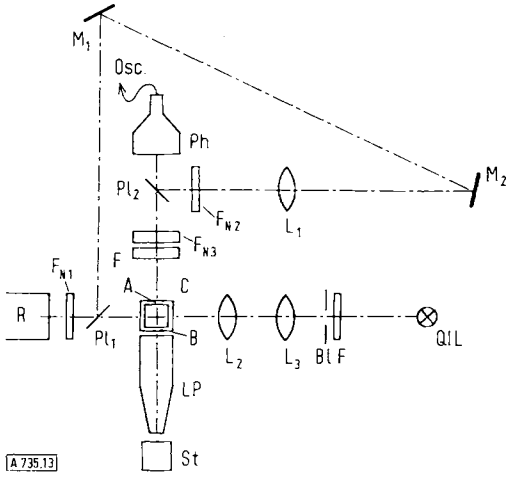


Fig. 13. Arrangement for the investigation of the stimulated fluorescence emission from dye solutions. R: ruby laser, C: cell containg dye solution, A,B: cell windows through which the stimulated fluorescence emerges, St: spectrograph, LP: light guide, Ph: photoelectric cell, $Pl_{1,2}$: glass plates, $M_{1,2}$:deflecting mirrors, F: spectral filter, $FN_{1,2,3}$: neutral density filters, $L_{1,2,3}$: lenses, Bl: aperture diaphragm, QIL: quartz-iodine lamp, Osc. = oscilloscope (after [45]).

light is split out as a reference signal and led by a separate path to the photoelectric cell. The spontaneously emitted or stimulated fluorescence light emerging from the cell, on the other hand, passes directly through a colored glass filter, which cuts out scattered light, and a neutral density filter (for specified intensity reduction) to the photoelectric cell. Part of the fluorescence light is introduced into the spectrograph through a light guide. Using the calibrated tungsten-iodine lamp and a system of lenses, apertures, and interference filters, the fluorescence of the cell can be excited continuously with the same geometry and spectral distribution as when pulse-stimulated by the ruby laser. In this case the cell C forms a resonator in which the plane-parallel windows A and B act as resonator mirrors, which reflect part of the emission back into the cell. The R value for the unsilvered cell due to reflection at the glass-air interface is 0.04, while the reflection for silvered cells can be varied over a wide range (maximum about $R = 0.95$) by varying the thickness of the vapor-deposited coating.

The dye emission output is found as a function of the excitation output by evaluation of the oscillogram; the results for the dye *(1d)* in 10^{-3} M methanol solution in an unsilvered cell are shown in Figure 14 [46]. It can be seen that the dye emission power suddenly increases by several powers of ten at an excitation power of about

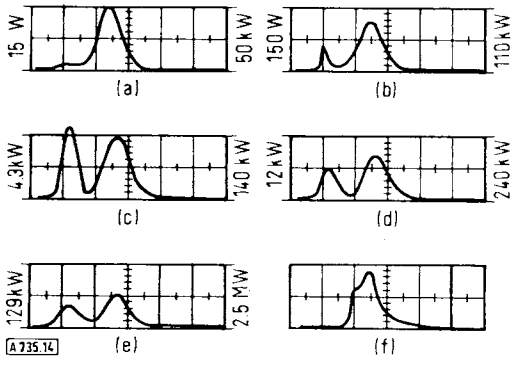


Fig. 14. Oscillograms (traced) recorded with the arrangement of Fig. 13. Deflection speed: a) to e): 10 ns/cm. b) to e): first pulse fluorescence, peak output indicated at left; second pulse pumping ruby laser; peak output at right; 10^{-3} M solution of *(1d)* in methanol; f: fluorescence pulse just above the laser threshold, as in b), but with a deflection speed of 2 ns/cm (after [46]).

100 kW, when the laser threshold is reached. The transition from spontaneous to stimulated emission can also be seen in the spectrum, as illustrated in Figure 15, which shows the absorption spectrum of the

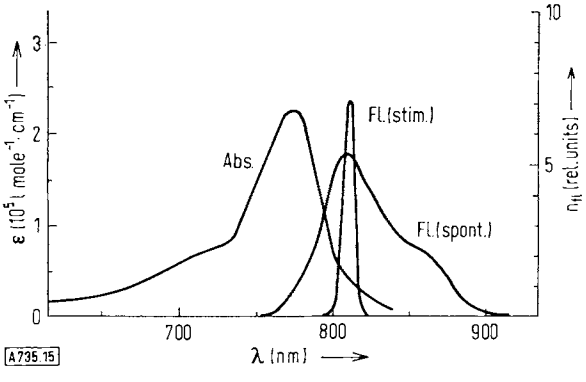


Fig. 15. Absorption spectrum and spontaneous and stimulated fluorescence spectra for a 10^{-4} M solution of *(1d)* in methanol in an unsilvered 1 cm cell (after [45, 46]).

dye *(1d)* together with the spontaneous fluorescence spectrum excited by the continuous light source and the spectrum of the stimulated fluorescence emission recorded with a pulse from the giant-pulse laser at an excitation power of 5 MW (for a 10^{-4} M solution).

[45] *J. Volze*, Dissertation, Universität Marburg 1969.

[46] *F. P. Schäfer, W. Schmidt*, and *J. Volze*, Appl. Physics Letters *9*, 306 (1966).

Repetition of these experiments with solutions of different concentrations gives the concentration dependence shown in Figure 16, which agrees very well with the expected behavior.

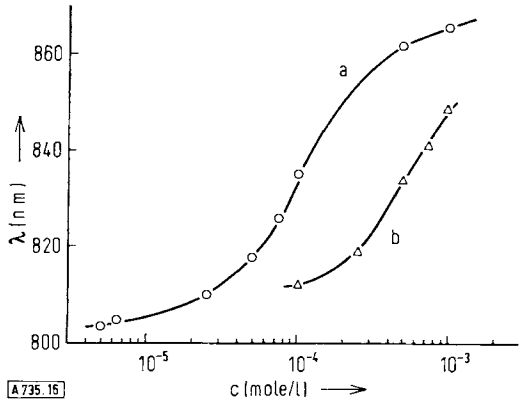


Fig. 16. Concentration dependence of the laser wavelength of *(1d)* in methanol solution. Measured wavelength of the emission maximum a) for a silvered and b) for an unsilvered cell (after [46]).

The diagram of Figure 12 can also be used to find the dependence of the laser wavelength on the length of the cell with the concentration as the parameter and with a reflection coefficient $R = 0.98$, which is readily obtainable by dielectric multilayer coating. It can be seen from Figure 17 that laser emission should be obtained even with layer thicknesses of only a few wavelengths.

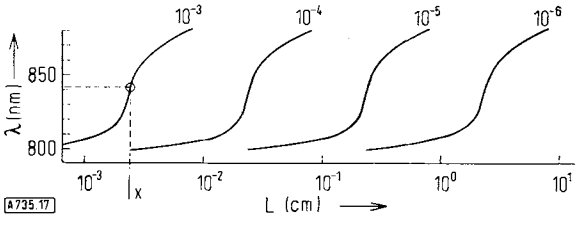


Fig. 17. Dependence of the laser wavelength λ on the layer thickness L for *(1d)* in methanol with laser mirrors having a reflection factor $R = 0.98$. The figures by the curves show the concentration (mole/l) of *(1d)*. X = 25 μm cell.

This has been confirmed (Fig. 18) experimentally by holding the dye solution between two reflecting plates separated by pieces of film.

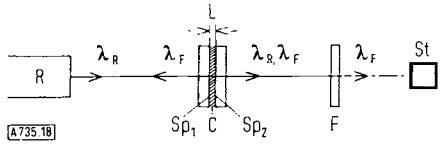


Fig. 18. Thin layer laser arrangement. $Sp_{1,2}$: reflective coatings, C: cell containing dye solution, F: colored filter (to absorb ruby laser light), St: spectrograph, R: ruby laser, λ_R, λ_F: wavelengths of ruby laser and dye laser emissions (after [45]).

The reflecting plates were coated with dielectric multilayers, which gave only a few percent reflection at the ruby wavelength but a reflection of more than 98% at wavelengths above 750 nm. The excitation with ruby laser pulses could thus be carried out through a reflective coating. The emission was recorded with a photoelectric cell and a spectrograph.

Densitometer curves for a number of layer thicknesses are shown in Figure 19. The curves show sharp equidistant maxima.

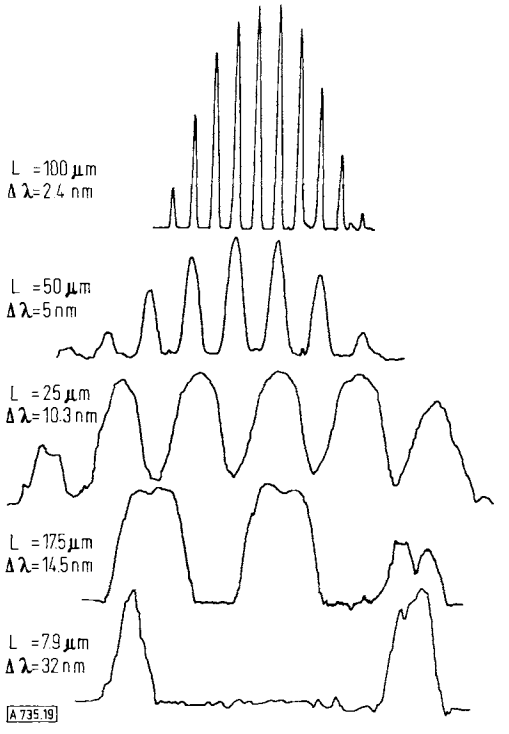


Fig. 19. Densitometer curves for the emission from the thin layer laser of Fig. 18 with the dye *(1d)*. L is the thickness of the layer of dye solution and Δλ is the distance between two adjacent maxima in the spectrum (after [45]).

The distance between the maxima can be easily calculated from the thickness of the pieces of film and the refractive index, bearing in mind that the forward and return light waves in the resonator can be superimposed to give stationary waves only if the length of the resonator is an integral multiple of half the wavelength. Thus $p\,\lambda/2 = n_B L$ where $p = 1,2,3,\ldots$, λ is the wavelength of the laser emission in air, and n_B is the refractive index of the solution at this wavelength. The distance Δλ between the maxima in the spectrum is then $\Delta\lambda = \lambda^2/2\,n_B L$.

For thicknesses of a few μm, there are only two maxima inside the fluorescence band width, and for a thickness of about 3 μm (not shown in Fig. 19) there is only one possible emission wavelength, whose position within the fluorescence band of the dye could be altered as desired by variation of the compression of the pieces of film. The above relations are valid for laser emission normal to the reflecting surface. Emission from other directions is discussed in [45].

Very many dyes (mostly cyanines [46,51,52]) can be stimulated with ruby lasers, and give laser emission between about 710 and 1300 nm. Nineteen cyanine dyes have been named with which this wavelength range could be covered without a gap [47]. Neodymium glass lasers can also stimulate laser emission in some cyanine dyes that still absorb sufficiently at 1.06 μm [48,49]. Other dyes that can be stimulated with the

[47] *Y. Miyazoe* and *M. Maeda*, Appl. Physics Letters *12*, 206 (1968).

[48] *L. D. Derkacheva, A. I. Krymova, V. I. Malyshev*, and *A. S. Markin*, JETP Letters *7*, 362 (1968).

[49] *P. Varga, P. G. Krynkov, V. F. Kupriskov* and *Yu. V. Senatskiĭ*, JETP Letters *8*, 307 (1968).

Table 2. Laser dyes. *(10a)* is fluorescein sodium, *(10b)* is Rhodamine B, *(10c)* is Rhodamine 6G, *(10g)* is eosin, *(12)* are pyrylium derivatives, and *(13)* are pyrene derivatives.

Compound	R	R^1	R^2	X	Solvent	λ (nm) of the excitation	λ (nm) of the laser dye	Ref.
(1a)	S	C_2H_5	$-(CH=CH)_2-$	I	CH_3OH, Acetone	694	710–735	[46, 47]
(1d)	S	C_2H_5	$-(CH=CH)_3-$	Br	CH_3OH, DMSO	694	798–870	[46, 47, 52, 52a, 72]
(1g)	S	C_2H_5	1,3; 7,9-Bis(neopentenylene)-decapentaenylene	I	CH_3OH	694	≈1100	[56]
					$C_6H_5NO_2$	1064	1093	[48]
(1i)	O	C_2H_5	$-(CH=CH)_2-$	I	CH_3OH	532	658	[54]
(2e)		C_2H_5	$-(CH=CH)_2$	I	Glycerol	694	750–790	[51]
(3a)		C_2H_5	$-CH=CH-$	I	Glycerol	694	745	[51]
(3b)		C_2H_5	$-CH=C(NO_2)-CH=CH-$	BF_4	CH_3OH	694	796	[46]
					Acetone	694	814	[46]
					C_5H_5N	694	821	[46]
(3d)		C_2H_5	$-(CH=CH)_3-$	I	Acetone	694	1000	[47]
(5a)			$-Al(Cl)-$		C_2H_5OH	694	755	[50]
(10a)	NaO	O	*o*-$NaOOCC_6H_4$	$R^3=H$	CH_3OH, H_2O	532, 347 [a]	527–556	[52a, 54]
(10b)	$(C_2H_5)_2N$	$N^{\oplus}(C_2H_5)_2$	*o*-$HOOCC_6H_4$	$R^3=H$	C_2H_5OH	347 [a]	597–628	[54]
(10c)	C_2H_5HN	$N^{\oplus}HC_2H_5$	*o*-$H_5C_2OOCC_6H_4$	$R^3=H$	C_2H_5OH, CH_3OH	347 [a]	567–610	[52a, 60, 61, 68, 70, 75]
(10d)	$(CH_3)_2N$	$N^{\oplus}(CH_3)_2$	H	$R^3=H$	CH_3OH	532 [a]	575–618	[57, 60, 73]
(10e)	$(CH_3)_2N$	$N^{\oplus}(C_2H_5)_2$	H	$R^3=H$	CH_3OH	532 [a]	575–618	[57, 60, 73]
(10f)	$(C_2H_5)_2N$	$N^{\oplus}(C_2H_5)_2$	H	$R^3=H$	C_2H_5OH	347 [a]	600–630	[52a, 58]
(10g)	NaO	O	*o*-$NaOOCC_6H_4$	$R^3=Br$	CH_3OH/NaOH, C_2H_5OH	347, 532	553–557	[52a, 60]
(11)		*o*-$CH_3C_6H_4$			CH_3OH	532	621–625	[60]
(12a)		C_6H_5	C_6H_5	BF_4	CH_3OH	347	485	[60]
(12b)		*p*-$CH_3C_6H_4$	*p*-$CH_3C_6H_4$	ClO_4	CH_3OH	347	492	[60]
(12c)		C_6H_5	*p*-$CH_3OC_6H_4$	BF_4	CH_3OH	347 [a]	566–573	[44, 60]
(13a)		CH_3CO			H_2O	347 [a]	441–453	[54, 56, 60]
					NaOH	347 [a]	566–574	[56, 60]
(13b)		C_2H_5			H_2O	347 [a]	547–554	[56, 60]
(14)					C_2H_5OH	347 [a]	432–435	[52a, 60]
(15)					CH_3OH	[a]	449–453	[60]
(16a)		OH			H_2O/NaOH	[a]	450–470	[59]
(16b)		$N(C_2H_5)_2$			C_2H_5OH	[a]	blue	[74]
(17)					$C_6H_5CH_3$	353	411–417	[55]
(18)					$C_6H_5CH_3$	353	383	[55]
(19)					C_6H_{12}	266	341	[55]

[a] Excitation with a flash lamp.

ruby laser are the phthalocyanines, in which dye laser emission has been observed for the first time[50] and methylene blue (dissolved in sulfuric acid)[53]. The choice is however greatly limited by the fact that the direct stimulation of dyes with ruby lasers occurs only in the longwave red region.

The number of suitable dyes is greatly increased *e.g.* by converting part of the light emitted from ruby or neodymium glass lasers into light of half the original wavelength in an ammonium dihydrogen phosphate crystal and using this light for excitation[54]. This forms the basis of a simple method for the visual observation of laser emission. The pumping light is allowed to enter a partly silvered cell containing dye solution, and the collimated dye laser beam emerging normal to the silvered surfaces is caught on a screen. Part of the frequency doubled neodymium laser light can be converted in another crystal into light of wavelength 266 nm. This wavelength allows a considerable further increase in the number of dyes that can be stimulated to laser emission[55]. In particular, many of the scintillator dyes used in nuclear technology can be stimulated to dye laser emission in this way. This gives laser emission even in the ultraviolet region at wavelengths down to 341 nm (*p*-terphenyl in cyclohexane). A selection is given in Table 2.

It was found that some dyes with fluorescence quantum yields close to 1 do not exhibit dye laser emission even with high excitation outputs. Examples are perylene in benzene or cyclohexane and some cyanines having the general formula *(22)* dissolved in methanol or water[56]. This is understandable if it is assumed that an absorption from the first excited singlet state

[50] *P. P. Sorokin* and *J. R. Lankard*, IBM-J. Res. Developm. *10*, 162 (1966).

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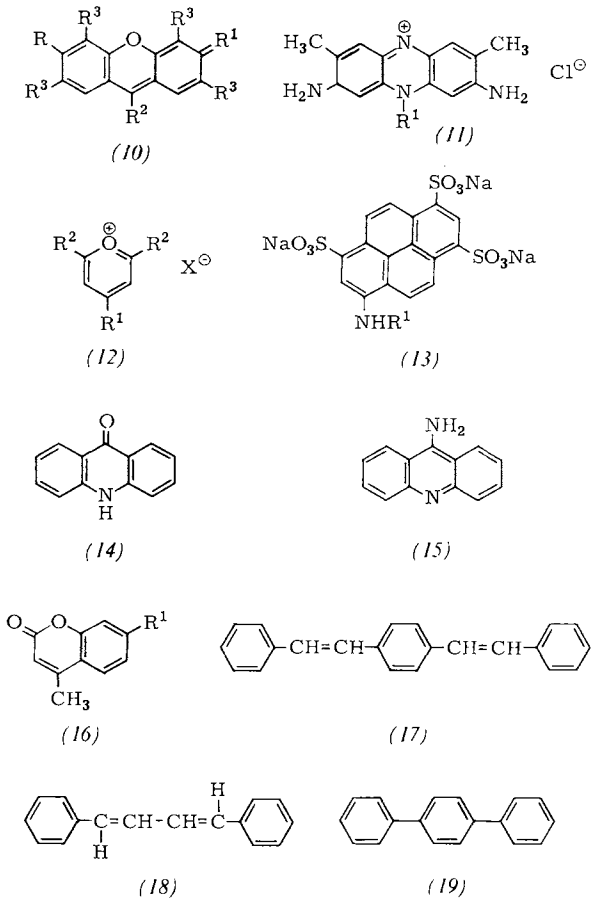
[52a] *P. P. Sorokin*, *J. R. Lankard*, *E. C. Hammond*, and *V. L. Moruzzi*, IBM-J. Res. Developm. *11*, 130 (1967).

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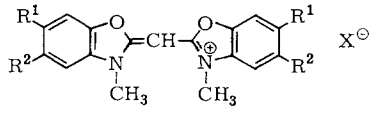
[54] *F. P. Schäfer*, *W. Schmidt*, and *K. Marth*, Physics Letters *24 A*, 280 (1967).

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into higher singlet states occurs in these dyes at the wavelength at which the laser emission of the dye would otherwise appear. The triplet-triplet absorption probably plays a minor role in these cases, since only



a very small fraction of the excited molecules can pass into the triplet state during the rise time of the stimulating light pulse, which lasts only a few nanoseconds, because of the high quantum yield of the dye.

The influence of the triplet-triplet absorption is very noticeable, on the other hand, when pumping light sources with slow rise-times are used. For example, if a ruby laser with normal-pulse operation (rise time about 150–500 ns) is used instead of a giant-pulse laser (rise time about 8 ns) for the excitation of a dye laser containing dye *(1d)*, no emission is obtained even when the excitation power is 30 times the threshold power found with giant pulses [57].

Since the life of the excited state of this dye is $\tau = 2$ ns [46] and its quantum yield is $\eta = 0.65$ [*], a very considerable fraction of the excited molecules pass into the triplet state during the rise time, which is long in relation to the lifetime, and they can remain in this state in liquid solution for periods of the order of a microsecond. The accompanying depopulation of the ground state and of the excited singlet state is sufficient under certain circumstances to make laser emission impossible because of the lower amplification. The increase in losses due to the triplet-triplet absorption probably has an even stronger effect for very many molecules.

Figure 20 shows the occupancies m_1 as a function of time for various fluorescence quantum yields and rise rates of the pumping pulse for a concentration of 10^{-4}

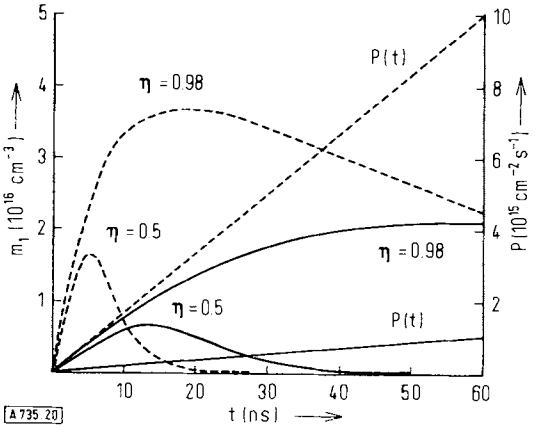


Fig. 20. Time variation of the occupancy of the first excited singlet state $m_1(t)$ (left-hand scale) for various pumping power curves $P(t)$ (right-hand scale) and various quantum yields η.
Broken: rapidly rising pumping power; continuous: slowly rising pumping power (after [57]).

mole/l and a life of 1 ns. It is assumed here for simplicity that the radiationless deactivation occurs exclusively *via* the lowest triplet level and that the life of this state is very long in relation to the life τ of the excited singlet state. It can be seen that the occupancy of the first excited singlet state passes through a maximum, the value of which for a given quantum yield η increases with the rate of rise of the pumping power P. To pump a dye laser with a flash lamp, the pulses of the latter must rise as rapidly as possible, and the fluorescence quantum yield of the dye must be as high as possible and its triplet-triplet absorption as low as possible in the region of the laser wavelength. Many dyes can be stimulated to laser emission with suitable flash lamps (see Table 2) [57–59].

It is to be expected from the calculated fluorescence emission curve in Fig. 20, which is based on simplifying assumptions, that the laser emission from most dyes will stop after only a short time, even if the pumping light output increases further.

Figure 21 shows this type of behavior for trisodium 6-triacetylaminopyrene-1,3,8-trisulfonate *(13a)* in 10^{-3} M aqueous solution [60]. The laser emission lasts only 100 ns, whereas the pumping lamp gives an output above the threshold value for more than 1 μs.

[57] *W. Schmidt* and *F. P. Schäfer*, Z. Naturforsch. *22a*, 1563 (1967).

[*] Estimated from the lifetime and the integrated absorption.

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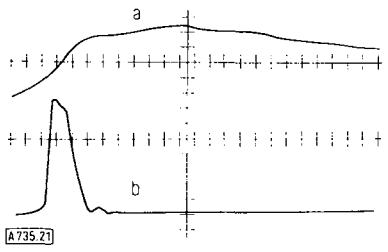


Fig. 21. Oscillogram (traced) of a) pumping light pulse and b) dye laser pulse for a 10^{-3} M aqueous solution of trisodium 6-acetylaminopyrene-1,3,8-trisulfonate *(13a)*. Deflection speed 100 ns/cm (after [60]).

Continuous dye laser emission thus seems impossible from Figure 21. It can however be obtained if the relaxation time of the molecules from the triplet state to the ground state can be reduced to such a degree that the depopulation of the ground state and the increase in the absorption at the laser wavelength due to the triplet-triplet absorption become insignificant. This has been achieved in solutions of Rhodamine 6G *(10c)* in methanol by saturation with atmospheric oxygen [61]. (It is well known that oxygen greatly shortens the life-times of triplet states.)

It has been estimated that the life τ_T of the triplet state of Rhodamine 6G in a solution saturated with oxygen should be at most about 0.2 μs. This gives a lower steady-state concentration of molecules in the triplet state and, as is shown by the oscillogram in Figure 22, makes it possible to obtain laser emission over a time

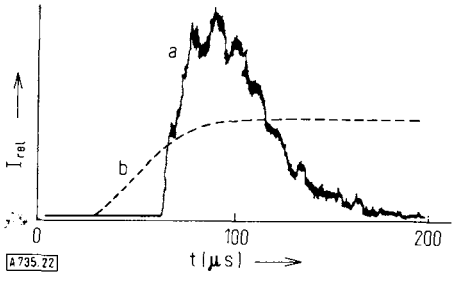


Fig. 22. Oscillogram (traced) a) of the dye laser emission of an air-saturated 5×10^{-5} M solution of Rhodamine 6G *(10c)* in methanol. The time variation b) of the pumping light pulse (recorded with higher sensitivity) is shown for comparison (after [61]).

that is long in relation to τ_T in a suitable laser resonator, even with an excitation source having a long rise time.

No laser emission was observed when nitrogen was passed through methanol solution or when 96% ethanol (which dissolves only half as much oxygen as methanol) was used. This shows that, for Rhodamine 6G at least, the accumulation of molecules in the triplet state is not so high that it prevents continuous emission. The cessation of the laser emission in Figure 22 after about 150 μs despite the fact that the excitation output was still constant is probably due to thermal and acoustic disturbance of the laser resonator by the excitation light source; this should not be a fundamental problem, but should be capable of being overcome by improved technical solutions. It is to be hoped that continuous dye laser emission will be obtainable with suitable continuous excitation light sources.

The possibilities of the dye laser are considerably extended by the use of compounds that are formed only in the excited state [41]. Three examples of this are shown in Figure 23–26.

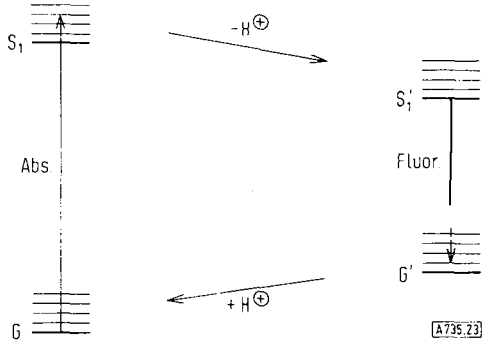
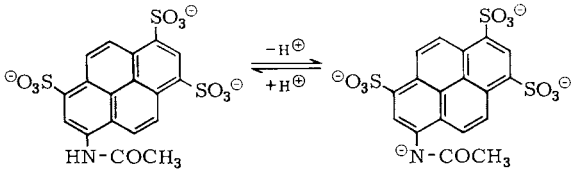


Fig. 23. Term diagram for absorption and fluorescence of 6-acetylaminopyrene-1,3,8-trisulfonate in alkaline solution.

It is well known that 6-acetylaminopyrene-1,3,8-trisulfonate is a much stronger acid in the excited than in the ground state [62]. In alkaline solution the trianion dissociates after transition to the excited state, and the fluorescence of the



tetra-anion predominates. A dye laser emission of longer wavelength is accordingly obtained, and the threshold output is greatly reduced, as can be seen from Figure 24, which was recorded under the same conditions as Figure 21 but in alkaline solution. The greater difference between the fluorescence and absorption spectra leads to smaller losses; moreover, the lower laser level is continuously being depopulated as a result of the rapid recombination of the anion in the ground state.

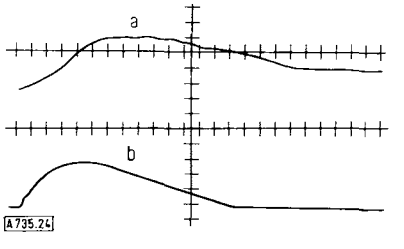


Fig. 24. Oscillogram as in Fig. 21, but in alkaline solution.

A significant lowering of the threshold output and displacement of the laser wavelength by about 10 nm has also been found for the pyrylium salt *(12c)* on addition of a small quantity of dimethylaniline, evidently as a result of the formation of a charge transfer complex in the excited state (Fig. 25), such as is known from other systems [63].

[61] *B. B. Snavely* and *F. P. Schäfer*, Physics Letters *28A*, 728 (1969).

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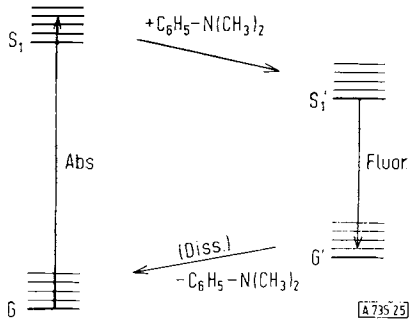


Fig. 25. Term diagram for absorption and fluorescence of a solution of 2,6-bis(*p*-methoxyphenyl)-4-phenylpyrylium tetrafluoroborate *(12c)* in methanol/dimethylaniline.

In the case of *p*-dimethylaminonitrostilbene we find, not a chemical reaction in the excited state, but a change in the solvation state of the molecule, whose dipole moment in the excited state is different from that in the ground state [64]. The threshold output in this case decreases when benzene/cyclohexane is replaced as the solvent by the more strongly polar ethyl acetate (Fig. 26).

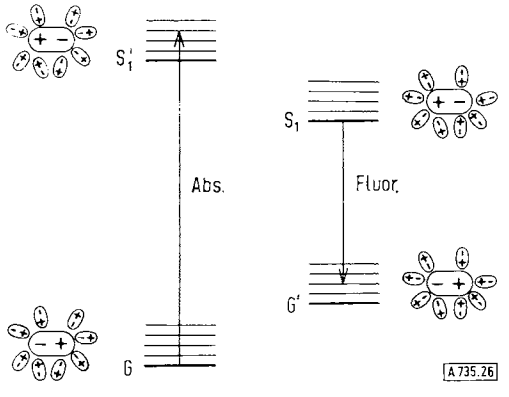


Fig. 26. Term diagram for absorption and fluorescence of *p*-dimethylaminonitrostilbene in a polar solvent.

As was mentioned earlier, the wavelength at which the dye laser emission begins for any dye can be adjusted as desired within the fluorescence band by variation of the concentration and cell length, as well as of reflection and other losses. If the losses change during excitation, as is the case particularly in dye lasers pumped with flash lamps, where *e.g.* the triplet-triplet absorption increases during the excitation, the laser wavelength also changes during the pulse [65–67]. It is essential for many applications that the laser wavelength should have a fixed, constant value, and that the spectral band width of the emission should be as small as possible. Both requirements can be satisfied if dispersing elements are introduced into the laser resonator.

The simplest solution is to replace one of the mirrors of the resonator with a reflection grating [68] (Fig. 27).

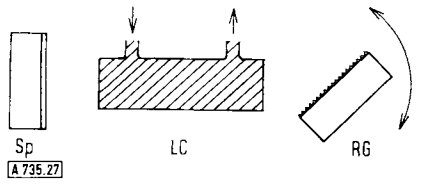


Fig. 27. Construction of a tunable laser. Sp: laser mirror, LC: laser cell, RG: reflection grating. The curved double-headed arrow shows the direction of rotation of the grating for adjustment of the wavelength.

A high reflection for a narrow range of wavelengths can then be obtained by rotating the grating about an axis parallel to the grating lines, and the reflection coefficient for adjacent ranges decreases to such an extent that the laser threshold is not reached.

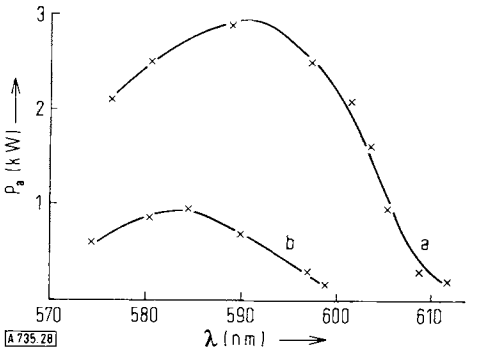


Fig. 28. Output P_a of a tunable laser in accordance with Fig. 27 with 10^{-4} M methanolic solution of Rhodamine 6G *(10c)* and a grating having 610 lines/mm.

a) First order,

b) second order (after [60]).

Figure 28 shows a plot of the laser output against the wavelength, which is adjusted by means of the grating angle for a grating having 610 lines per mm and a laser using Rhodamine 6G *(10c)*; the spectral band width for the first order was about 2 nm, and that for the second order was about 0.4 nm [60]. By insertion of one or more Fabry-Perot filters in the resonator, the width of this wavelength range can be reduced much further, without appreciable reduction of the laser output. The sodium concentration in the ionosphere up to an altitude of about 100 km has recenty been measured with a dye laser having a band width of 1.5 Å [*] and tuned exactly to the sodium resonance line (589.6 nm) [70].

The potochemical stability of dyes in dye lasers pumped with flash lamps has not been extensively studied. Some indication is provided by the fact that a laser of this type has been operated for several hours at a pulse frequency of 30 Hz with a few liters of a Rhodamine

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6G solution [71]. The further technical development of the dye laser should also provide fresh incentive to the detailed study of the photochemistry of laser dyes.

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The Coordination Number – an "Inorganic Chameleon"[1]

By R. Hoppe[*]

The purpose of the present article is to describe the changing ambiguous character of the term "coordination number" and its present-day definition in structural chemistry, particularly of typical solids (assemblies of particles with short-range and long-range order). An effort is made at the same time to describe the crystal structure of solids as simply as possible while also taking long-range order into account, i.e. by determining "effective" coordination numbers by the geometrical "polyhedron method" or from MAPLE (Madelung Part of Lattice Energy) values.

1. Introduction

The term "coordination number" comes from classical complex chemistry [2], and denotes the number of *ligands* arranged around a *central particle* "in the first coordination sphere". In this "naive" sense, the coordination number is always a whole number. Examples often given to illustrate a coordination number of 6 are compounds derived from the ions $[Cr(NH_3)_6]^{3+}$ and $[Co(NH_3)_6]^{3+}$, which have an octahedral structure.

Classical complex chemistry is essentially a chemistry of solutions, usually aqueous. It is now known that difficulties can be encountered in specifying "naive" coordination numbers even in the simple case of aquo complexes in solution.

Complicated equilibria occur in the fast exchange of the "aquo ligands" with "solution water molecules". One ionic species (*e.g.* $[Zn(OH_2)_6]^{2+}$) often predominates, but others (*e.g.* $[Zn(OH_2)_5]^{2+}$) are also present, though sometimes only in very small quantities. Owing to the rapidity of the exchange and the possibility of an associated change in the coordination number, the coordination number can only be specified as a space-time average, and is then not necessarily integral.

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[1] Based on a lecture (GDCH-Ortsverband Bonn, February 13, 1969) on the occasion of the 70th birthday of Professor *O. Schmitz-DuMont*.

[2] Cf. *A. Werner*: Neuere Anschauungen auf dem Gebiete der anorganischen Chemie, Braunschweig 1905, 1. Edit., p. 108ff.

Pfeiffer [3] was probably the first to apply the term "coordination number" to solids, soon after the elucidation of the structure of NaCl [4]. In using this term, he was making reference to the analogy between $[PtCl_6]^{2-}$ in which Pt^{4+} has a coordination number of 6, and the NaCl structure, in which Na^+ is surrounded by six Cl^-.

Since then the coordination number, like the terms ionic or atomic radius and bond angle, have come into use for the description and interpretation of crystal structures. The pioneering work of the 1920's showed even then the limits within which this is possible in principle.

It is admittedly advisable nowadays to place a clear question mark after these classical (and in practice still useful) basic concepts of crystal chemistry when their application is not restricted to pure "molecular lattices".

For example, the "centralistic" concept of coordination number, which relates only to the central ion of a complex (no one has so far raised the question of the coordination number of a ligand), is not strictly applicable in the NaCl structure, since the relation between the Na^+ and the Cl^- ions is reciprocal; in other words, six Na^+ surround one Cl^-, just as one Na^+ is surrounded by six Cl^-. Instead of a coordination, therefore, we have an adjunction. So far, moreover, the role of the "complementing ions" in complexes (*e.g.* Cl^- in $[Co(NH_3)_6]Cl_3$ or K^+ in $K_2[PtCl_6]$) has not received the attention that it merits.

[3] *P. Pfeiffer*, Z. anorg. allg. Chem. *92*, 376 (1915); 97, 161 (1916).

[4] *W. H. Bragg* and *W. L. Bragg*, Proc. Roy. Soc. (London) *88*, 428 (1913); cf. also, Z. anorg. allg. Chem. *90*, 169 (1915).

1.1. Subdivision of Chemistry

The following discussions are based not on the usual subdivision of chemistry but on one that distinguishes between molecular chemistry and solid state chemistry [5].

The chemical and physical behavior (even in the solid state) of many compounds, such as HCl, BF_3, CH_4, and C_6H_6 is determined by molecules. IR and Raman spectra provide detailed information about their structure and bond strengths within the discrete structural groups. In chemical reactions, *e.g.* in the oxidation of CH_4 to CO_2 and H_2O the reacting species is the individual molecule.

In the example mentioned, one molecule of CH_4 is the 'first' to be oxidized and another molecule is the 'last'. Some of the CH_4 molecules may even escape oxidation entirely. Thus, though subject to the laws of thermodynamics and of chemical kinetics, and hence to the law of large numbers, the individual particle in the assembly of molecules can, in a sense, have a fate of its own.

An entirely different state of affairs is found in typical solids (NaCl, Al_2O_3, *etc.*). The chemistry of these compounds and their crystal structure are largely determined by the existence of assemblies of particles [1]. The uniform (preferably so in the ideal case) behavior of the equivalent particles of an assembly is due to *long-range* as well as to *short-range* order.

Apart from transitions, reactions in the solid state occur mainly at the surface of the crystallites. Thus a given solid substance in the sense mentioned here can be prepared in forms that differ very markedly in their "reactivity", though their chemical compositions are the same.

It is interesting to observe how often thermodynamically unstable molecules can be reproducibly synthesized under mild conditions, often in high yields, whereas the preparation of definite unstable forms in the case of typical compounds is often problematic in solid state chemistry.

It was formerly difficult to obtain and interpret information from IR and Raman spectra for typical coordination lattices such as NaCl, since the vibrations cover comparatively large regions of the crystal at the same time and can react sensitively to imperfections of all kinds. Recent investigations (*e.g.* on NaCl, Nb_2O_5, *etc.*) have, however, shown that "sharp" spectral lines occur in this situation too.

The differences in these two subdivisions of chemistry are particularly noticeable in structural chemistry.

It is relatively easy to deduce the spatial arrangement of the atoms, often in detail, from the formulas of molecules (*e.g.* $SOCl_2$ or β-$C_{10}H_7SO_3H$) with the aid of certain fundamental concepts of chemical bonding. In the case of typical solids (*e.g.* NaCl or AgF_2), on the other hand, it is, as yet, still principally impossible to predict the arrangement of the particles in the "assembly". Thus no one can say with certainty what structure a still unknown but possibly obtainable modification of NaCl would possess that is thermodynamically unstable under normal conditions. Compounds that are chemically very similar, such as $BaMnF_6$ and $CaMnF_6$ ($=Ca_{0.5}Mn_{0.5}F_3$) can be structurally quite different [6]. For other compounds (*e.g.* $[-CH(CH_3)-CH_2-]_n$), the behavior of the assembly depends not only on the degree of polymerization n but also on the nature and variation of the arrangement (in the example, whether isotactic, syndiotactic, or atactic).

[5] Cf. *R. Hoppe* ('Madelung Constants as a New Guide to the Structural Chemistry of Solids') in *M. Stacey, J. C. Tatlow*, and *A. G. Sharpe*: Advances in Fluorine Chemistry, Butterworths, London, Vol. 7, in press.

1.2. Preliminary Remarks

The result of conventional crystal structure determinations is a geometrical arrangement, *i.e.* the positions of centers of gravity of particles in space.

The following discussion is concerned not with attempts to interpret such results from the point of view of chemical bonding but only with geometrical arrangements in solids. The conventional discussion of crystal structures takes no account of the difference between the two fields of chemistry defined in Section 1.1:

1. The actual "Gordian knot" of the cluster of structural problems in solid state chemistry is severed by crystallography with one radical cut, separating spacing from symmetry. The unusually rapid progress made in the structural investigation of solids during the last few decades would not otherwise have been possible. Spacing and symmetry can usually be unambiguously described by but few figures (lattice constants, space group symbol, occupied point positions, and corresponding position parameters).

2. The basic information about the crystal structure is given by the unit cell (cf. Fig. 1); this is the "motto" of the ideal structure, which is built up by translation of the unit cell in the three lattice directions.

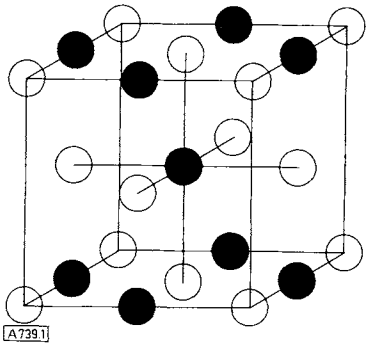


Fig. 1. Unit cell of the NaCl type (schematic).

The conventional description of a structure also includes the coordination numbers (*e.g.* coordination number = 6 for Na^+ with respect to Cl^- in NaCl) of the crystallographically different particles, the corresponding distances (*e.g.* d_{Na-Cl} = 2.81 Å), and possibly the bond angles (NaCl : 90 and 180 °).

3. However, these data characterize only the short-range order of the crystal structure, and are therefore sufficient in the case of solid molecular structures only.

[6] *R. Hoppe* and *K. Blinne*, Z. anorg. allg. Chem. *291*, 269 (1957).

For solid state structures such as the NaCl and CaF_2 types, the unit cell, like an ordinary molecule, is usually small, and this might easily blind one to the fact that the behavior of the solid compound in question is determined by an "assembly" possessing long-range order.

Our considerations, the aim of which is to show the changeable character of the term "coordination number" in the field of solid chemistry, arise from an attempt[5] to find the simplest possible way of describing the crystal structure of solids in such a manner that the long-range order is also accounted for.

2. An Excursion into Classical Complex Chemistry

For our first example we shall consider the hypothetical gaseous complex ions $[SnF_6]^{2-}$ and $[SnF_5I]^{2-}$ (Fig. 2).

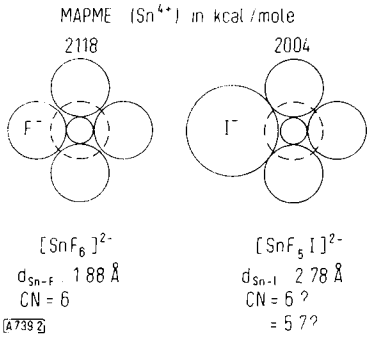


Fig. 2. Structure of "isolated" hexahalogenostannate(IV) ions.

Hexafluorostannates(IV) of the type $M_2SnF_6 \cdot aq$ have been known since *Marignac*[7], and have recently been the subject of numerous studies, particularly on the anhydrous compounds M_2SnF_6[8,9] (M = Li, Na, K, Rb, Cs). On the basis of these and further investigations on SnF_4[10], it may be assumed that the "isolated" complex $[SnF_6]^{2-}$ is octahedral; $d_{Sn-F} = 1.88$ Å.

No compounds containing the complex $[SnF_5I]^{2-}$ are known as yet. We shall assume that the six bond directions in this complex also possess octahedral symmetry, and that the interatomic distances are $d_{Sn-F} = 1.88$ Å and $d_{Sn-I} = 2.78$ Å.

There are then two possible answers to the question of the coordination number of Sn^{4+} in $[SnF_5I]^{2-}_{gas}$:

1. The greater Sn–I distance is merely due to the greater radius of I^-. If the ions are assumed to be spherical, Sn^{4+} and I^- would be in contact with each other as well as Sn^{4+} and F^-. On the basis that "anything in contact is to be taken as a neighbor" (a ligand in this case), the coordination number of Sn^{4+} is thus 6.
2. The Sn–I distance is much greater than the Sn–F distance. If it were very large (about 10 Å), it would be reasonable to ignore this ligand when counting neighbors. Conclusion: the effective coordination number of Sn^{4+} in $[SnF_5I]^{2-}$ is presumably smaller than 6 (about 5.7?).

This answer would also be supported by the fact that the "Madelung part of the molecular energy" (MAPME; see section 8) of $[SnF_5I]^{2-}_{gas}$ is 14 kcal/mole smaller than that of $[SnF_6]^{2-}_{gas}$ (cf. Fig. 2).

3. The *Wigner-Seitz* Polyhedron Method

We adopt the conventional answer[1] to the question of the coordination number of Sn^{4+} in $[SnF_5I]^{2-}$, *i.e.* the definition that anything in contact is a neighbor, and should accordingly be included in the determination of the coordination number.

3.1. The Coordination Number for the NaCl Type

It can be seen from Figure 3 that in KF, each K^+ particle and each F^- particle is in contact with six oppositely charged neighbors, *i.e.* K^+ and F^- both have a coordination number of 6.

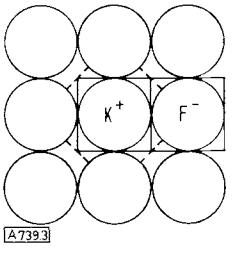


Fig. 3. Neighbors in KF.

In the case of LiI, as shown in Figure 4, application of the "contact definition" shows that Li^+ has the conventional coordination number 6, of the NaCl type, whereas I^- "is in contact" not only with the six Li^+ neighbors but also with twelve I^- neighbors. The coordination number of I^- in LiI is thus surprisingly found to be 18.

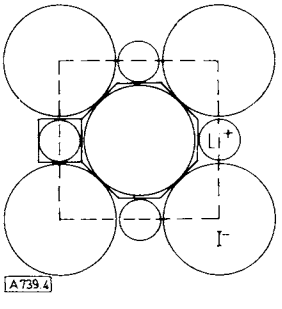


Fig. 4. Neighbors in LiI.

For compounds where there is some doubt as to whether ionic or atomic radii should be used for the construction of the touching "spherical" particles, the coordination number may be uncertain.

Quite apart from this practical difficulty, however, the "effective" coordination number defined by the number of touching neighbors can differ very considerably from the conventional values, and may not even be whole numbers.

[7] *Marignac*, Ann. Mineralogie (5) *15*, 221 (1859).

[8] *E. Weise* and *W. Klemm*, unpublished; see *W. Klemm*, Angew. Chem. *66*, 468 (1954); cf. *R. Hoppe*, Recueil Trav. chim. Pays-Bas *75*, 569 (1956).

[9] *Ch. Hebecker* and *R. Hoppe*, Naturwissenschaften *53*, 106 (1966); *Ch. Hebecker, H. G. v. Schnering*, and *R. Hoppe*, *ibid.* 53, 154 (1966).

[10] *R. Hoppe* and *W. Dähne*, Naturwissenschaften *49*, 254 (1962).

3.2. The Coordination Number for the CsCl Type

The CsCl type (cf. Fig. 5) can occur for AB compounds when the ratio of the atomic (or ionic) radius r_A/r_B is between 0.73 and 1.37. In the special case where $r_A/r_B = 1.0$, the structure corresponds metrically to the body-centered cubic structure found for many metals.

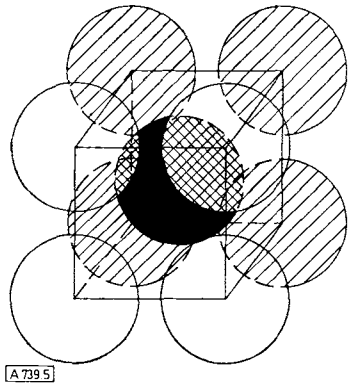


Fig. 5. Unit cell of the body-centered cubic structure. (The "atoms" are shaded differently for clarity.)

Figures 3 and 4 show schematic planes normal to the lines that join touching particles (*e.g.* from I^- to Li^+ and I^-) and that are situated at the point of contact of pairs of particles.

This type of polyhedron construction can be extended. If *e.g.*, in the CsCl type, an arbitrarily chosen ion Cs^+ is connected by straight lines to *all* of the other Cs^+ and Cl^- ions in the crystal and each connecting line divided by a perpendicular plane in the ratio of the ionic radii of the particles joined by the line, there emerges from the infinite number of these planes a "smallest" polyhedron around Cs^+ (cf. Fig. 6). The construction of the polyhedron corresponds to that described by *Wigner-Seitz* for metals.

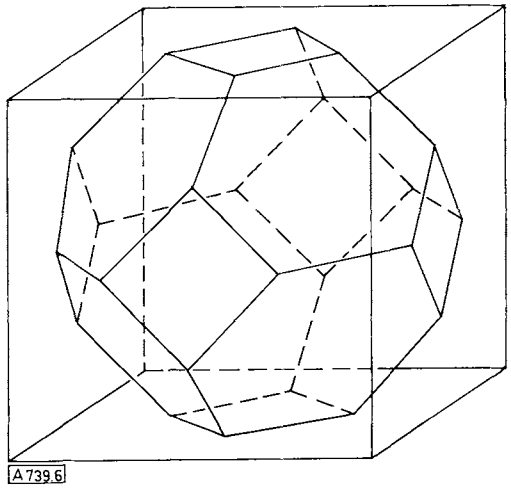


Fig. 6. Coordination polyhedron for CaCl (schematic).

In the case of the CsCl structure, and hence of the body-centered cubic structure, the polyhedron has 8 + 6 faces instead of only six; this polyhedron is a combination of an octahedron and a cube, the cube faces being smaller than the octahedron faces when $r_{A^+} = r_{B^-}$.

This points to an obvious "quantitative" refinement in the counting of "field neighbors"[11]. The areas of the individual faces of the "coordination polyhedron" are calculated and "normalized" to give the largest face a value of 1. The sum of the "normalized" areas of the faces of the polyhedron is then an "effective" coordination number. This gives a value of approximately 10 instead of the conventional 8 for the effective coordination number of a cubic body-centered metal (*e.g.* α-iron).

Table 1. The effective coordination number (ECN) of gallium metal (by the poly hedron method).

"Neighbors" No.	Area (normalized)	ECN
1	1.000	1.00
2	0.597	
3	0.585	
4	0.570	
5	0.517	
6	0.487	3.76
7	0.402	
8	0.255	4.42
9	0.123	
10	0.073	
11	0.073	
12	0.045	
13	0.030	
14	0.023	4.78

Table 1 shows the result of a polyhedron construction for gallium[12]. The effective coordination number is approximately 4.8.

In the very interesting Ga structure, which is difficult to explain theoretically, one neighbor is very close (d = 2.43 Å); others follow with d = 2.71 (2×), 2.74 (2×), 2.80 (2×), 3.72 (2×) Å, *etc.* No conventional coordination number can be given in this case.

The effective coordination number calculated by the polyhedron method fits satisfactorily into the sequence of coordination numbers for the series Cu (coordination number = 12), Zn (effective coordination number = 8–9[13]), Ga (effective coordination number ≈ 5), Ge (coordination number = 4). Table 1 shows that the effective coordination number of gallium is practically determined by the eight nearest of the fourteen neighbors considered here.

3.3. Close Packing of Spheres

Many metals crystallize with "close-packed" structures, of which there are an infinite number of variants. Those found most often in practice are cubic close packing (*every* metal atom occupies a center of symmetry) and hexagonal close packing (*no* metal atom occupies a center of symmetry), and simple (Pr, Nd) or fairly complicated (Sm) alternating structures are occasionally encountered. A 'pure' metal[14] only

[11] Cf. also *K. Schubert*: Kristallstrukturen zweikomponentiger Phasen. Springer, Berlin 1964, p. 18ff.

[12] *R. Hoppe*, unpublished; cf. *R. Hoppe*, 18. IUPAC-Congress, Montreal 1961, Abstr. sci. Papers, p. 73; *G. E. R. Schulze*, Kristall u. Techn. *1*, 375 (1966).

[13] Cf. ECN of Cd (Fig. 8).

[14] For example, hexagonal close packing occurs in Ca metal only when it is stabilized by impurities.

rarely (Co?, Ce) crystallizes in more than one close packing[15]; the reasons for this are unknown.

The coordination polyhedron of cubic close packing, for example, is a dodecahedron, and the effective coordination number is 12.0. The packing factor, *i.e.* in the case of wooden spheres, for example, the proportion of the volume that is occupied by wood, is 74.0% for any close packing of spheres in three-dimensional space. The effective coordination number for primitive cubic packing of spheres (cf. Fig. 7) is 6, and the packing factor is only 52.4% [four examples are known at present: α-Po, SbII (high pressure form: 20 °C, 70 kbar), metastable phases in the systems Ag/Te and Au/Te].

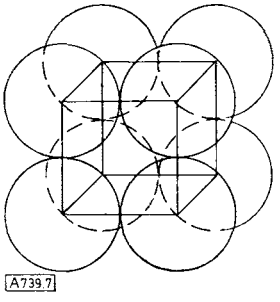


Fig. 7. Primitive cubic close packing (α-Po).

3.4. The Body-Centered Cubic Crystal Structure

There are however metals, such as the elements of the group Vb triad, that crystallize with a body-centered cubic instead of a close packed structure. One of the modifications of polymorphic metals often belongs to this type (Ba, Np, Pu, *etc.*). It is interesting to note that the body-centered cubic form of polymorphic metals is always the highest-temperature form "from which the metal melts"[15]. Even iron, which changes from the body-centered cubic form to the cubic close packing of γ-iron at 910 °C, changes back into the body-centered cubic δ-modification at 1390 °C.

The packing factor of 68.0% for the body-centered cubic structure is higher than one would expect for the conventional coordination number of this type of structure, which is 8. An empirical plot of the coordination number against the packing factor (Fig. 8) indicates that the packing factor for a coordination number of 8 should be only 60%, while a packing factor of 68% corresponds to an "effective coordination number" of 9.6 according to this curve.

This remarkable situation is connected with the fact that the ratio of the distances to nearest and to next-nearest neighbors in cubic close packing, as in primitive cubic packing, is $1 : \sqrt{2}$, whereas the corresponding ratio for the body-centered cubic structure is $1 : 2/\sqrt{3}$. In addition to the eight nearest neighbors, therefore, there are six others for which the distance is increased by a factor of $2/\sqrt{3}$ only (cf. Table 2). It is thus understandable to some extent why many metals change from close packing into this form before melting. Other metals (such as Mn or Pu) that exhibit unexpectedly low packing factors at

[15] *R. Hoppe*, lecture, Tagung der Gesellschaft für Metallkunde, Clausthal-Zellerfeld 1947; *Ch. Zener*, Physic. Rev. *71*, 846 (1947); *L. Kaufman*, Progr. Mater. Sci. *14*, 2 (1969). – With the exception of Co these are usually 4f and 5f elements only.

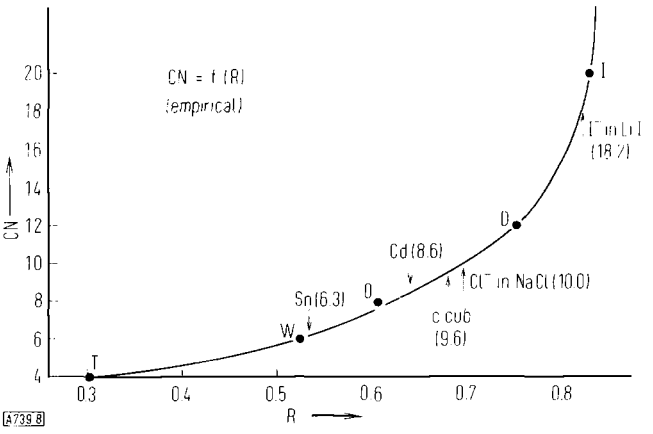


Fig. 8. Empirical relation between coordination number and packing factor. T = tetrahedron, W = cube, O = octahedron, D = dodecahedron I = icosahedron.

low temperatures (γ-Pu: 62.7%), possibly because of directed bonds, also change into the body-centered cubic structure after "breakdown" of the directed bonds when heated.

4. An Excursion into the Fourth Dimension

Let us consider an ionic compound of the type AB, *e.g.* Na^+Cl^-.

In the one-dimensional crystal space there is only one electrostatically favorable crystal structure for such a compound (Fig. 9), and there is again only one electrostatically favorable arrangement of the ions in a two-dimensional crystal (Fig. 10).

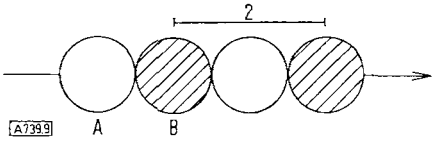


Fig. 9. Electrostatically most favorable structure of a one-dimensional AB ionic crystal.

In both cases we find a similarity to the known NaCl type of the three-dimensional crystal space in the "alternating" principle $Na^+Cl^-Na^+ \ldots$ along lattice lines. However, they both also show a similarity to the CsCl type (cf. Fig. 5) with respect to the "centering" principle, as shown in Figure 10. It is only in the three-

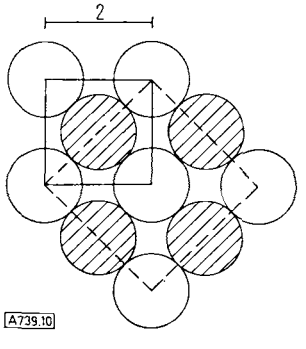


Fig. 10. Electrostatically most favorable structure of a two-dimensional AB ionic crystal.

dimensional crystal space that alternation and centering separate to give the NaCl and CsCl types; however, the two types are still energetically so similar that compounds such as CsCl and RbCl occur in both forms.

It can be seen from Figure 11 that the ratio of the shortest cation-cation/cation-anion distances for the CsCl type decreases rapidly as we pass from one-dimensional to three-dimensional space, and reaches a value of 1 in four-dimensional space. In a four-dimensional space, therefore, this type of structure would scarcely be possible for ionic compounds like Na^+Cl^-, but occur at best in the case of intermetallic compounds similar to NaTl and its structural relatives in three-dimensional space.

In this light the CsCl type is an oddity of structural chemistry in three-dimensional space.

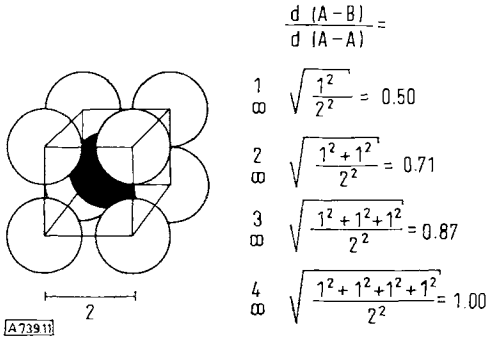


Fig. 11. Ratio of the shortest cation-anion/cation-cation distances for the CsCl type in one- to four-dimensional crystal space.

The same is true of the closely related body-centered cubic structure (cf. Table 2). It can be seen that a four-dimensional body-centered metal has 24 (*i.e.* 16 + 8) "exactly equally" distant neighbors, and the special position of the body-centered cubic structure in three-dimensional space becomes comprehensible.

It is astonishing, that not one of the known crystal structures has, as yet, been investigated and/or discussed with respect to the question of which observed facts are to be considered as "trivial for 3-dimensional space" and which of the known structural peculiarities is a singularity of this common space!

Table 2. Numbers (n_1 and n_2) and distances (d_1 and d_2) of "nearest" and "next-nearest" neighbors for centered packing of spheres in n-dimensional space.

Dimension,	n_1	n_2	d_1	d_2	d_2/d_1	CN
1	2	2	1	2	2.00	2
2	4	4	$\sqrt{2}$	2	1.41	4
3	8	6	$\sqrt{3}$	2	1.15	8 + 6
4	16	8	$\sqrt{4}$	2	1.00	24

5. Packing Factor and the Coordination Polyhedron

Let us now consider the diamond structure, the primitive cubic structure, and cubic close packing from among the crystal structures of elements. Each of these types is associated with a certain coordination number and a certain packing factor; in the order given, these are coordination number = 4 (34.0%) coordination number = 6 (52.4%), and coordination number = 12 (74.0%).

Application of the polyhedron method, on the other hand, shows that each type is associated with a certain coordination polyhedron, *i.e.* tetrahedron (coordination number = 4), cube (coordination number = 6), and dodecahedron (coordination number = 12).

It seems reasonable to extend the considerations to the other regular polyhedra, *i.e.* the octahedron and the icosahedron.

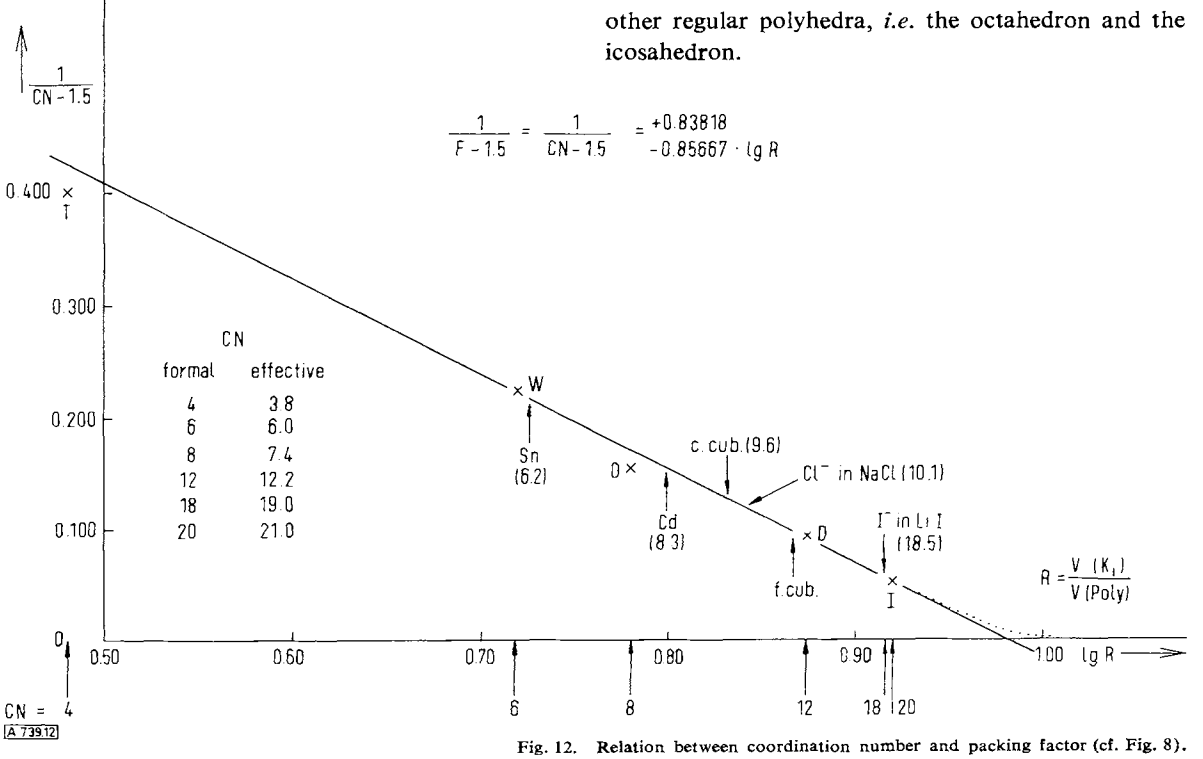


Fig. 12. Relation between coordination number and packing factor (cf. Fig. 8).

The packing fraction in every case is the ratio of the volume of the "inscribed sphere" to the volume of the regular polyhedron (Table 3).

Table 3. Regular polyhedra and the largest "inscribed" spheres.

Polyhedron	$R = \frac{\text{Volume (sphere)}}{\text{Volume (polyhedron)}}$	log R
Tetrahedron	0.3023	0.4804−1
Cube	0.5236	0.7190−1
Octahedron	0.6046	0.7815−1
Dodecahedron	0.7547	0.8778−1
Icosahedron	0.8288	0.9184−1

When the reciprocal of the number of faces of the regular polyhedron minus 1.5 is plotted against the logarithm of the packing factor (cf. Fig. 12), the values for cubes, dodecahedra, and icosahedra lie practically on a straight line. This line therefore gives "reasonable" values of the effective coordination number against the packing factor for the body-centered cubic structure (and *e.g.* also for the ion I^- in LiI, cf. Section 3.1).

The practically linear relation can be used to find the effective coordination number from the packing factor. The (small) deviation of the octahedron and its hemihedral form, the tetrahedron, from this very relation is presumably due to far-reaching geometrical causes.

6. Thermodynamic Cycles

Figure 13 shows the Born-Haber cycle for the formation of KF from the elements. Step I brings the reactants (K metal and F_2 gas) to the "same starting conditions". Step II is characterized by the very simplicity of physically definite processes.

Step III on the other hand, is complicated, and its mathematical treatment is difficult, since it leads to an ordered "solid state" collection of particles. The bonding will in reality rarely be purely ionic. Polarization, repulsion, covalency, *etc.* must be taken into account in order to obtain satisfactory values for the lattice energy in step III. This lattice energy can be expressed as the sum of a series of individual contributions, as follows:

$$E_L = E_M + E_{Pol} + E_{Rep} + E_{Cov} + \text{----------} + E_{Corr}$$

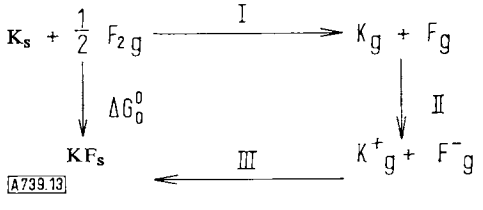


Fig. 13. Born-Haber cycle for KF (schematic).

For compounds consisting of ions, such as KF, the most important term is E_M, the "Madelung part of the lattice energy" (MAPLE). E_{Pol} takes polarization, including ion-dipole and dipole-dipole interactions *etc.*, into account, and can make a decisive contribution. E_{Rep} takes into account the Born repulsion, which is also important, and E_{Cov} allows for the covalent bonding component. The sum of all the terms generally still differs from the "experimental" lattice energy, and this difference can be allowed for by the additional term E_{Corr}.

This cycle, which is important in principle, involves difficulties in practice. This is because it is adapted to the formation of salts from their components, *i.e.* usually from a metal and a non-metal. The calculation of ΔG_0° (*e.g.* for the formation of KF_{solid} from K_{solid} and F_{2gas} at 0 °K) from steps I–III thus necessarily involves substances that represent the three principal limiting cases of chemical bonding, *i.e.* metallic, atomic, and ionic bonding.

Cycles of the type shown in Figure 14 are much simpler. In this case we consider the formation of a ternary fluoride from the binary components. If we assume for simplicity that the ions are "rigid" and take only E_M into account in the calculation of the lattice energies, remarkable differences may be found between this MAPLE value and the "true" lattice energy.

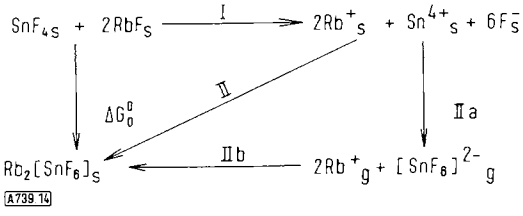


Fig. 14. Born-Haber cycle for $Rb_2[SnF_6]$ (schematic).

On the other hand, the Rb–F bond in RbF is undoubtedly very similar to that in $Rb_2[SnF_6]$, and the same is true of the Rb–F distances. The Sn–F bond in solid SnF_4 (with an octahedral environment according to $^2_\infty[SnF_{4/2+2}]$) will also be very similar to that in $Rb_2[SnF_6]$. Finally, the Sn–F distances in SnF_4 and in $Rb_2[SnF_6]$ are expected to be very similar. The errors resulting from the radical simplification of step I (Fig. 13) are therefore cancelled out by the "analogous" errors with opposite signs in step II. Such calculations on various examples have shown that MAPLE-data often provides a reasonable representation of the lattice energy in such cycles. However, the influence of E_{Pol} in particular must be taken into account in more detailed calculations.

The MAPLE values are still more definite and reliable in cycles of the type shown in Figure 15. Here, we

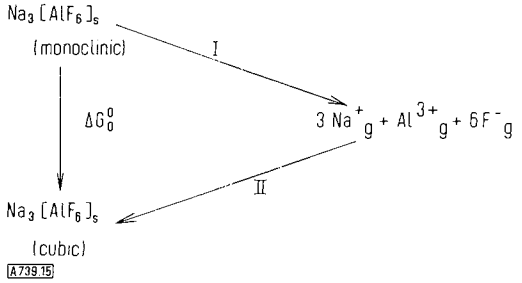


Fig. 15. Born-Haber cycle for $Na_3[AlF_6]$ (schematic).

discuss the transitions of compounds into structurally very similar (observed or hypothetical) modifications [16].

7. Madelung Constants and MAPLE Values [5]

In order to calculate the lattice energy, it is necessary to know the corresponding Madelung constant [17] which is a number characteristic of the structure. The Madelung Constant is the sum of Partial Madelung Constants. For example

$$MC(CaF_2) = PMC(Ca^{2+}) + 2 \cdot PMC(F^-) \quad (1)$$

The MAPLE values can be calculated from the Partial Madelung Constants *e.g.* in accordance with

$$MAPLE(Ca^{2+})_{CaF_2} = \frac{331.81 \cdot PMC(Ca^{2+})_{CaF_2}}{d_{Ca-F}} \quad (2)$$

d_{Ca-F} (in Å) is the shortest cation-anion distance, on which all Madelung Constants and Partial Madelung Constants are based as the unit distance (cf. Table 4). The factor of 331.81 $[e^2.10^8 N_L]$ effects the conversion into kcal/mole.

Table 4. Partial Madelung Constants and MAPLE values for CaF_2 ($d_{Ca-F} = 2.365_5$ Å).

Particle	PMC	MAPLE (kcal/mol)	$^*_i$MAPLE (kcal/mol)
Ca^{2+}	3.276116	459.5	272
F^-	0.881337	123.6	292
Σ (CaF_2)	5.03879	706.8	

The numerical value of the MAPLE depends on the geometry of the charge distribution in the crystal space, the magnitude of the charge assigned to the individual particles, and the magnitude of the reference distance *d*. To allow the comparison of MAPLE values for different structures and particles having different charges, the value must be reduced to unit charge and unit distance [18]:

$$^*_i MAPLE = \frac{MAPLE}{z_i^2} \cdot d_{ki} \quad (3)$$

Table 5. $^*_i$MAPLE as a function of Q_i.

Q_i	$^*_i$MAPLE (kcal/mol)	Q_i	$^*_i$MAPLE (kcal/mol)
8	292	3	254
7	291	2	230
6	290	1.5	204
5	282	1.0	166
4	272		

The values given are representative for binary compounds if the ratio of the shortest anion-anion distance, d_{AA}, and the shortest cation-anion distance, d_{KA}, is $d_{AA}/d_{KA} = \sqrt{2}$. Deviations occur for tertiary compounds when the d_{ki} values are very different from one another.

z_i is the charge on the particle in question, and d_{ki} is the shortest cation-anion distance (in Å) (cf. Table 4). The $^*_i$MAPLE values for typical coordination lattices are a function of Q_i (cf. Table 5).

For simple structures in which all the short cation-anion distances are exactly equal,

$$Q_i \approx \sum_{j=i}^{j=j} n_j \cdot z_j/z_i \quad (4)$$

where z_j is the charge of the neighbors, n_j is their number, and z_i is the charge of the particle in question. Thus *e.g.* for CaF_2:

$$Q(Ca^{2+}) = 8 \times 1/2 = 4; \quad Q(F^-) = 4 \times 2/1 = 8$$

In more complicated structures, the distances to the "nearest" neighbors are not necessarily all equal (cf. *e.g.* Table 6). In such cases the empirical equation

$$Q_i = \sum_{j=i}^{j=j} n_j \cdot z_j \left(\frac{d_{ki}}{d_j}\right)^6 \quad (5)$$

is often useful for the calculation of Q_i. The meanings of n_j, z_j, and z_i are the same as before. d_{ki} is the shortest of all the distances from the particle in question to others, and d_j denote all other distances.

Table 6. Na_{II}–F distances in $Na_3[AlF_6]$. The coordination of Na_{II} in $Na_3[AlF_6]$ is unusually complicated. The "spectrum" of the Na_{II}–F distances begins at 2.20_3 Å; no definite conventional coordination number can be given.

d_{kj} (Å)	Contribution to Q_i	ECN
$2.20_3 \equiv d_{ki}$	1.000	1.000
2.324	0.726	1.7
2.330	0.714	2.4
2.442	0.539	3.0
2.454	0.523	3.5
2.670	0.316	3.8
2.774	0.251	4.1
2.859	0.209	4.3
3.125	0.123	4.4
3.524	0.060	4.5
3.535	0.059	4.5
3.982	0.029	4.5

Thus $Q_i = 4.5$.
Expected $^*_i$MAPLE (Na^+) from Table 5: 270 kcal/mole; found: 277 kcal/mole.

Reduced MAPLE values are structure-specific (cf. the example of AuF_3 in Table 7); owing to the relatively slow decrease in the potential energy with $1/r$, they also take into account the long-range order of assemblies. The combined application and discussion of MAPLE and $^*_i$MAPLE values is a new and often valuable aid to the elucidation of crystal structures [19–21].

The specific short-range and long-range order of typical molecular lattices of essentially covalent compounds such as BrF_3 or XeF_2 can also be expressed in

[16] Cf. *e.g. R. Hoppe*, Z. anorg. allg. Chem. *364*, 263 (1969).
[17] Cf. *R. Hoppe*, Angew. Chem. *78*, 52 (1966); Angew. Chem. internat. Edit. *5*, 95 (1966).
[18] This reduction is strictly correct only for simple binary types of compounds; cf. [5].
[19] *F. Stewner* and *R. Hoppe*, Z. anorg. allg. Chem., in press.
[20] *K. Seeger* and *R. Hoppe*, Z. anorg. allg. Chem., in press.
[21] *G. Dittrich* and *R. Hoppe*, Z. anorg. allg. Chem., in press.

Table 7. Distances, MAPLE values, and $^{*}_{i}$MAPLE values for AuF_3.

a) Distances (Å)

Particle	d_{kj}
$Au-F_I$	2.03_5 (2×); 3.94_2 (2×)
$Au-F_{II}$	1.91_3 (2×); 2.68_7 (2×); 3.16_6 (2×)
Au–Au	3.46_0 (2×) (for comparison)

$\frac{d_{Au-Au}}{d_{Au-F}} = 1.80!$

b) MAPLE-values (kcal/mole)

Particle	MAPLE	$^{*}_{i}$MAPLE	for Q_i=	$^{*}_{i}$MAPLE (expected)
Au^{3+}	959.9	204	1.3	195
F^-_I	152.5	310 [a]	6.0	292
F^-_{II}	133.5	255	3.0	254

[a] The bridge position of F_I is particularly obvious from the $^{*}_{i}$MAPLE value.

terms of structural geometry by $^{*}_{i}$MAPLE values of this type, if we assign charges to the particles corresponding to their oxidation states, *e.g.* $Br^{3+}(F^-)_3$ (cf. Table 8 and the supplementary example of ICl_3, Table 9). We are, of course, not concerned with the absolute calculation of lattice energies, but wish only to express structural-geometrical facts by a number such that the long-range order is also taken into account.

$^{*}_{i}$MAPLE calculations are very useful even in the case of compounds such as Hg_2Cl_2, B_2F_4, or C_2H_6 if the approach is suitably modified [22].

Table 8. Distances and MAPLE values for BrF_3(solid).

Particle	d_{kj} (Å)
$Br-F_I$	1.71_5; 3.26_1 (2×); 3.62_8 (2×)
$Br-F_{Ii}$	1.84_7; 3.36_7 (2×); 3.78_7 (2×)
$Br-F_{III}$	1.84_2; 2.49_2; 3.51_0 (2×)
Br–Br	4.04_5 (2×) (for comparison)

$\frac{d_{Br-Br}}{d_{Br-F}} = 2.36$

Particle	MAPLE (kcal/mole)	$^{*}_{i}$MAPLE (kcal/mole)
Br^{3+}	983	187
F^-_I	141	242
F^-_{II}	125	231
F^-_{III}	152	281 [a]

[a] It can be seen that F_{III} tends to form Br–F .... Br bridges, a tendency that is more pronounced in $ICl_3 = I_2Cl_6$ (cf. Table 9).

Table 9. Distances and MAPLE values for ICl_3(solid).

Particle	d_{kj} (Å)	
$I-Cl_I$	2.67_8; 2.72_0;	3.83_2
$I-Cl_{II}$	2.38_5;	3.86_7
$I-Cl_{III}$	2.37_6;	4.03_0

$\frac{d_{I-I}}{d_{I-Cl}} = 1.70$

Particle	MAPLE (kcal/mole)	$^{*}_{i}$MAPLE (kcal/mole)
I^{3+}	715	189
Cl_I	126	338 [a]
Cl_{II}	78 [b]	188
Cl_{III}	105	249

[a] The bridge position of Cl in I_2Cl_6(solid) is clear from the $^{*}_{i}$MAPLE value.

[b] The abnormally low MAPLE(Cl_{II}) value is surprising.

8. $^{*}_{i}$MAPLE Values, Q_i Values, and Coordination Numbers

Equations (4) and (5) relate Q_i to the number n_j of neighbors for typical "coordination lattices"; on the basis of Table 5, a Q_i value can be assigned to each $^{*}_{i}$MAPLE value, and can then be used to deduce n_j. Thus by a method that is quite different from the "geometrical polyhedron methods" one obtains data about "effective" coordination numbers, which must be treated differently because of their different source. Eq. (5) in particular leads to interesting information in comparisons of similar variants of the same structural type [23] (see the example of Na_{II} in $Na_3[AlF_6]$; Table 6).

Similarly, the "Madelung Part of the Molecular Energy" (MAPME) can also be plotted as a function of Q_i of the central particle in the case of discrete molecules or complex ions (Fig. 16).

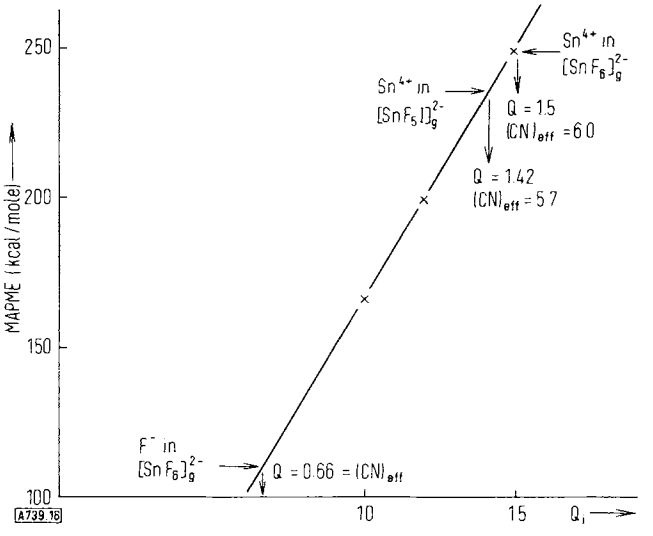


Fig. 16. Relation between MAPME and Q_i values and the "effective" coordination number.

A value of 5.7 is obtained in this way as the effective coordination number for Sn^{4+} in $[SnF_5I]^{2-}$, cf. Section 2. Finally, it is also possible to try to find the effective coordination numbers of ligands by this method. The value found for F^- in $[SnF_6]^{2-}$ is 0.7.

[22] *R. Hoppe*, unpublished.

[23] Cf. [16] and *H. Henkel*, and *R. Hoppe*, Z. anorg. allg. Chem. *364*, 253 (1969).

9. Closing Remarks

MAPLE calculations are of direct practical interest for the comparison of commensurable structures.

An example is *Holmberg*'s discussion on the structure of ScOF[24], where X-ray and structure-chemical methods failed to distinguish between three alternatives. The MAPLE values calculated by us (cf. Table 10) show clearly that in agreement with *Holmberg*'s suggestion, only alternative I can be seriously considered[25]. Many other examples have similarly shown the value of MAPLE calculations for detailed structural discussions.

The discrepancy between the accuracy of modern X-ray structure determinations and the possibility of understanding and critically interpreting their results, even only semiquantitatively, is amazing, and never since the "golden twenties", with their exceptionally fruitful symbiosis of physics, chemistry, mineralogy, and crystallography has it been so striking as it is today. Solid state chemistry in the true sense begins only with crystal chemistry, and is in fact a lot more in the eyes of the experimental chemist. But even the value of the advance in structural chemistry as a first step of solid state chemistry is, however, doubtful so long as structural facts cannot be critically and quantitatively evaluated and checked for internal consistency or inconsistency. We are conscious of the limitations of the very one-sided structure-geometrical view taken here, but we nevertheless hope to stimulate further discussion.

Table 10. Crystal structure of ScOF [24]: MAPLE values in kcal/mole.

MAPLE	Alternative I	Alternative II	Alternative III (statistical distribution of O^{2-} and F^-)
Sc^{3+}	1122.0	1043.5	1083.3
O^{2-}	543.1	393.1	365.2
F^-	138.9	215.2	251.7
Σ	1804.0	1651.8	1700.2

[24] *B. Holmberg*, Acta chem. scand. *20*, 1082 (1966).

[25] Cf. also *W. Barker*, Acta crystallogr. *A 24*, 700 (1968). Our values differ from those of *Barker*'s values in that they show in detail the changes during the transition from one individual alternative to another.

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From Planck to Bohr

The First Fifteen Years in the Development of the Quantum Theory

By Armin Hermann[*]

The quantum theory, which is nowadays a fundamental basis of chemistry that is regarded as self-evident, initially presented immense difficulties to human thought. An insight into many particulars of its fascinating evolution is provided by the correspondence of those involved in the development of the theory between 1899 and 1913, which has now been thoroughly sifted for the first time by the author.

1. The Continuity Principle

The principle "*natura non facit saltus*", *i.e.* all natural processes take place continuously and not spasmodically, had played a very important part in the development of science during the 17th century. This is shown particularly clearly in the creation of differential and integral calculus, the spirit of which is also the spirit of physics. The entire philosophy of *Leibniz* in particular is permeated with the continuity principle in its widest sense.

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Leibniz clearly stated "that the present always conceals the future in its bosom, and that any given state can only be explained naturally by the state immediately preceding it. Unless we accept this, there will be many things in the universe that defy the principle of sufficient reason and force us to marvel or to have recourse to chance for the explanation of the phenomena". The principle of the continuity of all natural processes was expressed by many scientists and philosophers in the 18th and 19th centuries, though it was not usually formulated as self-evident.

"An act of despair" was how *Max Planck* later described his theoretical proof of the law of black body radiation: "The entire affair can in short be described as an act of despair. I am peaceful by nature, and averse to hazardous adventures. However, ...a theoretical interpretation had to be... found at all costs... The two principal laws of heat seemed to me

to be all that had to be retained in any circumstances. Apart from these, I was ready to make any sacrifice of my physical beliefs" [1].

2. The Birth of the Quantum Theory

December 14, 1900, the day on which *Planck* described the derivation of his radiation law to the Physical Society in Berlin, saw the birth of the quantum theory. As an unwilling revolutionary, *Planck* had smashed the principle of the continuity of natural processes by postulating discrete energy steps for the linear oscillator, expressed by the formula

$$\varepsilon = h\nu$$

Contrary to a widely held belief, however, *Planck* had no suspicion of this corollary at the turn of the century. If he had no impression in 1900 of having overthrown the continuity principle, what did he mean by "act of despair" and the "sacrifice of physical beliefs"?

The sacrifice that *Planck* had knowingly made was the surrender of the purely axiomatic thermodynamic view of the second law of heat and the acceptance of the atomistic-probabilistic interpretation, which he had until then vigorously rejected. Only a few years earlier, in 1896, he had carried on an argument on this topic in the Annalen der Physik, through his assistant *Ernst Zermelo*, with *Boltzmann*.

And *Planck* was now forced to adopt the detested "Boltzmann method" to derive the law of black body radiation! The need to divide the energy into discrete atomistic portions was then only a minor additional difficulty: "This was a purely formal assumption, and I did not really think too much about it, since my only concern was to obtain a positive result, whatever the cost."

Following *Planck*'s work, the theory of radiation was investigated in the first few years of the present century by *Rayleigh*, *Jeans*, and *Lorentz*. By various routes, but always adhering rigidly to the thought processes of classical physics, they all arrived at the Rayleigh-Jeans formula. It was felt that this had to be accepted; it had been shown that there is no true equilibrium of black body radiation, and the energy passes from the resonators into the radiation and to ever-decreasing wavelengths. This viewpoint was still defended by *Hendrik Antoon Lorentz* in April 1908 at the International Congress of Mathematicians in Rome.

Willy Wien commented on this in a letter to *Arnold Sommerfeld*: "I am very disappointed by the lecture given by *Lorentz* in Rome. I take a poor view of the fact that he merely presented the old Jeans theory without adding any new point of view ... In my opinion the theory is not worth considering, since observations show enormous deviations from the Jeans formula. It also seems rather odd to me to regard as the advantage of the Jeans theory the fact that the entire unlimited multiplicity of the electronic vibrations can be retained, despite its complete failure to represent the true facts. And the spectral lines? *Lorentz* has not shown himself to be a leader of science this time."

Lorentz's caution was in line with his personality, but it was undoubtedly also stamped with the prejudices of the turn of the century: Anyone who shook the foundations of science, whatever his motives, was suspected of being a revolutionary.

Rayleigh, *Jeans*, *Lorentz*, and *Planck* were all alike in this respect. In the early years the only difference between *Planck* and the others was that *Planck* had been familiar with the natural constant h at least since May 1899, and he knew that its value can be found very accurately from radiation measurements. In *Planck*'s eyes the constant h existed and had to be explained, however inconvenient this might often appear to be. As late as 1910 he addressed the following warning to the innovators, and above all to *Albert Einstein* and *Johannes Stark*: "In introducing the quantum of action h into the theory, one must proceed as conservatively as possible, *i.e.* changes in the existing theory should be restricted to those that have proved absolutely essential."

3. The Appearance of *Einstein*

In 1905 *Albert Einstein*, who was at that time 26 years of age and an "Expert, 3rd Class" at the Swiss Patent Office in Bern, published three papers of great importance in the celebrated Volume 17 of the Annalen der Physik: The Theory of Brownian Movement, The Special Theory of Relativity, and The Light Quantum Hypothesis.

With his later almost proverbial independence of thought and his intellectual lack of respect, unlike *Planck*, *Lorentz*, and *Rayleigh*, he did not look upon the electromagnetic theory of light and mechanics as venerable structures that had to be treated "as conservatively as possible". From the very beginning he considered the Maxwell equations to be valid only for average values in time and space. Thus matter could often be successfully dealt with on the basis of the continuum concept, as *e.g.* in the theory of elasticity, and it became necessary to consider the corpuscular structure only for finer effects.

According to *Einstein*, the same was true in electrodynamics. The Maxwell equations are valid for optical interferences, but the corpuscular structure of light must be taken into account for the "groups of phenomena concerned with the production and transformation of light". Also according to *Einstein* (in 1909), the electron is "an alien in electrodynamics", since it is still not understood how the finite electronic charge is stably concentrated in a small space despite the very large Coulomb repulsion forces between the various elements of charge.

Early in 1909, *Einstein* came to the conclusion that the two deficiencies of the Maxwell theory must be linked

[1] The sources of the quotations reproduced here are to be found in *A. Hermann*: Frühgeschichte der Quantentheorie (1899 to 1913). Physik-Verlag, Mosbach/Baden 1969. This book also includes a complete review of the published and unpublished literature.

with each other. He tried to explain both the quantum structure of radiation and the electron, *i.e.* he tried to derive a single theory embracing both the electron and the light quantum. Einstein believed in 1909 that the key to the solution of this problem was the fact that e^2/c and h have the same dimensions, those of an action. "It seems to me from the relation

$$h = e^2/c$$

that the same modification of the theory that contains the elementary quantum e as a consequence will also contain the quantum structure of radiation." It should be mentioned that *Max Planck* had put forward a similar (though more cautiously formulated) view in a letter to *Ehrenfest* as early as 1905. *Planck* thought it possible that from the elementary quantum of electricity, "there is a bridge to the existence of an elementary quantum of energy h".

The elementary quantum of electricity e and *Planck*'s quantum of action h are nowadays regarded as independent natural constants, and it is considered a prerequisite of any future theory of elementary particles that the value of the Sommerfeld fine structure constant

$$2\pi e^2/hc = 1/137$$

can be calculated from it.

Einstein's paper in the Physikalische Zeitschrift of March 1909 elicited a comment from *Willy Wien*. It was around that time that *Wien* was composing his article on radiation theory for the Mathematische Enzyklopädie, in which he wrote: "I cannot at present accept *Einstein*'s opinion ... that the magnitude of the element of energy is related to that of the elementary quantum of electricity... The element of energy, if indeed it has any physical significance, must derive from a universal property of the atom."

This was entirely different from *Planck*'s view. Faced with the need to find a derivation for the radiation law, *Planck* had overcome the positivistic objection of *Mach* and *Ostwald* to atomism, and even did atomism a considerable service by his interpretation of the Planck-Boltzmann constant k. However, *Planck*'s linear oscillator remained a physically anemic object; it did not occur to *Planck* at first to look for a way of bridging the gap between this and real atoms. *Planck* had always regarded the "search for the absolute as the highest aim of research", and the "absolute" was precisely what was independent of the special properties of matter.

Einstein and the majority of the German physicists and chemists had likewise scarcely thought about the question of the constitution of atoms. *Max Born* said about this: "Well, the atom was the central problem at that time, and the Germans didn't known it." It must however be added that the most important idea was the quantum concept, and the French and English didn't know that.

4. The First Model of the Atom Based on the Quantum Theory

Who then was the first to attempt a quantum-theoretical treatment of the atom? Well, it was not one of the leading physicists or chemists, but a historian of physics named *Arthur Erich Haas*: In 1909, *Haas* had submitted a paper on the history of physics as his thesis for habilitation at the University of Vienna. This paper was not appreciated by the physicists of the faculty, and they imposed upon *Haas* the additional condition that he prepare another purely physical paper. To satisfy this condition, *Haas* started to read the latest physical literature. This was firstly the book by *Joseph John Thomson* on "Electricity and Matter", which deals almost exclusively with the structure of atoms, and secondly the newly published Mathematische Ezyklopädie containing *Wien*'s article. *Haas* combined *Wien*'s suggestion of deriving the element of energy from a universal property of atoms with the Thomson model of the atom, and so produced an important forerunner of the Bohr theory of the atom.

In the Thomson model, which consisted of an extended positively charged atomic sphere with point electrons, *Haas* considered only the electron orbitals on the surface of the atomic sphere; his model is therefore mathematically equivalent to *Rutherford*'s. For the forces acting on the surface and in the external space of a spherically symmetrical charge distribution, one can think of the total charge as being united in the center.

To determine the two unknowns, *i.e.* the radius of the electron orbital and the frequency of revolution, *Haas* needed another equation as well as the classical expression that equates centrifugal force to the Coulomb attraction force. This second equation can be obtained only by a "quantum-theoretical" approach. *Haas* was very fortunate in that he equated potential energy to the Planck element of energy $h\nu$.

This agrees with the later Bohr condition for the ground state of the hydrogen atom, and *Haas* therefore correctly obtained the "Bohr" radius of the hydrogen atom, which we could thus historically call the "Haas" radius. It is significant, however, that he wrote

$$h = 2\pi e\sqrt{am}$$

and not the equation solved for a. *Haas*, like *Wien*, considered the property of the atom to be the fundamental quantity from which the quantum of action h was derived.

The Bohr radius a is not a measurable quantity, so that the Haas relation provides no basis for numerical calculations. Using a similar hypothesis, however, *Haas* also derived an expression for the Rydberg frequency, which was thus traced back, as it was later by *Bohr*, to the fundamental quantities of the electron theory and the quantum of action. *Haas*'s determination is wrong by a factor of only 8, which is due to the inaccuracy of the numerical values used for the elementary charge and the quantum of action.

The reaction to his ideas was described very vividly by *Haas* in his autobiography: "In Vienna I at first met only scorn, and even ridicule. When I lectured to the Wiener Physikalisch-Chemische Gesellschaft, *Lecher* thought he was being very funny when he called the whole thing a carnival joke ... *Hasenöhrl* explained that I could not be taken seriously, as I had naively mixed up two branches of science that could have absolutely nothing to do with each other, namely quantum theory (which was concerned with the theory of heat) and spectroscopy (which was optical)" [2].

Thus the attempt to produce a quantum theory of the atom had apparently come to nothing in February 1910. However, the ideas developed by *Haas* were soon re-examined and pursued further by *Schidlof*, by *Sommerfeld*, and by *Hasenöhrl*. At about the time of *Haas*'s "carnival joke", a decisive *volte-face* in favor of the quantum concept had occurred. Everyone that had supported a quantum theory had hitherto been treated as an outsider, whereas from 1910 onward the quantum concept became, so to speak, respectable. How did this change of opinion come about? To find the answer to this question, we must dig a little deeper.

5. *Einstein*'s Influence on *Stark*, *Sommerfeld*, and *Nernst*

Einstein's light quantum hypothesis was regarded by the experts as the most radical attempt to derive the law of black body radiation, and it was accordingly received with much skepticism. Using the corpuscular theory of light, *Einstein* was able to provide a simple model for the interaction of light with atoms, molecules, and solids. As is well known, the "Einstein equation" for the photoelectric effect, which was deduced in 1905, consists simply of the application of the energy theory. In this way *Einstein* was able to extend the range of validity of the quantum concept. This valuable extension remained only a theory at first, since the experimental verification of these effects dragged out over several years, *e.g.* up to 1915/16 in the case of the photoelectric effect.

In the search for new quantum phenomena, the first to follow *Einstein*, from about 1907 on, was *Johannes Stark*. He named a whole series of processes in which the quantum law should, in his opinion, be evident. In addition to many that were correct, such as the ultraviolet boundary of X-ray bremsstrahlung, these included many that were not.

Like *Einstein*, *Stark* thought nothing of opposing the prevailing opinion. Opposition to dogma seemed to him to be a necessity of life. When the many quantum approaches were united in the Bohr theory in 1913 (and this theory,more over, was confirmed by his own experiments), *Stark* suddenly turned against the quantum concept and continued to oppose it until his death. Up to 1913, however, he fought with the same vehemence in favor of the quantum idea, and for this reason *Stark*, who is still remembered as a conservative physicist of the older generation, had his merits at the time as an avantgardist.

In late 1909, *Johannes Stark* tried to wring an agreement with the quantum theory from *Sommerfeld*, virtually by brute force. However, *Sommerfeld* had no difficulty in demonstrating embarrassing physical errors to *Stark*. Thus *Sommerfeld* wrote: "Nothing could be further from my intention than to start a quarrel with you. This would be very unequal, since you are far above me *in* experimental ideas, and I above you in theoretical lucidity." *Sommerfeld* and *Stark* carried on a lively discussion of the quantum concept in X-ray bremsstrahlung in the Physikalische Zeitschrift and in their correspondence. They entered into an argument that was the start of a deadly enmity, which was to affect the subsequent lives of both men.

The outcome for *Sommerfeld*, *Planck*, and the experts was essentially a corroboration of the wave theory of light and of X-rays. *Sommerfeld* expressly demonstrated in 1910 that the quantum of action had nothing to do with X-ray bremsstrahlung.

In March 1910, however, *Arnold Sommerfeld* was subjected to pressure by his own assistant *Peter Debye*. The latter had developed what was perhaps the shortest and clearest derivation of the Planck radiation law. Like *Rayleigh* and *Jeans*, he considered the characteristic vibrations of the cavity, which, however, are now provided with the quantum-theoretical energy average. *Debye* told *Sommerfeld* that he had now reached a firm opinion in his considerations on radiation, and that he wished to publish his views. *Sommerfeld* felt responsible for all the work done by his co-workers. What should he do? It was recorded with surprise at *Sommerfeld*'s institute that he suddenly felt in need of a rest in the middle of the year and went off to spend a week in Switzerland. As his pupil *Paul S. Epstein* commented, *Sommerfeld*'s idea of recreation was to talk physics all day with *Einstein*.

Like the other experts, *Sommerfeld* had first met *Einstein* in 1909 at the Salzburg Naturforscherversammlung, where the two men had formed a friendship based on mutual respect. *Einstein* now wrote in a letter to *Johann Jacob Laub* that *Sommerfeld* had spent a whole week with him "to discuss the question of light and some matters concerning relativity. His presence was a real occasion to me. He has largely accepted my ideas ..."

For *Sommerfeld*, *Einstein*'s power of persuasion was based not only on the force of his personality but also on the proven success of the relativity theory. This had very rapidly gained acceptance among those that mattered up to about 1908. Though the two most important physical theories of the beginning of the 20th century, *i.e.* the quantum theory and the theory of relativity, have no direct logical connection, they are closely linked from a historical standpoint. The success of the theory of relativity now also accelerated the development of the quantum theory.

The quantum theory gained an important champion in the person of *Sommerfeld*. Unlike *Planck*, *Sommer-*

[2] *A. E. Haas*: Der erste Quantenansatz für das Atom (= Dokumente der Naturwissenschaft. Vol. 10). Battenberg, Stuttgart 1966, see p. 16.

feld had a large circle of pupils, with whom he was constantly exchanging ideas, and on whom he made a strong impression. Thus from about the beginning of 1911, enthusiastic efforts were being made even among the younger scientists to solve the quantum problem.

6. *Nernst* and the First Solvay Congress

Even before *Sommerfeld*, the quantum theory had won another important adherent, who also enjoyed absolute and authoritative rule over a large institute. This was *Walther Nernst*. *Nernst* was interested in thermodynamics. He had formulated the third law of thermodynamics in 1906, and had deduced from it that the specific heat of all substances must tend toward a constant limiting value as the temperature approaches absolute zero. *Nernst* had therefore already set out to measure specific heats at low temperatures over a wide front when the Einstein theory of specific heat came to his notice in late 1909 or early 1910.

When the term ended, in March 1910, *Nernst* hurried off to *Einstein* in Zürich with the results of his measurements. Both men were delighted. A letter written by *Einstein* reads: "There is no doubt in my mind about the correctness of the quantum theory. My predictions about specific heats appear to have been brilliantly confirmed."

In addition to thermal radiation, there was now a second field whose experimental results could be explained with the aid of the quantum concept, and only with its aid. The quantum concept now rested, in *Sommerfeld*'s words, on "two stout supporting pillars", and *Einstein* stated that *Nernst* had freed the problem from its "theoretical shadow existence" [3].

Nernst was filled with enthusiasm by this encounter with a problem of the utmost importance to the foundations of science, and he looked around for further work. He initiated moves to acquire *Albert Einstein* for the Preussische Akademie, and in June 1910 he began preparations for an international "Quantum Conference" to enable the leaders in the field to reconsider the foundations of their science. *Nernst* wanted this conference, like the Karlsruher Chemikertagung in 1860, to be a landmark, and this aim was achieved in full. The preparations for the congress, which attracted a great deal of attention, the Solvay Congress itself, which started on October 30, 1911, in Brussels, and the official and unofficial congress reports won over many who had previously been mere by-standers.

In this trail-blazing atmosphere, the Haas idea was also activated. *Sommerfeld* had adopted this idea, but in Brussels he switched to the opposite view, *i.e.* that "h is not explained by molecular dimensions; on the contrary, the existence of molecules may be regarded as a function and a consequence of the existence of an elementary quantum of action".

After the Solvay Congress, *Sommerfeld* expected *Einstein* to provide the fundamental clarification of the constitution of the atom with the aid of the quantum theory, as is shown by the correspondence that passed between *Einstein* and *Sommerfeld* [4]. On October 29, 1912, *Einstein* made the following reply to a question by *Sommerfeld*:

"Your letter perplexes me still further. I assure you, however, that I have nothing new of any interest to say about the quantum problem. I am in complete agreement with the Debye-Born view, and can find nothing in it to criticize. However, this achievement is of little help in the solution of the principal difficulties."

Sommerfeld subsequently wrote to *Hilbert*: "My writing to *Einstein* was in vain, as you can see from this. *Einstein* is evidently so steeped in gravitation that he is deaf to everything else."

7. The Bohr Model of the Atom

As everyone knows, it was *Bohr* that made the breakthrough in February and March 1913 with his quantum theory of the atom. This success was largely due to *Bohr*'s conviction that it was the quantum of action that was responsible for the stability of the planetary atom. This conviction was essentially the result of *Sommerfeld*'s lecture in Brussels.

The international congress in Brussels carried the quantum concept beyond the boundaries of the German-speaking world. It had a deep impression on the young *Léon Brillouin* and *Louis de Broglie* in France and on *William Nicholson* and *Niels Bohr* in England. The quantum concept found a fertile soil particularly in the traditions of English natural science. The positivistic objection to atomism had played no part in England, and unlike in Germany, the constitution of the atom had long been a center of interest here.

As a guest at *Rutherford's* Institute in Manchester, *Bohr* witnessed the new experiments on radioactivity and the scattering of α and β rays at the beginning of 1912, and like the rest of *Rutherford*'s coworkers he was convinced of the correctness of the planetary model of the atom. *Bohr* was interested by the questions that followed directly from the experiments, and he found the answer. In an interview of the Sources for History of Quantum Physics with *Georg von Hevesy* we find: "I asked *Rutherford*: ... 'Where do the beta particles come from?'. *Rutherford* answered: Ask *Bohr! Bohr* with no difficulty answered that electrons involved in radioactive transmutation process come from the nucleus, and all of the other electrons come from the exterior of the atom".

Bohr deduced information about many important properties of the atom on what was still, so to speak,

[3] Cf. *Einstein, Debye, Born, Kármán*: Die Quantentheorie der spezifischen Wärme (= Dokumente der Naturwissenschaft. Vol. 8). Battenberg, München 1967

[4] *A. Einstein, A. Sommerfeld*: Briefwechsel. Sechszig Briefe aus dem goldenen Zeitalter der modernen Physik. Schwabe Verlag, Basel/Stuttgart 1968, see p. 26.

a pre-quantum-theoretical basis. This was a frequently overlooked prerequisite for the successful treatment of the problem. Toward the end of 1912 *Bohr* was clear:

about the correctness of the planetary model of the atom,

about the concept of atomic number, *i.e.* about the assignment of the models with one, two *etc.* electrons to the actual atoms,

about the separation of the "nuclear" from the "atomic" phenomena,

about the possibility that one and the same atom can exist in various "states",

about the ability of the Planck quantum of action to ensure the stability of the atom,

and that no further "explanation" of such a quantum theory is necessary.

On *Rutherford*'s advice that he avoid unnecessary complications and calculations, *Bohr* concentrated on the simplest model, that of the hydrogen atom, with one electron. In a letter to *Rutherford*, *Bohr* wrote that he was considering only the ground state of the atom, the "natural permanent state", and had no intention of trying to apply his ideas to the line spectra. That was on January 31, 1913. On March 6, 1913, however, he submitted the finished article on the theory of the spectrum of hydrogen to *Rutherford* for publication in the Philosophical Magazine.

The decisive step must therefore have been made in February 1913. Who or what persuaded *Niels Bohr* to embark on a theory of spectral lines? And how did he achieve such speedy success?

On October 31, 1962 less than three weeks before his death, *Bohr* himself was asked about this by *Léon Rosenfeld* and *Thomas S. Kuhn* on behalf of the Sources for History of Quantum Physics [5]. The record reads: "*Rosenfeld*: 'How did you come to examine the spectra?' *Bohr*: 'The spectra was a very difficult problem... And I discovered it, you see ... And I found the hydrogen spectrum. I was just reading the book of *Stark*, and at that moment I felt now we'll just see how the spectrum comes.' *Kuhn*: 'Was this at Manchester that you were reading *Stark?*' *Bohr*: 'No, no, that was later in Copenhagen ... it was in January, I think of 1913."

The author must confess that he was quite bewildered by this information. Having been in possession of the major part of *Stark*'s scientific legacy for a number of years [6], he had repeatedly referred to the importance of *Stark*'s contribution to the development of the early quantum theory. He had never dared, however, to assume that it had had such a direct influence on the emergence of the Bohr theory. We know from *Rutherford*'s letter of January 31, 1913, that the date of this decisive stimulus was February 1913, and not January.

What, then, were the ideas of *Stark*'s that had such an unusual outcome? According to *Stark*, even a single electron can emit an entire spectrum of lines. The electron returns from the almost completely separated state to a very eccentric elliptic orbital near the center of the atom. The orbital is strongly curved at the perihelion, and the acceleration of the electron is accordingly high. At this point electromagnetic energy is emitted in the form of a light quantum.

Stark wrote: "The electron's residual kinetic energy carries it away from the center Z again; because of the loss of energy, however, it can no longer move away to its original distance, but curves back again at a shorter distance." According to *Stark*, this repeated return of the electron to the atom is accompanied by emission of a light quantum at the aphelion and at the perihelion of the movement.

Stark developed these ideas in 1908, and reproduced them in 1911 in his book "Prinzipien der Atomdynamik. II. Die elementare Strahlung" (Principles of Atomic Dynamics. II. Elementary Radiation). *Bohr* obtained this book in February 1913.

When one accepts, as *Bohr* did, the planetary model of the atom with Coulomb forces between the nucleus and the electron, the application of *Stark*'s ideas follows automatically:

The path of the electron is an ellipse before the emission of radiation.

The path is again an ellipse after the emission, but this ellipse is situated closer to the nucleus. The energy of the electron is now lower.

The question how the electron moves from one ellipse to another need not be answered immediately.

Application of *Stark*'s concept to the basis of the Rutherford model of the atom thus gives families of ellipses, which must be classified according to their electronic energy.

"As soon as I saw *Balmer*'s formula the whole thing was immediately clear to me", *Bohr* told *Rosenfeld* more than once. Compare this with *Bohr*'s other statement: "I was just reading the book of *Stark*, and at that moment I felt now we'll just see how the spectrum comes." Thus *Niels Bohr* must have read *Stark*'s book and seen the Balmer formula at roughly the same time, *i.e.* in February 1913.

Bohr's copy of *Stark*'s "Prinzipien der Atomdynamik II" was found among his books at the Niels Bohr Institute in Copenhagen. This book contained a scrap of paper on which *Bohr* had noted two references to articles published in 1912. It appears, therefore, that *Bohr* procured these articles in direct connection with the reading of *Stark*'s book. One of the two deals with the theory of spectral lines, and contains the formula

$$\nu = N\left(\frac{1}{n^2} - \frac{1}{m^2}\right)$$

"As soon as I saw *Balmer*'s formula the whole thing was immediately clear to me": taken together with the idea of various elliptic orbitals, this formula gave the

[5] The American-financed "Sources for History of Quantum Physics" has been recording the relevant source material for some years, and has also arranged interviews with the workers involved. The Director for Europe is Prof. *F. Hund* (Göttingen).

[6] *Stark*'s legacy is now in the possession of the Staatsbibliothek der Stiftung Preussischer Kulturbesitz in Berlin-Dahlem.

"transitions" between pairs of elliptic orbitals m and n. Since there was evidently no suggestion of classifying the elliptic orbitals on the basis of energy, *Bohr* could apparently write the following formula directly for the energy emitted in a spectral line:

$$h\nu = h \cdot N \left(\frac{1}{n^2} - \frac{1}{m^2} \right)$$

All that remained now was to classify the various elliptic orbitals according to their energy; in other words, to complete the work, *Bohr* merely had to derive the formula

$$E_n = h \cdot N \cdot \frac{1}{n^2}$$

Without knowing about *Haas*, *Bohr* had tried in the middle of 1912 to relate the kinetic energy to the frequency of revolution. In an unpublished manuscript by *Bohr* dated July 1912, which was edited by *Léon Rosenfeld* to celebrate the 50th anniversary of the Bohr model in 1963, we find the formula

$$E_{kin} = K \cdot \nu$$

which at that time referred only to the ground state. The K in this formula should be closely related to the Planck constant.

It was now a simple matter for *Bohr* to find the correct expression by trial and error. Thus the "mechanism" of spectral lines, which had been sought since the discovery of spectral analysis by *Kirchhoff* and *Bunsen*, was found.

It is well known that the Bohr model of the hydrogen atom was then developed, by the addition of *Sommerfeld*'s quantum conditions, into a system of formulas that really deserved to be called a quantum theory. "Your spectral investigations", wrote *Einstein* to *Sommerfeld*, "are among my finest physical experiences. It is only through them that *Bohr*'s idea becomes totally convincing" [7].

Since the majority of physicists had accepted the quantum concept since 1912 and a corresponding theory had now been produced, developments entered a new phase. The early history of the quantum theory was closed.

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Translated by Express Translation Service, London

[7] Cf. Ref. [4], p. 41.

Polyurethane Ionomers, a New Class of Block Polymers

By D. Dieterich, W. Keberle, and H. Witt[*]

Dedicated to Professor K. Hansen on the occasion of his 60th birthday

Linear polyurethanes containing ionic centers at wide intervals are heteropolymers having a pronounced segment structure, i.e. ionomers. As a result of interactions between chains (Coulomb forces and hydrogen bonds), their properties are similar to those of crosslinked elastomers. They are strongly associated both in organic and in aqueous solutions. Polyurethane ionomers in polar organic solvents spontaneously form stable aqueous dispersions on addition of water, with the ionomer as the disperse phase. The particle size can be varied between 20 nm and 1 mm.

1. Polyelectrolytes by the Diisocyanate Polyaddition Process[1–3]

By reaction of diisocyanates *(1)* with diols containing tertiary amino groups *(2)*, *Schlack* obtained basic, linear polyurethanes, which dissolve in aqueous acids to form polyurethane polyammonium salts *(3)* [4].

Diisocyanates react with diaminobenzenesulfonates, or diaminobenzoates to form water-soluble polyurea polysulfonates or polycarboxylates *(4)* [5].

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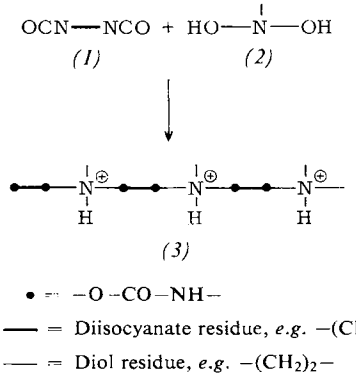
[1] *O. Bayer, H. Rinke, W. Siefken, L. Orthner*, and *H. Schild*, DRP 728981 (Nov. 13, 1937), I.G. Farben: Chem. Zbl. *1940* II, 1796.

[2] *O. Bayer*, Angew. Chem. *60*, 257 (1948).

[3] *O. Bayer* and *E. Müller*, Angew. Chem. *72*, 934 (1960); *E. Müller*, Kautschuk u. Gummi, Kunststoffe *18*, 67 (1965); *H. Oertel*, Melliand Textilber. *46*, 51 (1965); *E. Windemuth*, Kunststoffe *57*, 337 (1967); *H. Rinke*, Chimia *22*, 164 (1968); other literature cited therein.

[4] *P. Schlack*, DDR-Pat. 5367 (April 25, 1942); 5379 (June 19, 1942); 5381 (June 24, 1942); all VEB Filmfabrik Agfa Wolfen; Chem. Zbl. *1956*, 10345, 10816, 11577.

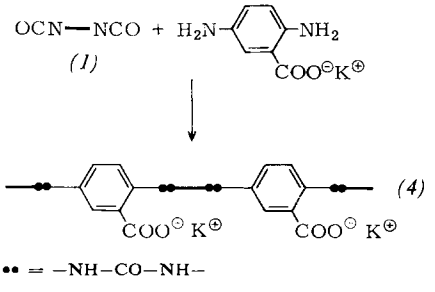
[5] *W. Thoma, O. Bayer*, and *H. Rinke*, DAS 1067212 (Dec. 15, 1959); DAS 1042892 (April 6, 1957); both Farbenfabriken Bayer; Chem. Abstr. *55*, 10912f, 2184d (1961).



• = $-O-CO-NH-$

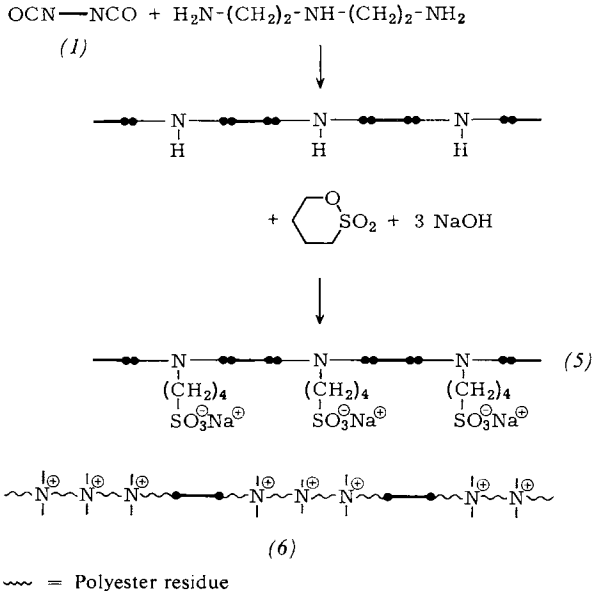
—— = Diisocyanate residue, *e.g.* $-(CH_2)_6-$

—— = Diol residue, *e.g.* $-(CH_2)_2-$



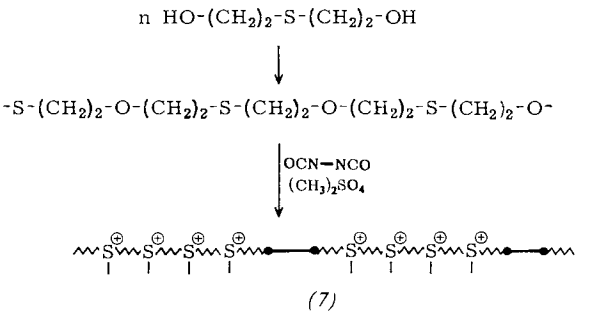
•• = $-NH-CO-NH-$

Polyelectrolytes such as *(5)*, *(6)*, and *(7)* have also been prepared by polymer-analogous reaction of polyureas containing secondary amino groups with sultones or acid anhydrides in the presence of bases [6], by quaternization of basic polyester urethanes [7], and by ternization of polythioether urethanes [8].



~~~ = Polyester residue

A feature common to the isocyanate-based polyelectrolytes is the more or less random distribution of numerous (250 to 800 milliequivalents/100 g of polymer) of ionic centers over the macromolecule; the

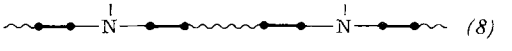


www = Ether residue

products are accordingly soluble in water, but not in organic solvents. These polyelectrolytes are of no importance in the field of plastics.

2. Segment Polyurethanes

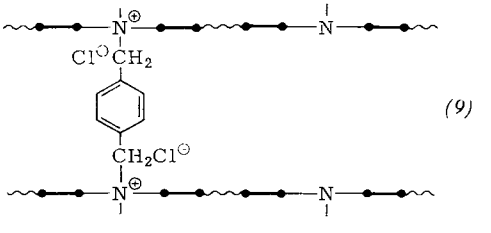
The diisocyanate polyaddition process also permits the production of nonrandom distributions of the ionic center. Thus reaction of a high molecular weight polyester diol that is free from (potentially) ionic centers with excess diisocyanate yields a polyester diisocyanate (NCO prepolymer), which reacts with *N*-methylimino-2,2'-diethanol (*N*-methyl-*N*,*N*-bis(2-hydroxyethyl)-amine) to give a segment polymer having the structure *(8)*.



In this structure, organophilic, apolar polyester segments (molecular weight about 2000; this corresponds to a length of about 120–210 Å) alternate with shorter basic polar urethane segments (length about 40–70 Å) formed from the diisocyanate and the basic chain-lengthening agent. These reactions can also be carried out with polyether diols.

2.1. Difunctional Quaternization – Crosslinked Elastomers

The thermoplastic rubber-like material can be "vulcanized" with bifunctional quaternizing agents such as 1,4-bis(chloromethyl)benzene [9]; chemical linkage of the chains occurs to give a three-dimensional network *(9)* of the type found in elastomers.



[6] *G. Pieper*, *O. Bayer*, *H. Weese*, and *W. Wirth*, DBP 922736 (Jan. 4, 1952), Farbenfabriken Bayer; Chem. Abstr. *52*, 7355f (1958).

[7] *R. Pütter*, *H. Raab*, *F. Suckfüll*, and *P. Zervas*, DBP 880465 (July 2, 1944), Farbenfabriken Bayer.

[8] *E. Enders* and *H. Holtschmidt*, DAS 1062014 (June 19, 1957), Farbenfabriken Bayer; Chem. Abstr. *55*, 6892g (1961).

[9] *D. Dieterich*, *O. Bayer*, *J. Peter*, and *E. Müller*, DBP 1156977 (June 5, 1962), Farbenfabriken Bayer; Chem. Abstr. *60*, 1911e (1964); *H. Wieden*, *W. Rellensmann*, *D. Dieterich*, and *G.-E. Nischk*, Brit. Pat. 1150634 (German Priority, June 15, 1965), Farbenfabriken Bayer.
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2.2. Monofunctional Quaternization – Linear Elastomers

If the quaternization is carried out instead with a monofunctional agent such as dimethyl sulfate or methyl chloride, chemical crosslinking is impossible. Nevertheless, this again gives an elastomer, which, at $N^{\oplus}$ contents of more than 0.4%, differs characteristically from the basic starting material (Table 1) [10].

Table 1. Change in the properties of basic uncrosslinked segment polyurethanes on quaternization (salt formation) (measurements on films 0.3 mm thick).

	1% N	1% $N^{\oplus}$
Tensile strength	<10 kg/cm² plastic, soft	200–300 kg/cm² highly elastic
Elongation at break	–	600–800%
Modulus (100% elongation)	<1 kg/cm²	40 kg/cm²
Tear propagation	<5 kg/cm¹	30–40 kg/cm²
Elastic range	nonexistent	−40 to 120 °C
Thermoplasticity	from −40 °C	from 120 °C
Swelling in water at room temperature after 24 hours	<10%	50–100%
Solubility in benzene	+	–
in acetone	+	–
in water	–	–
in 70% aqueous acetone	–	+

The tensile strength of the elastomer depends on the $N^{\oplus}$ content (Table 2). 0.2% of $N^{\oplus}$ has little effect on the properties; the material remains plastic.

The dependence of the elastomeric range on the content of quaternary ammonium groups is illustrated by the shear modulus curves obtained by free torsional oscillation (Fig. 1).

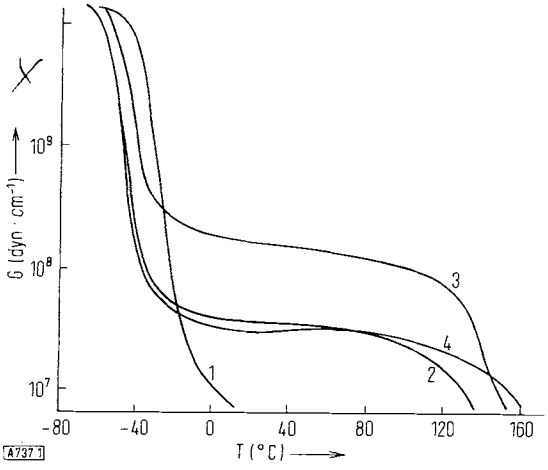


Fig. 1. Shear modulus G as a function of temperature for polyurethanes with various degrees of quaternization.

G > 10^9: glass state; G = 10^7–10^9: elastic range; G < 10^7: plastic range. 1: 0.12% $N^{\oplus}$; 2: 0.86 $N^{\oplus}$; 3: 1.06% $N^{\oplus}$; 4: 1.06% $N^{\oplus}$ and chemical crosslinking with hexakis(methoxymethyl)melamine.

Whereas the polyurethane 1 passes directly from the glass state into the thermoplastic range, the polyurethanes 2 and 3 exhibit pronounced elastomeric character between −40 and +130 °C. The additional chemical crosslinking in polymer 4 gives only a slight increase in the elastic range, extending it to 150 °C.

Table 2. Properties of polyurethane ionomers based on poly-1,2-propylene ether diol (molecular weight 2000) (measurements on films 0.3 mm thick).

MDE (%) [a]	Desmodur 44 (%) [b]	Quaternizing agent	$N^{\oplus}$ (%) [c]	Tensile strength kp/cm² [d]	Breaking elongation (%) [d]	Tension value 100% Elongation (kp/cm²) [d]	500% Elongation (kp/cm²) [d]	Permanent elongation [e] 1′ (%)	1 h (%)	24 h (%)	H_2O-vapor permeability at 0.3 mm thickness [f] (g · m⁻² · d⁻¹)
2	14.1	DMS [g]	0.19	14	>3000	7	11	40	10	4	123
4	16.8	CH_3Cl	0.37	16	>1300	6	11	42	10	5	110
6	19.1	DMS	0.51	31	1280	13	22				115
8	21.3	CH_3Cl	0.67	115	994	22	61	48	21	13	90
10	23.4	DMS	0.76	156	924	27	65	48	16	10	94
12	25.2	DMS	0.86	183	760						103
12	25.2	CH_3Cl	0.90	172	714	50	105	92	50	34	100
15	27.7	CH_3Cl	1.06	240	668	86	158	141	104	94	
18	29.9	CH_3Cl	1.20	129	722	73	108				99
24	33.7	CH_3Cl	1.43	96	551	56	92				
12	25.2	12% quatern.	0.86	172	714	50	105				
12	25.2	8% quatern.	0.57	132	820	24	68				
12	25.2	4% quatern.	0.28	90	900	14	36				76
12	25.2	2% quatern.	0.14	70	1000	11	29				60
12	25.2	0% quatern.	0	20	>3000	< 5					

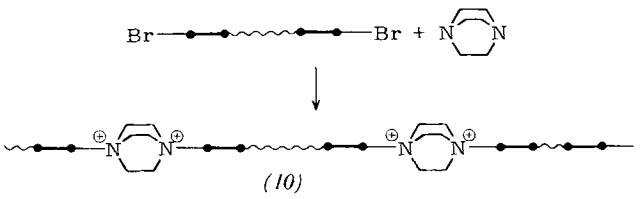
[a] MDE: *N*-methylimino-2,2′-diethanol, percentage based on polyether. [b] Desmodur 44: 4,4′-diisocyanatodiphenylmethane, percentage based on total ionomer. [c] $N^{\oplus}$: percentage based on total ionomer. [d] DIN 53504. [e] Elongation after the times indicated and after 600% pre-elongation. [f] DIN 53379. [g] DMS = dimethyl sulfate.

In the last five examples of Table 2, the content of quaternary ammonium groups was varied while the content of urethane groups was kept constant. Comparison with the earlier examples shows the influence of the urethane group content on the tensile strength. Both the quaternary ammonium groups and the urethane groups are evidently essential to the elastomer character.

It had been observed earlier that the reaction of polyester urethane dibromides with diazabicyclooctane, which is a polyquaternization addition, leads not to plastic but to elastic products with high tensile strengths, such as *(10)* [10a], though no chemical crosslinking has evidently taken place, since these products dissolve in 80% aqueous tetrahydrofuran.

[10] *D. Dieterich, O. Bayer,* and *J. Peter,* DBP 1184946 (Oct. 26, 1962), Farbenfabriken Bayer; Chem. Abstr. *62,* 7984h (1965).

[10a] *D. Dieterich, E. Müller, O. Bayer,* and *J. Peter,* Brit. Pat. 1006151 (German Publ. Pat. Appl. 1495693 of Aug. 30, 1962), Farbenfabriken Bayer; Chem. Abstr. *62,* 701e (1965).



(10)

2.2.1. Solvent Effects

Alkylation of the basic segment polyurethane in benzene (20%) leads to a marked increase in viscosity and formation of a solid elastic gel, which does not exhibit thermoreversible liquefaction and does not dissolve in benzene or acetone. In sufficiently dilute benzene solution (*e.g.* 5%), considerable turbidity appears with formation of microgel dispersions, which settle in time and undergo syneresis to form an elastomer. In polar media, (tetrahydrofuran, acetone), on the other hand, no gel is formed at concentrations below 10%. The solutions exhibit an anomalous dependence of the viscosity on concentration, so that the apparent molecular weight found from viscosity measurements increases rapidly with increasing concentration (Table 3).

Table 3. Viscometrically determined apparent molecular weight of a polyurethane polyammonium ionomer as a function of concentration.

Conc. (g/100 ml acetone)	Mol.-wt.
0	10000
0.5	11500
1.0	13000
2.0	20000
4.0	200000
6.5	400000
8.0	$>10^6$

In a solution of 6.5 g of the quaternized product in 100 ml of acetone, the viscosity is reduced to about 1/10th of the original value by 3% of water. The apparent molecular weight decreases from 400000 to 100000.

quaternization [10]. Neutralization of the basic polyurethane dissolved in polar organic solvents with *e.g.* hydrochloric acid gives a polyurethane polyhydrochloride that forms colloidal solutions in water and yields films having the same properties as the quaternized products.

Weaker acids (pK value >4, *e.g.* acetic acid and aspartic acid) readily give the hydrophilic polyurethane salts, which can be transferred into the aqueous phase, but these dry to give soft to tacky coatings. Thus elastomer formation no longer occurs. Polyurethane polyacetates are so strongly hydrolyzed in water that the acetic acid evaporates with the water on drying, to leave the rubbery, hydrophobic, basic starting polyurethane.

By subsequent treatment in baths containing 1–10% of acid, basic groups still present in a thin surface region of the polyurethane can be converted into salts. The reaction can be detected from the change in the mechanical properties (Table 4 and Fig. 2). (The bifunctionality of oxalic acid is of practically no importance.)

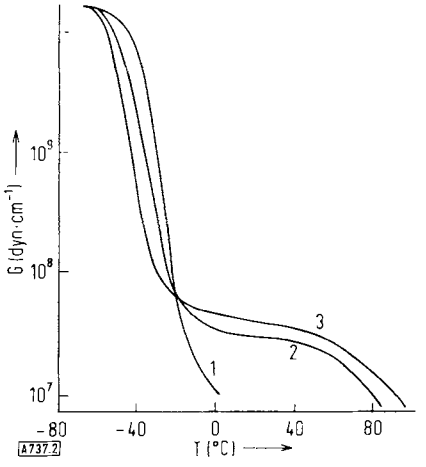


Fig. 2. Shear modulus G of an incompletely quaternized polyurethane film before and after storage in aqueous oxalic acid.
1: Partly quaternized with CH_3Cl, approx. 0.2% $N^{\oplus}$; 2: subsequently treated for 16 h in 1% oxalic acid; 3: subsequently treated for 16 h in 5% oxalic acid.

Table 4. Change in the properties of an incompletely quaternized polyurethane film on subsequent treatment with aqueous oxalic acid.

Salt formation	Tensile strength (kp/cm²) [a]	Breaking elongation (%) [a]	Tension value 100% | 500% Elongation (kp/cm²) (a)		Permanent elongation 1′ | 1 h | 24 h (%) [b]			H_2O-vapor permeability at 0.3 mm thickness [c] (g · m⁻² · d⁻¹)
CH_3Cl 4 h 80 °C	31	1176	5	13	25	3	0	62
+16 h in 1% oxalic acid	83	738	19	48	33	12	9	69
+16 h in 5% oxalic acid	138	715	26	76	40	40	9	85

[a] DIN 53504. [b] Elongation after the indicated times at an elongation of 500%. [c] DIN 53379.

The ionomer is not precipitated even by large quantities of water, but forms an opaque sol. The product obtained when this sol is dried is insoluble in water.

2.3. Action of Acids

Polyurethane polyammonium ionomers are obtained even more readily by the action of acids [11] than by

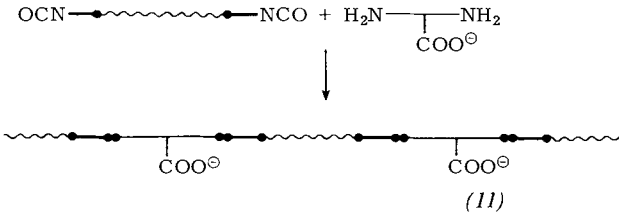
[11] *D. Dieterich, E. Müller,* and *O. Bayer,* DBP 1178586 (Dec. 5, 1962); DBP 1179363 (Feb. 28, 1963); Chem. Abstr. *62,* 6633f, 2900g (1965); *D. Dieterich* and *H. Meier,* Netherlands Publ. Pat. Appl. 67/03743 (German Priority, March 12, 1966), all Farbenfabriken Bayer.

2,2′-diethanol (bis(2-hydroxyethyl) sulfide) into the polysulfonium ionomers[12] and into anionic polyurethane ionomers.

2.4. Anionic Ionomers

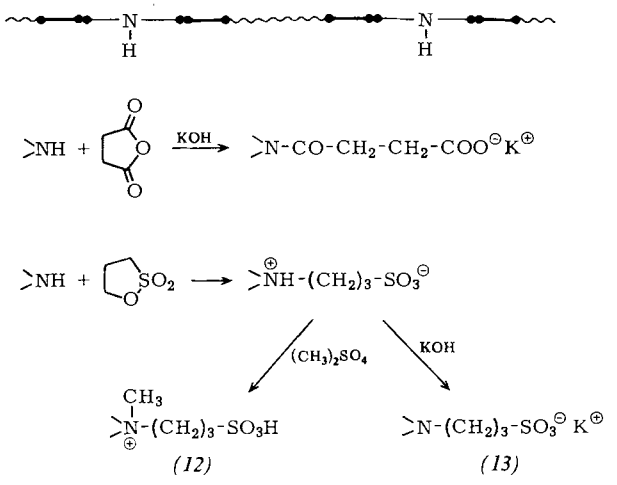
Quaternary ammonium groups can be readily introduced into the polyurethane macromolecule to form cationic ionomers by means of tertiary amines containing hydroxyl or amino groups. The preparation of anionic segmented polyurethane ionomers by reaction with bifunctional anionic "chain lengtheners"[12a,13] such as dihydroxy- and diaminocarboxylic acids, on the other hand, is more difficult, since the free carboxyl groups can react with the isocyanates and insoluble inner salts can be formed. The anionic component is therefore preferably introduced as the sodium or potassium salt.

Salts of aliphatic diamino acids such as *N*-(2-aminoethyl)-3-aminopropanesulfonate, *N*-(2-aminoethyl)-β-aminopropionate, and lysinate give the best results in the chain lengthening of NCO prepolymers formed from polyester or polyether diols and excess diisocyanate.



(11)

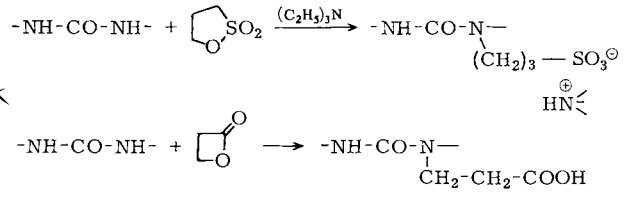
The polyaddition to give the macromolecule, *e.g. (11)*, takes place within a few minutes. Owing to hydration of the anionic groups, no abnormal viscosity increase is observed. The resulting polyurethane urea ionomers have a particularly high tensile strength and solvent resistance. Soft products are obtained *e.g.* by incorporation of tartaric acid, the carboxyl groups of which are neutralized by triethylamine immediately upon addition.



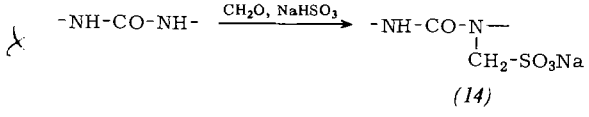
(12) *(13)*

Special methods for the introduction of ionic centers are the reaction of high molecular weight segmented polyurethanes or polyureas with cyclic compounds such as sultones, lactones, or anhydrides in the presence of strong bases[14]. The reaction can take place on secondary amino groups, and the products obtained with sultones are zwitterion ammoniosulfonates, which can be converted into cationic ionomers *(12)* by quaternization and into anionic ionomers *(13)* by reaction with bases.

A procedure of greater practical interest is the modification of existing polyurethanes containing urea groups[14].

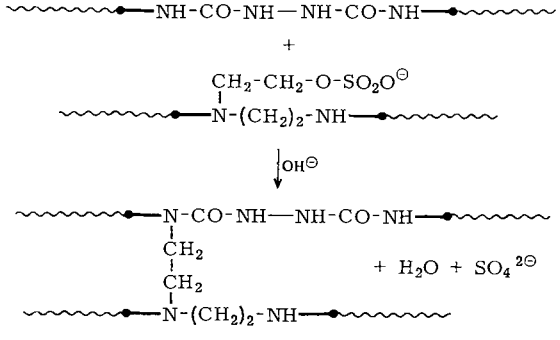


Ionomers such as *(14)* can also be prepared by sulfomethylation or aminomethylation[15].



(14)

If a salt of a sulfuric acid half ester is introduced as the anionic group, the ionomers can be crosslinked by heating with alkalis, with elimination of sulfate[16].



The segmented polyurethane ionomers containing carboxylate or sulfonate groups also have high tensile strength and elasticity with predominantly linear structures.

Plastic ionomers such as *(15)* on the other hand are obtained when low molecular weight diisocyanates are allowed to react with high molecular weight polyesters containing sulfonate groups[16a].

[12] a) *D. Dieterich* and *O. Bayer*, Brit. Pat. 1078202 (German Publ. Pat. Appl. Sept. 19, 1963); b) *D. Dieterich*, Brit. Pat. 1080590 (German Publ. Pat. Appl. 1544892) (Dec. 28, 1964); both Farbenfabriken Bayer; Chem. Abstr. *67*, 91314c (1967).

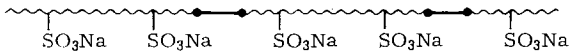
[13] *W. Keberle* and *D. Dieterich*, Brit. Pat. 1076688 (German Priority, Dec. 8, 1964), Farbenfabriken Bayer.

[14] *W. Keberle*, *D. Dieterich*, and *O. Bayer*, DBP 1237306 (Sept. 26, 1964), Farbenfabriken Bayer.

[15] *W. Keberle* and *D. Dieterich*, Brit. Pat. 1076909 (German Priority, (April 3, 1965), Farbenfabriken Bayer.

[16] *W. Keberle* and *E. Müller*, Brit. Pat. 1146890 (German Priority, June 8, 1966), Farbenfabriken Bayer.

[16a] *W. Keberle*, *H. Wieden*, and *D. Dieterich*, French Pat. 1496584 (German Priority, Oct. 16, 1965), Farbenfabriken Bayer.



(15)

3. Interaction Between Chains

The most suitable subjects for the investigation of the characteristic physical behavior of linear polyurethane ionomers are polyurethane polyammonium salts, since these can be obtained simply and specifically from the basic starting polyurethanes in a polymer-analogous reaction, and can be compared with these.

3.1. Coulomb Forces

The character of a segment polymer is greatly intensified by the formation of the ammonium ion from the tertiary nitrogen atom. Apolar polyether segments are separated by salt-like segments, which are held in the unraveled state by repulsion between neighboring positively charged nitrogen atoms.

In nonaqueous media, the unsolvated "salt segments" are brought together by Coulomb forces to form a sort of microionic lattice (Fig. 3), as a result of which the viscosity can increase by a factor of 1000 within a few seconds.

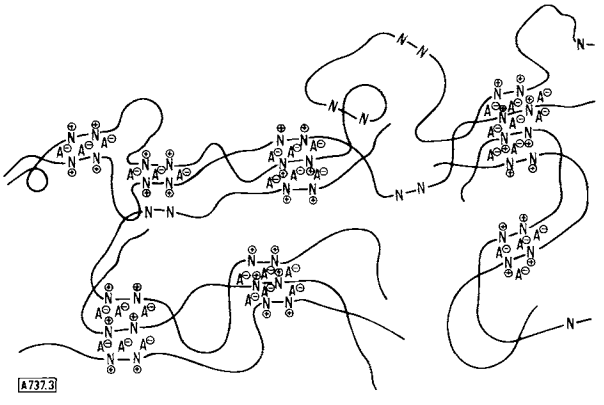


Fig. 3. Interchain association of the ionic segments of polyurethane ionomers in non-aqueous organic solution. $A^{\ominus}$ = anion.

When the association of the ionic centers (an intermolecular or intramolecular salt precipitation, so to speak) occurs at least twice (intermolecularly) in each macromolecule, it leads to the formation of aggregates ("micelles") whose length is many times that of the original molecules, and which are responsible for the observed enormous increase in viscosity. As in the case of soaps, the association is strongly dependent on concentration.

The morphology of the associates depends *inter alia* on the length of their structural units. Whereas high molecular weight polyurethane ionomers form a clear elastic gel in anhydrous acetone (uniform network), similar ionomers with lower molecular weights (approx. 10000) can form milky dispersions that exhibit the Tyndall effect and remain very fluid. Discrete sphereocolloid associates appear to be present in this case.

Interchain or, at high dilution, intrachain association due to Coulomb forces is indicated by the following observations:

The association decreases with increasing size of the organic residue on the quaternary nitrogen atom. A butyl group has a greater association-reducing effect than a methyl group, because of its bulk and better solvation by the organic solvent. Polarizable anions have the same effect.

The association also decreases with increasing dielectric constant, and also with the polarizability of the solvent (dioxane).

3.2. The Influence of Water

The association is very greatly reduced or eliminated by the addition of small quantities of water. Formamide and formic acid have the same effect, though to a smaller degree (Fig. 4). Similar associate formation and its disturbance by traces of water have been observed for solutions of soap in *e.g.* paraffin oil [17].

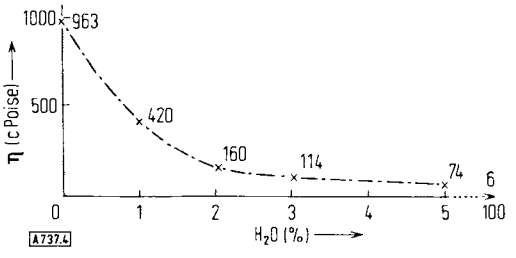


Fig. 4. Decrease in the viscosity of a 6.5% solution of polyurethane in acetone on addition of water.

Polyurethane ionomers are evidently completely solvated only in aqueous organic media (*e.g.* 80% acetone) (Fig. 5).



Fig. 5. Solvation of polyurethane ionomers in approx. 80% acetone +20% water (schematic). / / / = acetone, v v v = water.

3.3. Hydrophobic Interaction

A further increase in the water content of the water-acetone ratio leads again to an increase in viscosity, until finally the viscosity decreases again and the solution simultaneously becomes opaque.

As a result of the decrease in the acetone content, the polyether segments lose their solvation sheath, and they come together to form hydrophobic associates (Fig. 6), the viscosity again increasing at first. With decreasing acetone concentration, the associates rearrange into spherocolloids with the result that the solution becomes cloudy and its viscosity decreases considerably. The result is an aqueous colloidal sol having a low viscosity (Fig. 7).

[17] *J. G. Honig* and *C. R. Singleterry*, J. physic. Chem. *58*, 201 (1954); cf. *J. Stauff*: Kolloidchemie. Springer, Berlin 1960.

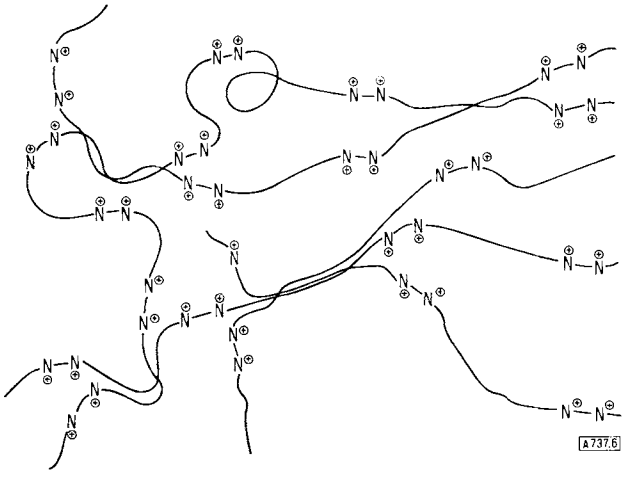


Fig. 6. Interchain association of the hydrophobic segments of polyurethane ionomers in approx. 60% acetone +40% water (schematic).

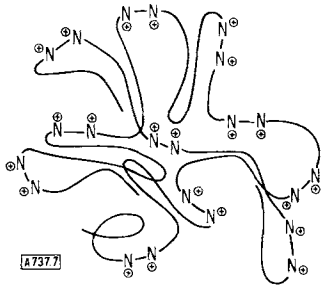


Fig. 7. Interchain association of the hydrophobic segments of polyurethane ionomers after rearrangement into the spherocolloid in approx. 40% acetone +60% water (schematic).

The increase in viscosity on addition of water is particularly pronounced when the tetracoordinate nitrogen carries a butyl group instead of a methyl, with the result that the hydrophobic bonding is strengthened.

The dissolved particles in the purely aqueous polyurethane sols are thus again associates, the size of which varies according to their hydrophilicity.

The polyurethane ionomers, like soaps, inverse soaps, and many dye salts thus belong to the group of association colloids. However, whereas the other substances mentioned are low molecular weight compounds that assume pseudo-high molecular weight character only on association to form micelles, the polyurethane ionomers are already high molecular weight segment polymers, which associate to form super macromolecules (according to *Staudinger*: "macromolecular associations"), giving particle weights (micelle weights) of more than 500000 and, in particular, "crosslinking" occurs by association.

3.4. Hydrogen Bonds

The polymer chains should also be oriented in the solvent-free state, polar segments tending to associate with polar segments, and apolar with apolar.

Thus the two types of association that are observed in succession on transition from the organic to the aqueous phase are now present together, so that we have an alternation of hydrophobic and hydrophilic heteropolar micelle segments. The X-ray diagram of stretched films shows two types of short-range order, which is in agreement with the above views.

On quaternization, the band due to the urethane NH group in basic segment polyurethanes, which is normally situated at 3340 cm^{-1}, shows a bathochromic shift of 30 to 80 cm^{-1}, depending on the degree of quaternization, with simultaneous broadening.

This observation can be interpreted as follows: The urethane groups, whose probability of encountering a urethane group of a neighboring chain was low before quaternization, are now arranged opposite one another (Fig. 8). Hydrogen bonds can therefore be formed, and these are responsible for the surprisingly high mechanical strength and the pronounced elastomeric character of the materials. Thus crosslinking has occurred as a result of molecular orientation, the forces responsible for this crosslinking being Coulomb forces and hydrogen bonds, and its strength being equivalent to that of chemical crosslinking.

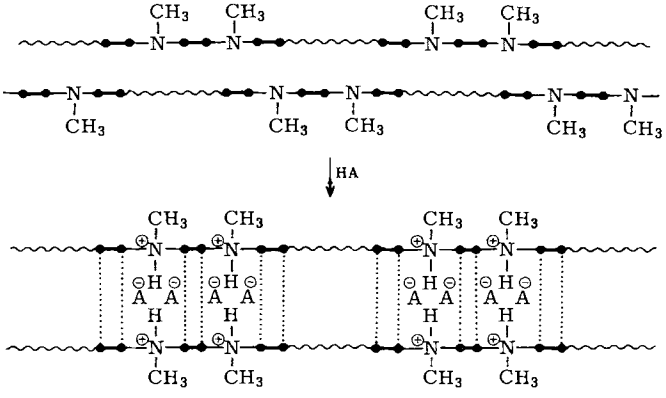


Fig. 8. Alignment of the polymer chains.

This view provides a plausible explanation for the influence of the position and number of the polyurethane groups on the "physical crosslinking". The anomalous increase in the permanent elongation with increasing degree of crosslinking, which is never found with covalently crosslinked elastomers, is now also understandable. Under tensile loads, strong forces are exerted on the hydrogen bonds, so that bonds are broken and reformed where the energy conditions are more favorable. The result is reorientation with partial slipping. The forces leading to reorientation are greater for the more strongly "crosslinked", less yielding materials, as are the possibilities for "engaging" during the slipping process; these materials accordingly exhibit higher permanent elongations.

If the ionomers are prepared from 4,4'-diisocyanatodiphenylmethane, NH-π-electron interaction cannot be ruled out.

However, bonding *via* protonated basic nitrogen, such as is assumed to occur in "HCl-crosslinked" butadiene/2-methyl-5-vinylpyridine copolymers [17a], is unlikely, since there is no great difference between polyurethane ionomers prepared with HCl and those prepared with CH_3Cl.

3.5. Tertiary and Quaternary Structure

Linear polyurethane ionomers are thus very stable "secondary-valence gels" as a result of the combined

[17a] *I. S. Ochrimenko, A. A. Petrov,* and *V. V. Vercholanzev,* Vysokomolekuljarnye Soedinenija *3*, 724 (1961); *4*, 1463 (1962).

action of electrostatic forces and hydrogen bonds. Chemical modification of the primary macromolecule, *i.e.* salt formation, leads to a tertiary structure, which has a greater influence on the properties of the polymer than might be expected from the small chemical change. This phenomenon is extremely important in natural polymers, such as collagen, pectins, and nucleic acids.

It must be assumed that "hydrophobic bonds", and hence quaternary structure [18], are also formed, since the properties are also influenced by the nature and length of the hydrophobic residues. This is true in particular of the polyether or polyester segments, but also applies to isocyanates and to the alkylating group of the quaternizing agent.

The presence of hydrophobic bonds would explain the facts that films and coatings deposited from aqueous polyurethane sols are insoluble in water and that such sols are in fact formed.

It would also explain the surprising aging resistance of aqueous polyester urethane sols. Whereas unstabilized polyester urethane elastomers suffer hydrolytic degradation by water, even finely divided sols of polyester urethane ionomers show practically no decomposition after three years.

The unsolvated hydrophobic polyester segments are tightly packed into the interior of the sol particles, while the strongly hydrated urethane segments with the mutually repelling ammonium groups are situated on the outside. The polyester groups are thus protected against hydrolysis as effectively as in the dry solid [19].

If on the other hand the ester groups are situated close to the ammonium nitrogen atom, as is the case in polyurethanes made from basic polyester after quaternization, sols prepared from these substances undergo hydrolytic degradation within a short time.

3.6. Comparison with Polypeptides

Polyurethanes are characterized by three types of interchain and intrachain interactions: 1. electrostatic forces, 2. hydrogen bonds, and 3. hydrophobic interactions. A comparison with proteins thus seems appropriate.

It is assumed [20] that the primary structure (chemical composition and sequence of the covalently bonded chains) of the polypeptides determines the total structure (*i.e.* secondary, tertiary, and quaternary structures) even of complicated proteins with very high molecular weights. The structures of higher order follow from the primary structure as a result of the three types of interactions mentioned.

Model substances for proteins must consist of covalent chains, and must satisfy the requirements for these interactions. Thus, by allowing salts to diffuse into solutions of degraded native polypeptides ("ionotropy"), *Thiele* was able to form anisometric associates that largely corresponded to the initial natural products [21].

Preliminary experiments showed that sols of polyurethane ionomers can also be solidified by electrolytes to give ionotropic gels. Hence it is to be expected that polyurethane ionomers can also form anisometric, complex structures, and they have the advantage of great versatility. In particular, the hydrophilic character can be decreased and the "plastic character" increased by variation of the structure and length of the hydrophobic segment.

The physico-chemically protein-like character of the polyurethane polyelectrolytes and of the ionomers is indicated *e.g.* by their excellent compatibility with gelatin [4, 22]. The use of polyurethane ionomers in medicine thus appears possible [23].

4. Aqueous Dispersions of Polyurethane Ionomers

The most remarkable and technically the most important property of all polyurethane ionomers is their ability to form stable dispersions with water spontaneously under certain conditions [10–16]. The products are binary colloidal systems in which a discontinuous polyurethane phase is dispersed in a continuous aqueous phase. The diameter of the disperse polyurethane particles can be varied between about 20 and 5000 nm.

Solutions of polyurethane ionomers in polar solvents such as acetone, methyl ethyl ketone, and tetrahydrofuran spontaneously form dispersions when water is stirred in. The organic solvent can then be distilled off to give solvent-free sols and latices of the ionomers. There is no need for the usual emulsification [24–28].

[18] *H. Sund* and *K. Weber*, Angew. Chem. *78*, 217 (1966); Angew. Chem. internat. Edit. *5*, 231 (1966).

[19] Cf. *e.g. J. C. Kendrew et al.*, Nature (London) *190*, 666 (1961), according to whom all the phenylalanine and methionine side chains in myoglobin are directed inward toward hydrophobic regions of the molecule.

[20] Cf. *H. Zahn*, Kolloid-Z. *197*, 14 (1964); *S. J. Singer*, Advances in Protein Chem. *17*, 1 (1962); *J. D. Bernal*, Disc. Faraday Soc. *25*, 7 (1958).

[21] *H. Thiele et al.*, Kolloid-Z. *197*, 26 (1964).

[22] *D. Dieterich*, *O. Bayer*, *W. Himmelmann*, and *H. Ulrich*, DBP 1179109 (April 13, 1963); Chem. Abstr. *61*, 16253g (1964); DBP 1260974 (US Priority, March 25, 1964); Chem. Abstr. *68*, 100658t (1968); *W. Keberle*, *W. Himmelmann*, *D. Dieterich*, *O. Bayer*, and *F. Nittel*, US-Pat. 3397989 (German Priority, March 17, 1965); *W. Keberle*, *W. Himmelmann*, *F. Nittel*, and *G. Oertel*, French Pat. 1533689 (German Priority, Aug. 6, 1966), all Farbenfabriken Bayer.

[23] Cf. *R. D. Falb*, Rubber Chem. Technol. *39*, 1288 (1966); *J. W. Boretos* and *W. S. Pierce*, Science (Washington) *158*, 1481 (1967); *D. J. Lyman*, Ann. New York Acad. Sci. *146*, 30 (1968); *S. N. Levine*, *ibid. 146*, 3 (1968).

[24] DRP 255129 (March 13, 1912), Farbenfabriken Bayer; Chem. Zbl. 1913 I, 362.

[25] *H. Fikentscher*, Kunststoffe *53*, 734 (1963).

[26] *P. Schlack*, DBP 920512 (June 16, 1943), Bobingen AG für Textilfasern.

[27] *H. Gensel* and *E. Windemuth*, DBP 819086 (Sept. 24, 1949); DBP 957564 (April 29, 1952); *E. Windemuth*, *H. Gensel*, and *W. Kreutzmann*, DBP 865593 (Nov. 30, 1950), all Farbenfabriken Bayer; Chem. Abstr. *49*, 3549h (1955); *53*, 12698c (1959); *52*, 14182 (1958).

[28] *J. E. Mallonee*, DAS 1097678 (US Priority, June 30, 1953), du Pont; Chem. Abstr. *52*, 19224d (1958).

4.1. Precipitation Dispersion

If 100 g of the polymer contains more than about 70 milliequivalents of cationic or anionic groups, the transition from the organic solution to the aqueous sol is perfectly continuous, and involves the stages described above (ion association, molecular solution hydrophobic association). The process can be referred to as "precipitation dispersion", since the addition of water leads first to precipitation of the hydrophobic polymer components, which are however stabilized by the ionic segments.

4.2. Dispersion by Phase Inversion

Polyurethane solutions with lower contents of ionic groups (even 5 milliequivalents/100 g of polymer can be sufficient for the formation of stable dispersions without emulsifiers) can also take up water with initial formation of a water-in-polymer emulsion (W/O type), which becomes more viscous with increasing water content until it undergoes phase inversion to give a nonviscous O/W emulsion. The water penetrates from the ionic groups into the body of the polymer, with the result that the structure changes and the polymer finally divides into spherical globules surrounded by water. The hydrophobic polyether or polyester segments are contained in the interior of these globules, while the urethane, or urea and salt groups are situated outside in the hydrated region.

4.3. The Boundary Layer

Whereas a polystyrene latex stabilized with soaps forms a clearly defined two-phase system (anhydrous disperse polystyrene phase and polymer-free continuous aqueous phase with a unimolecular layer of soap at the interface), the polyurethane ionomer dispersions have a more or less extensive boundary layer, where the water content increases in the outward direction. This effect becomes more pronounced as the concentration of ionic groups is increased; the turbidity decreases, and almost clear sols are ultimately obtained. The degree of swelling as found from light scattering and its angular variation is between 1.2 and about 5, depending on the content of ionic groups; this corresponds to effective concentrations of swollen particles of 60–85%. The pronounced structure viscosity points to a strong interaction between the dispersed particles, and together with other characteristics, such as the chemical crosslinking of concentrated sols as a whole, indicates that the state is similar to that of a solution.

For this reason and because of the hydration of the particles, care is necessary in the determination of particle sizes, since the particle diameter is a definite quantity only for the dried and unswollen material, which can be determined *e.g.* by electron microscopy. However, this method fails for soft ionomers with small particles (<200 nm), owing to the tendency of the particles to coalesce and form films.

The particle size distribution is generally narrow in dispersions prepared by "precipitation dispersion", and much broader in the coarser dispersions obtained by phase inversion (Fig. 9, curves 1 and 2, 3 and 4).

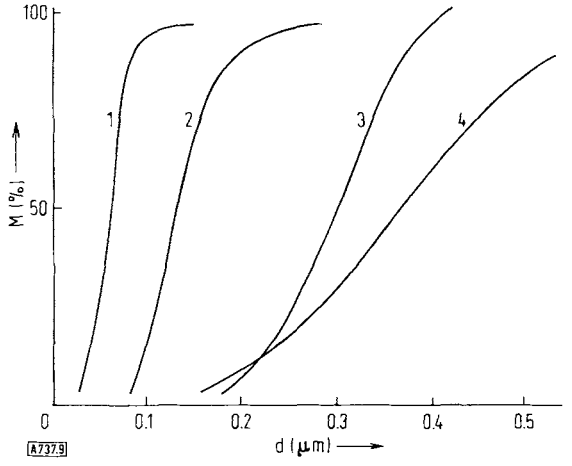


Fig. 9. Particle size distribution of some polyurethane dispersions, calculated from the change in light transmission, *i.e.* of the concentration, with time in the ultracentrifuge. Correction according to *Mie*, taking into account the degree of swelling (determination Dr. *Scholtan* and Dr. *Lie*).
M = weight fraction; d = diameter; 1–4: see text.

Dispersions containing *e.g.* 2–5 milliequivalents of ionic groups/100 g of polymer exhibit only slight swelling and give particle sizes of around 1 μm. Dispersions of this nature can thus be prepared with solids contents of 45–60% and with low viscosities, even when their molecular weights are very high.

Rheopexy, *i.e.* a sudden increase in viscosity under mechanical stress, is often observed with particle diameters of between 2 and 5 μm and with concentrations greater than 45%. In the extreme case, sampling is impossible, since *e.g.* insertion of a spoon leads to reversible solidification of the surrounding dispersion. The interaction between the particles must be particularly strong in this case because of the absence of a film of emulsifier.

4.4. Redispersible Suspensions

If the content of ionic groups is reduced still further, dispersion yields polyurethane suspensions with particle diameters greater than 5 μm and up to about 1–2 mm. Such suspensions are generally uninteresting; they sediment rapidly, with the result that the particles stick together and coalesce. If however chemical crosslinking is carried out during or after dispersion, the result is a suspension of elastomer particles, and though these particles sediment, they can be suspended at any time by simple stirring. Polyurethane powders can also be prepared in this way [29].

Polyurethanes can also be obtained in the form of fine, short fibers suspended in water (Fig. 10). Depending on the structure and the method of preparation, therefore, polyurethane ionomer particles ranging in size

[29] *H. Witt* and *D. Dieterich*, DBP 1282962 (April 28, 1966); *D. Dieterich* and *H. Witt*, Brit. Pat. 1158088 (German Priority, Feb. 1, 1967), both Farbenfabriken Bayer.

from a few macromolecules (Fig. 11) to the mm range can be obtained (Fig. 12). The unswollen dispersion particles in Figure 13 are typical of ionomers.

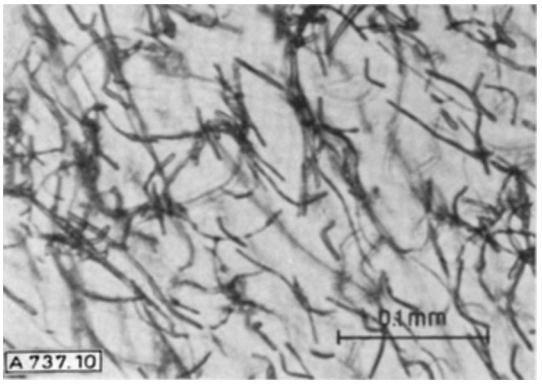


Fig. 10. Polyurethane suspension, fibrous, optical microscope, 200×

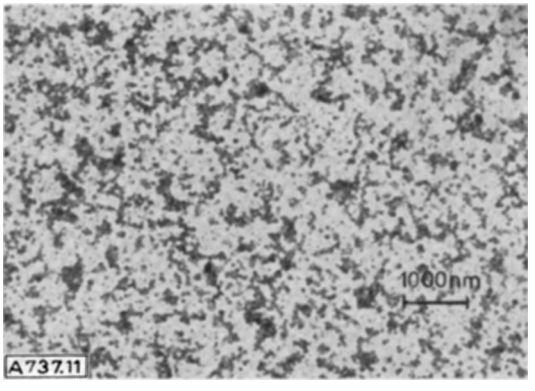


Fig. 11. Polyurethane sol, electron microscope, 7500× (recorded by Dr. *Born*).

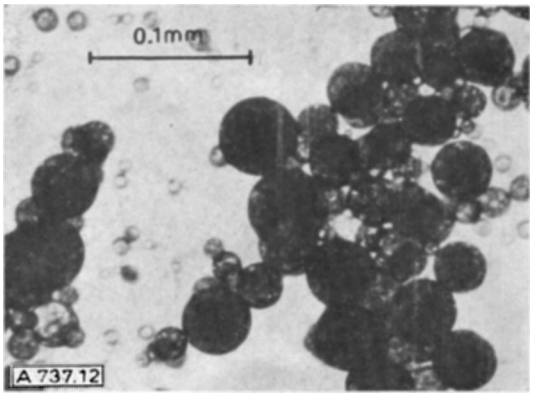


Fig. 12. Polyurethane suspension spherical, optical microscope 220×.

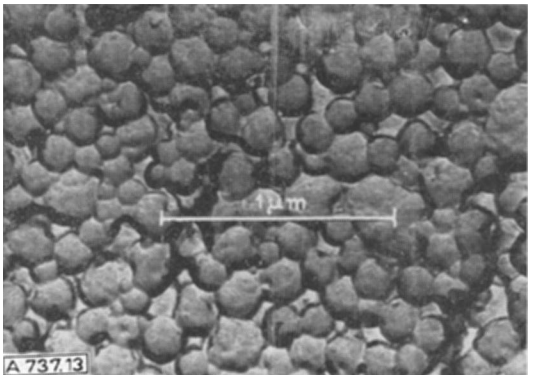


Fig. 13. Polyurethane latex, freeze-dried (carbon replica), 31 000× (recorded by Dr. *Menold*). The rough surface of the particles indicates shrinkage of the particles during freeze-drying.

5. Use

Polyurethane ionomers allow the controlled modification of the flexibility, dimensional stability, and swellability of photogelatin [22]. The two components evidently form a sort of simplex by interaction of the cationic or anionic centers of the polyurethane with the amphoteric zwitterionic centers of the gelatin and by hydrogen bonding between urethane and amide groups.

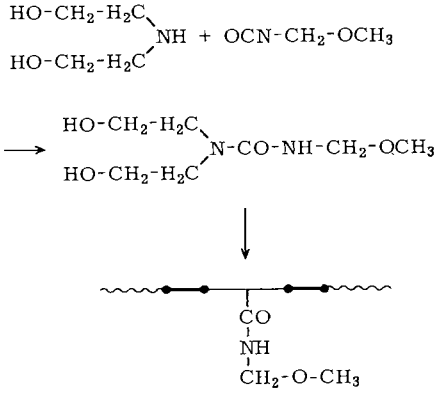
Polyurethane dispersions, as aqueous one-component systems that have reacted to completion, can be used wherever reactive polyurethane systems from organic solvents have been used in the past, or where the application of such systems has been impossible because of the solvent content, despite the desirability of the valuable properties of the polyurethane (elasticity, tensile strength, abrasion resistance, good low-temperature behavior, and high solvent resistance).

The most interesting characteristic of these dispersions is their outstanding film-forming ability which is practically equal to that of organic solutions. Even dispersions of very hard polyurethanes, such as are required for paints, dry even at room temperature or below to give high-gloss coatings.

Soft polyurethane ionomers are suitable for the coating and impregnation of textiles, where their good resistance to perchloroethylene is valuable.

To improve their water-resistance, polyurethane ionomers can also be chemically crosslinked *e.g.* by polyisocyanates or polyfunctional alkylating agents. Formaldehyde and its derivatives have proved particularly useful for this purpose [30]. They react even at room temperature in the presence of aliphatic urethane or urea groups.

Methoxymethyl isocyanate may be used for the synthesis of one-component systems containing reactive groups [31].



[30] *D. Dieterich* and *E. Müller*, DBP 1187012 (March 13, 1963); *E. Müller* and *D. Dieterich*, DAS 1284963 (May 3, 1965); both Farbenfabriken Bayer.

[31] *G. Oertel*, *H. Holtschmidt*, *K. Wagner*, and *K. E. Zenner*, DBP 1244410 (Feb. 3, 1965); *D. Dieterich*, *W. Keberle*, and *E. Müller*, DBP 1241104 (June 5, 1965); *W. Keberle* and *D. Dieterich*, Belg. Pat. 682689 (German Priority, June 18, 1965); all Farbenfabriken Bayer.

Anionic polyurethane dispersions are more stable than their cationic counterparts toward electrolytes (particularly in the presence of sulfonate groups), and hence have a better pigment tolerance, and they have the additional advantage that they can be combined with commercial polymer dispersions and additives. Cationic products exhibit particularly good adhesion, *e.g.* even to glass.

There are possibilities for the use of crosslinked redispersible polyurethane ionomer suspensions in the production of microporous sheet materials (synthetic leather).

Our own work in this field has been supported by a number of colleagues from the applications, analytical, engineering, and technological departments. Special contributions were made by Dr. M. Hoffmann (Polymer Analysis) and Dr. Erwin Müller, who directed this development. We are grateful to all those mentioned. Special thanks are due to the former head of the Scientific Laboratories, Prof. Dr. O. Bayer, who initiated this work in 1962 and furthered its progress by numerous discussions.

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Reactions with Addition Compounds Containing Activated Formic Acid

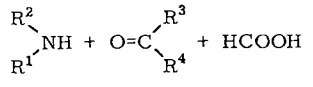
By K. Wagner[*]

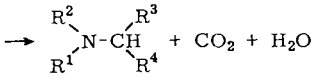
Dedicated to Professor K. Hansen on the occasion of his 60th birthday

Addition compounds of formic acid with tertiary organic bases in ratios higher than that required for salt formation (3 : 1 and 2 : 1 adducts) contain formic acid in a highly activated form. In particular, the 3 : 1 adducts of formic acid with trimethylamine and triethylamine are liquid reducing agents that are convenient to handle and are suitable for use in many selective reductions. These addition compounds have a surprisingly strong reducing action on sulfur dioxide, which is rapidly converted, even at low concentrations, into crystalline rhombic sulfur. Sulfones and polysulfones can be prepared in good yields by three-component reactions from activated formic acid, sulfur dioxide, and polarized vinyl compounds.

1. Introduction

In the Leuckart-Wallach reaction, formic acid acts as a strong reducing agent in the presence of carbonyl compounds.





R^1 - R^4 = H, Alkyl, Aryl

This method of aminoalkylation was greatly extended by *Wietzel*[1] and *Clarke*[2] with the use of formaldehyde as the carbonyl component in the reduction. The reaction is widely used as an elegant method of permethylation.

In studies on cleavage reactions of hexamethylenetetramine with acetic anhydride[3] and phosgene[4], anhydrous formic acid[5] was also used. Liquid, distillable cleavage products, whose compositions were unknown at first, but which possessed reducing properties, were isolated. The reducing power of these compounds was much greater than the well-known reducing action of formic acid.

2. Methods for the Preparation of Addition Compounds Containing Activated Formic Acid and their Thermal Behavior

2.1. Preparation and Constitution of the Addition Compounds

The reaction of concentrated formic acid with hexamethylenetetramine yields a liquid, distillable reaction product having the analytical composition $C_6H_{15}NO_6$

[*] Dr. K. Wagner
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509 Leverkusen-Bayerwerk (Germany)

[1] *R. Wietzel*, German Pat. – 12 q I. 19. 30(5)(1930), I.G. Farben.

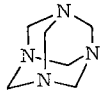
[2] *H. T. Clarke*, J. Amer. chem. Soc. *55*, 4571 (1933).

[3] *H. Holtschmidt*, unpublished.

[4] *H. Holtschmidt* and *K. Wagner*, DBP 1132118 (Feb. 1, 1961), Farbenfabriken Bayer.

[5] *H. Holtschmidt* and *K. Wagner*, unpublished.

(b.p. 87 °C/14 torr), together with small quantities of dimethylformamide and methylformamide. When this reaction is followed with the aid of gas analysis, it is found that the compound $C_6H_{15}NO_6$ can be obtained in practically quantitative yield and without by-products only if formaldehyde is also present, the proportions being at least 6 moles of formaldehyde and 24 moles of formic acid per mole of hexamethylenetetramine.



$$+ 6\ CH_2O + 24\ HCOOH \qquad (1)$$

$$\longrightarrow 4\ C_6H_{15}NO_6 + 12\ CO_2 + 6\ H_2O$$

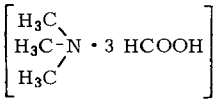
The CO_2 balance found under these conditions clearly points to a permethylation corresponding to the Leuckart-Wallach reaction. The unknown compound should therefore contain bound trimethylamine and this is in fact the case as is shown by equations (2) to (4).

$$C_6H_{15}NO_6 + 3\ NaOH \rightarrow (CH_3)_3N + 3\ HCOONa + 3\ H_2O \quad (2)$$

$$C_6H_{15}NO_6 + 3\ C_6H_5{-}N{=}C{=}O \rightarrow (CH_3)_3N + 3\ C_6H_5{-}NH{-}CHO + 3\ CO_2 \quad (3)$$

$$C_6H_{15}NO_6 + HCl \rightarrow [(CH_3)_3NH]^{\oplus}Cl^{\ominus} + 3\ HCOOH \quad (4)$$

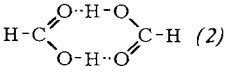
The liquid addition compound $C_6H_{15}NO_6$ [6] has the constitution *(1)*. An identical adduct can be obtained



(1)

in quantitative yield by passing one mole of gaseous trimethylamine into three moles of anhydrous formic acid.

The IR spectrum of *(1)* contains characteristic bands for both the carboxyl and the carboxylate groups. The very pronounced broadening of the OH bands indicates that extremely strong hydrogen bonds must be present. This agrees with the molecular structure found for formic acid, for which an eight-membered cyclic chelate *(2)* [7,8] with hydrogen bonds has been detected both in the liquid phase and in the vapor within a certain temperature range.



(2)

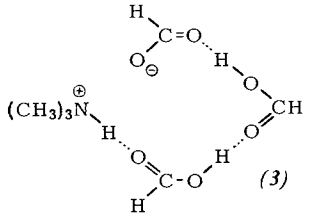
Comparison of the ^{1}H-NMR spectra of the addition product and of the corresponding 1 : 1 salt of trimethylamine and formic acid shows that the electron density in the position of the alkyl protons is lower in the addition compound than in the salt.

[6] *K. Wagner* and *H. Holtschmidt*, German Pat. 1233398 (March 14, 1964), Farbenfabriken Bayer

[7] *J. Karle* and *L. O. Brockway*, J. Amer. chem. Soc. *66*, 574 (1944).

[8] *R. Hofstadter*, J. chem. Physics *6*, 540 (1938).

On the basis of IR-spectroscopic observations, elementary analysis, and osmotic molecular weight determinations in halogenated hydrocarbons such as chloroform, the constitution *(3)* has been proposed for the addition product of three moles of formic acid with one mole of trimethylamine [9].



(3)

2.2. Thermal Properties of the 3 : 1 and 2 : 1 Addition Compounds

The formation of these adducts is not restricted to trimethylamine as the organic base. Many tertiary aliphatic, cycloaliphatic, and heterocyclic amines react with formic acid beyond the salt formation stage, often with formation of liquid 1 : 2 or 1 : 3 adducts. The 1 : 3 adducts are the more stable, and are also the more interesting from the chemical point of view. They are stable up to about 140 °C, and can be distilled under reduced pressure (see Table 1); they decompose above 140 °C in the absence of catalysts [eq. (5)] or below 140 °C in the presence of cuprous chloride and noble metals [eq. (6)] [10].

$$[R_3N \cdot 3\ HCOOH] \xrightarrow{> 140°\ C} R_3N + 3\ CO + 3\ H_2O \quad (5)$$

$$[R_3N \cdot 3\ HCOOH] \xrightarrow[\substack{Cu_2Cl_2\\ \text{noble metal}}]{90\text{–}120°C} R_3N + 3\ H_2 + 3\ CO_2 \quad (6)$$

Table 1. Distillable adducts of formic acid and tertiary bases.

	B.p. (°C/14 torr)
$(H_3C)_3N + 3\ HCOOH$	87
$(C_2H_5)_3N + 3\ HCOOH$	94
$(C_4H_9)_3N + 3\ HCOOH$	102
$(C_2H_5)_3N + 2\ HCOOH$	84

The addition compounds with *N*-methylpiperidine, *N*-methylmorpholine, and *N,N*-dimethylbenzylamine readily decompose in accordance with eq. (5) on distillation. Adducts of imidazole and substituted imidazoles and of 1,4-diazabicyclo[2.2.2]octane cannot be distilled.

3. Reductions with Addition Compounds containing Activated Formic Acid

The study of the decomposition of the adducts containing activated formic acid by traces of Cu_2Cl_2 and palladium in accordance with eq. (6) led to two reduction methods based on different reactions.

[9] *M. Pestemer*, *N. Joop*, and *K. Wagner*, unpublished.

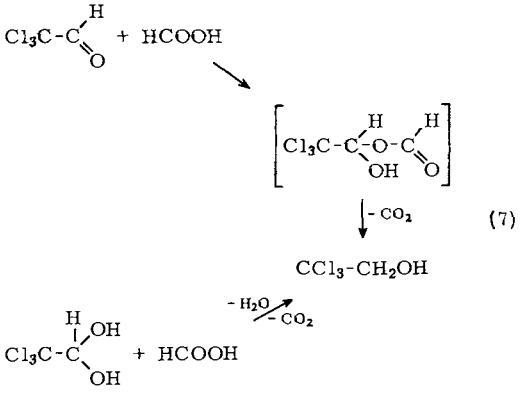
[10] *K. Wagner*, unpublished.

One of these reductions (cf. Section 3.2) is a true hydrogenation, in which the actual reducing agent is hydrogen formed from the adducts in accordance with eq (6) and then catalytically activated by copper(I) chloride and noble metals. The other method, in which no free hydrogen occurs (see Section 3.1), allows the selective reduction of α-halogenated carbonyl compounds in good yields.

3.1. Selective Reduction of Polarized Carbonyl Compounds with Activated Formic Acid

The selective reduction of α-halogeno aldehydes and ketones to the alcohols does not proceed by hydrogenation following reaction (6); there is consequently no need to add copper(I) chloride, noble metals, or hydrogenation catalysts such as Raney nickel. On the contrary, these additives greatly reduce the yield, since they make the reduction less selective, and reductive dehalogenation occurs.

A simple laboratory method will be described for the selective reduction of chloral hydrate to trichloroethanol [11] [*].



(7)

The driving force for this reaction is probably the tendency of formic acid to add to polarized double bonds; in the case of carbonyl compounds this yields hemiacylals of aldehydes, which are then decarboxylated by nucleophilic attack by the tertiary base.

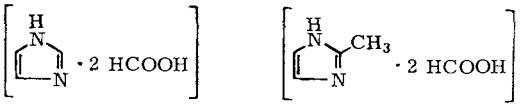
Application of this reduction to chloral, chloral hydrate, or chloral-ethanol adduct yields trichloroethanol in yields of more than 87%. This reduction is simpler and much faster than the classical method for the preparation of trichloroethanol, *i.e.* the *Meerwein-Ponndorf* reduction of anhydrous chloral.

The preferred reducing agents are the liquid 3 : 1 adducts of formic acid with trimethylamine, triethylamine, dimethylethylamine, or diethylmethylamine, since these can be purified by distillation. The compound to be reduced is largely dissolved in the liquid addition compound, and fresh formic acid is continuously added to the system at a rate corresponding to the rate of liberation of CO_2 at 95 to 100 °C, so that the 3 : 1 adduct is still present in the reaction mixture at the end of the reaction.

[11] *K. Wagner*, US-Pat. 3397963 (April 1, 1965), Farbenfabriken Bayer.

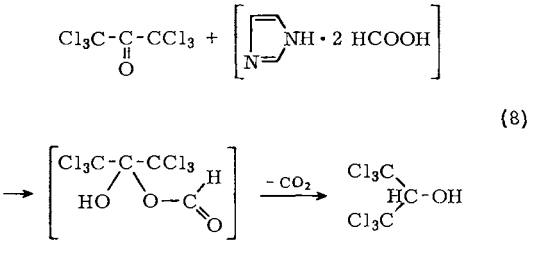
[*] The abbreviation $HCOOH_a$ is used for $[(CH_3)_3N \cdot 3\,HCOOH]$ and $[(C_2H_5)_3N \cdot 3\,HCOOH]$.

Even unstable ketones such as hexachloroacetone and fluorinated ketones can be reduced to the secondary alcohols in good yields and under mild conditions by activation of formic acid with imidazole or 2-methylimidazole. The resulting adducts *(4)* and *(5)* are remarkably fluid, and have a viscosity of about 34 cp at room temperature.



(4) *(5)*

Hexachloro-2-propanol has only recently been described [12]. It was prepared, not by reduction of hexachloroacetone, but by reaction of anhydrous chloral with alkali metal trichloroacetates; the yields are low (35–36%) and the purity of the compound (m.p. 85–86 °C) is only moderate. The selective reduction in accordance with eq. (8) [13], on the other hand, can be carried out very simply.



(8)

Hexachloroacetone is added dropwise over about 2 hours to the imidazole-formic acid adduct at 55 to 65 °C. Concentrated formic acid is added continuously at a rate of about 2.1 g of formic acid per liter of carbon dioxide liberated. After the reduction the water-soluble imidazole adduct is removed by extraction with water, and hexachloro-2-propanol crystallizes out immediately (m.p. 89 °C); the yield is about 89%.

3.2. Hydrogenations by Catalytic Decomposition of the Addition Compounds

Under the influence of catalysts such as platinum, rhodium, and iridium, formic acid slowly decomposes even at room temperature into hydrogen and carbon dioxide [14]. This decomposition of formic acid can be greatly accelerated in the addition compounds by the use of copper(I) chloride and palladium on active charcoal as the catalyst.

The hydrogen formed in this case is activated by the noble metal catalyst, so that many aldehydes, ketones, and functional groups such as $-NO_2$, $-NO$, $-NHOH$, $-N(\rightarrow O)=N-$, $-N=N-$, $-NH-NH-$, $-NH-NH_2$, $=NOH$, $=NH$, and $=N-R$ can be hydrogenated in good yields, or $>N-N<$ bonds can be reductively broken. This reduction method practically corre-

[12] *R. Haszeldine, R. Farmer*, and *H. Goldwhite*, Brit. Pat. 1019891 (Feb. 9, 1966); Chem. Abstr. *64*, 12549 (1966).

[13] *K. Wagner*, German Pat. Appl. P 1793243.3 (April 21, 1968), Farbenfabriken Bayer.

[14] *I. E. Adadurow*, Ž. fiz. Chim. *2*, 142 (1931); Chem. Zbl. *1933*, I 1240.

sponds to the conventional hydrogenation methods, but proceeds at atmospheric pressure. It is recommended in the laboratory for the reduction of sparingly soluble compounds or for cases where it is desirable to obtain the *N*- or *O*-formylated derivatives of the hydrogenation products in a single operation. Nitriles, dinitriles, and polyacrylonitrile cannot be hydrogenated, since addition of the activated formic acid to the nitrile group predominates over hydrogenation.

4. Reactions of Addition Compounds Containing Activated Formic Acid with Sulfur Dioxide

4.1. Reduction of Sulfur Dioxide to Crystalline Sulfur

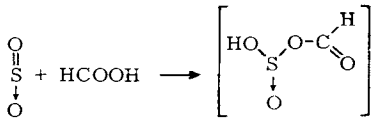
Probably the most striking example of the high activity of the formic acid in the addition compounds is the fast and practically quantitative reduction of sulfur dioxide to crystalline rhombic sulfur[15]. Sulfur dioxide itself is well known to be a relatively strong reducing agent; however, it behaves as a strong oxidizing agent toward these addition compounds. Since even very dilute sulfur dioxide can be readily reduced and the resulting crystalline sulfur can always be filtered out extremely easily, this reaction has been investigated in connection with the cleaning of industrial waste gases.

Overall reaction:

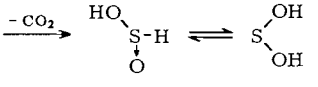
$$8\,SO_2 + 16\,HCOOH \rightarrow S_8 + 16\,CO_2 + 16\,H_2O \qquad (9)$$

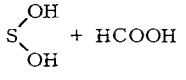
Under normal conditions, 44.8 liters of CO_2 are liberated per g-atom of sulfur.

Reaction steps:

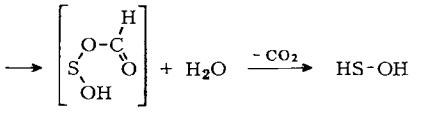


(10)



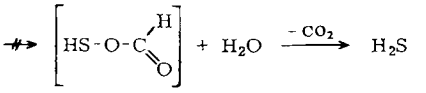


(11)



HS-OH + HCOOH

(12)



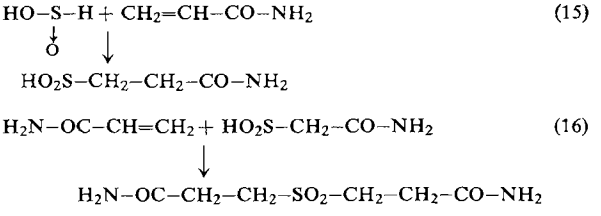
$$2\,H_2S + SO_2 \longrightarrow 3\,S + 2\,H_2O \qquad (13)$$

$$8\,HS\text{-}OH \longrightarrow S_8 + 8\,H_2O \qquad (14)$$

It can be concluded from the investigation of the reaction by gas analysis that sulfur dioxide is not reduced to hydrogen sulfide, and therefore that the sulfur formation cannot be explained by the well known reduction in accordance with eq. (13). When the reduction is carried out at various temperatures and with simultaneous checking of the CO_2 balance, it is found that the reduction leads first in accordance with eq. (10) to sulfoxylic acid (H_2SO_2), which it in turn reduced to the very unstable hydroxysulfane (H_2SO) [eq. (11)]. The hydroxysulfane is so unstable that instead of undergoing further reduction in accordance with eq. (12) it decomposes readily, as a sulfur homolog of hydrogen peroxide, into water and probably free-radical sulfur, which achieves stability by formation of S_8 and is obtained as rhombic sulfur eq. (14).

4.2. Interception of Short-Lived Intermediates of the Reduction of Sulfur Dioxide by Three-Component Reactions

The intermediates involved in the reduction, such as sulfoxylic acid and hydroxysulfane, can be used for a simple preparation of organic sulfinic acids, sulfenic acids, and sulfoxides, and particularly of monosulfones and polysulfones (see Table 2)[16]. These preparations can be carried out very readily and in excellent yields by dissolving vinyl compounds in the adducts containing activated formic acid before the introduction of sulfur dioxide, adding small quantities of polymerization inhibitors, and introducing SO_2 into the reaction mixture at 90 °C.



(15)

(16)

Table 2. Monosulfones prepared by three-component reactions.

Vinyl compound	Monosulfone	M.p. (°C)
$CH_2=CH-COOH$	$(HOOC-CH_2-CH_2)_2SO_2$	220
$CH_2=CH-CO-NH_2$	$(H_2N-OC-CH_2-CH_2)_2SO_2$	228
$CH_2=C(CH_3)-CO-NH_2$	$(H_2N-OC-CH(CH_3)-CH_2)_2SO_2$	178
$CH_2=CH-COOC_2H_5$	$(C_2H_5OOC-(CH_2)_2SO_2$	86
$CH_2=CH-CN$	$(NC-CH_2-CH_2)_2SO_2$	86–87
$CH_2=CH-SO_2-CH_3$	$(CH_3-SO_2-(CH_2)_2)_2SO_2$	268

The sulfones listed can in most cases be very readily isolated, whereas the primary products, *i.e.* the organic sulfuric acids, can be obtained only with difficulty because of their instability.

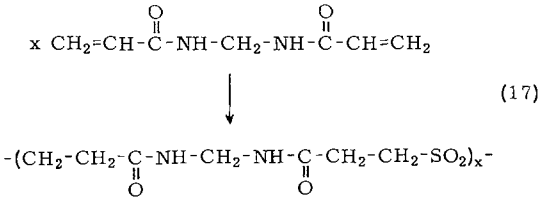
4.3. Interception of Short-Lived Intermediates of the Reduction of Sulfur Dioxide for the Synthesis of High Molecular Weight Polysulfones

As is shown by equations (15) and (16), sulfoxylic acid (H_2SO_2) reacts as a bifunctional compound. It reacts

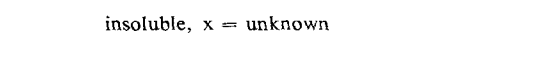
[15] *K. Wagner*, German Pat. Appl. P 1442692.7 (April 4, 1964); US-Pat. 3397963 (April 1, 1965).

[16] *K. Wagner*, DBP 1222048 (Dec. 8, 1964), Farbenfabriken Bayer.

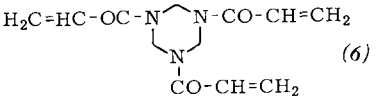
with suitable vinyl compounds to form sulfinic acids, and if the reaction mixture still contains activated vinyl compounds, sulfones are very rapidly formed. High molecular weight polysulfones can thus be readily prepared by polyaddition reactions with sulfoxylic acid if suitable divinyl compounds are used as acceptors.



(17)



insoluble, x = unknown



(6)

insoluble, three dimensionally crosslinked polysulfone

With introduction of sulfur dioxide at a suitable rate during the preparation of polysulfones, water-soluble polysulfones with sulfinic acid end groups can also be prepared by this method.

The results obtained in the reduction of sulfur dioxide have led to the investigation of the action of activated formic acid on nitrous gases, dinitrogen trioxide, and nitrous acid. It is difficult to isolate intermediates of the reduction. The utmost care is necessary in the treatment of even small reaction mixtures from the reduction of potassium and sodium nitrites, since violent decompositions have sometimes been observed.

5. Addition Compounds Containing Activated Formic Acid as Formylating Agents and as Solvents

Many of the liquid adducts, particularly those of one mole of trimethylamine or triethylamine with three moles of formic acid can be used as formylating agents for *N*- and *O*-formylations, since the addition compounds are generally good solvents for high molecular weight polyols and polyamines, and the formylations are accelerated in these solvents. Reductive degradations of natural polymers such as cellulose and polypeptides proceed particularly readily.

I am grateful to Professor Dr. Holtschmidt for the use of his unpublished experimental results on the hexamethylenetetramine-formic acid cleavage reaction, to Professor Dr. Pestemer for spectroscopic studies, to Dr. Joop for NMR measurements, to Dr. Fauss for osmotic molecular weight determinations, and to Dr. Klauke for the preparation of partly fluorinated ketones.

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Chlorosulfenylated Carbonic Acid Derivatives

By G. Zumach and E. Kühle[*]

Dedicated to Professor K. Hansen on the occasion of his 60th birthday

The present article deals first with the synthesis of chlorocarbonylsulfenyl chloride and its imino analogs. The chemical behavior of these bifunctional compounds is illustrated for selected examples. Special attention is given to the syntheses of five-membered heterocycles containing sulfur, oxygen, and/or nitrogen.

1. Introduction

The present article deals with compounds that can be regarded both as carbonic acid derivatives and as sulfenic acid derivatives. Two compounds of this series, *i.e.* trichloromethanesulfenyl chloride *(1)* and *N*-dichloromethylenesulfenylamide chloride *(2)*, have been known for a long time.

Trichloromethanesulfenyl chloride *(1)* consists formally of an orthocarbonyl trichloride group and a sulfenyl chloride group. It was first synthesized more than 100 years ago by *Rathke*[1] by chlorination of carbon disulfide in the presence of iodine, and is still produced on the large scale by the same method.

$$S{=}C{=}S + 3\,Cl_2 \xrightarrow[I_2]{} Cl_3C{-}SCl + SCl_2 \qquad (1)$$

In 1924, *Kaufmann* and *Liepe*[2] obtained "thiocyanogen trichloride" by chlorination of thiocyanogen; this product was later found to be *(2)*[3].

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[1] *B. Rathke*, Ber. dtsch. chem. Ges. *3*, 858 (1870).

[2] *H. P. Kaufmann* and *J. Liepe*, Ber. dtsch. chem. Ges. *57*, 923 (1924).

[3] *E. Kühle*, *B. Anders*, and *G. Zumach*, Angew. Chem. *79*, 663 1967; Angew. Chem. internat. Edit. *6*, 649 (1969).

$$NCS{-}SCN + 3\,Cl_2 \rightarrow 2\,ClSN{=}CCl_2$$
(2)

Whereas *(2)* behaves in most reactions as a masked sulfur dichloride, with elimination of cyanogen chloride, the chlorosulfenylated carbonic acid derivatives to be described here are derived from trichloromethanesulfenyl chloride *(1)*:

$$Cl{-}\overset{\overset{X}{\|}}{C}{-}S{-}Cl$$

(1), X = Cl, Cl
(7), X = O
(3), X = S
(9), X = N–R
(4), X = Cl, SCl

We shall now consider chlorocarbonylsulfenyl chloride *(7)*, the iminochloromethanesulfenyl chloride *(9)* [4], chlorothiocarbonylsulfenyl chloride *(3)*, and dichloromethanebis(sulfenyl chloride) *(4)*. Chlorothiocarbonylsulfenyl chloride *(3)*, which should occur as an intermediate in the chlorination of carbon disulfide, has not yet been prepared so far as we know, but was described by *Klason* [5] as the product of the thionation of thiophosgene.

$$Cl{-}\overset{\overset{S}{\|}}{C}{-}Cl + S \xrightarrow[130-150\,^\circ C]{} Cl{-}\overset{\overset{S}{\|}}{C}{-}SCl$$
(3)

The very high boiling point of 140 °C at about 15 torr given by *Klason* cannot be correct for this compound, since thiophosgene boils at 73–74 °C under normal pressure.

Dichloromethanebis(sulfenyl chloride) *(4)*, which is also an intermediate of the chlorination of carbon disulfide, has however been obtained in this way in the presence of UV light as a compound that can be isolated only in the cold, and that has an extrapolated boiling point of 183 °C [6]:

$$S{=}C{=}S \xrightarrow[UV]{Cl_2} Cl_2C(SCl)_2$$
(4)

2. Syntheses

2.1. Syntheses of Chlorocarbonylsulfenyl Chloride

Chlorocarbonylsulfenyl chloride *(7)* (b.p. = 98 °C, n_D^{20} = 1.5165) was first obtained by thermolysis of alkoxydichloromethanesulfenyl chlorides *(6)* at 60 to 70 °C [7]. Since the required starting compounds are obtainable only from alkyl *S*-methyl dithiocarbonates *(5)* [8], this synthesis is of little preparative value.

$$\text{Alkyl-O}{-}\overset{\overset{S}{\|}}{C}{-}SCH_3 \xrightarrow{Cl_2} \text{Alkyl-O}{-}CCl_2{-}SCl + CH_3S{-}CCl_3$$
(5) *(6)*

$$(6) \xrightarrow{60-70\,^\circ C} O{=}C{-}SCl + \text{Alkyl-Cl}$$
Cl
(7)

Chlorocarbonylsulfenyl chloride *(7)* is now obtainable on the industrial scale by a simple process that proceeds smoothly. This process makes use of trichloromethanesulfenyl chloride *(1)*, which is subjected to partial hydrolysis with sulfuric acid [9]. Concentrated sulfuric acid is used with the quantity of water required for the hydrolysis, and the components are heated at 45 to 50 °C. Chlorocarbonylsulfenyl chloride *(7)* separates out as an oil that is immiscible with sulfuric acid.

$$Cl_3C{-}SCl \xrightarrow[H_2SO_4]{H_2O} ClC(=O){-}SCl + 2\,HCl$$
(1) *(7)*

2.2. Syntheses of Iminochloromethanesulfenyl Chlorides

Iminochloromethanesulfenyl chlorides *(9)* always occur as intermediates in the chlorination of isothiocyanates *(8)* to form isocyanide dichlorides *(10)* [3].

Whereas aliphatic compounds *(9)* are mostly unstable and can be handled only with special precautions (dis-

$$R{-}N{=}C{=}S \xrightarrow{Cl_2} R{-}N{=}C(Cl)(SCl) \xrightarrow[-SCl_2]{Cl_2} R{-}N{=}CCl_2$$
(8) *(9)* *(10)*

Table 1. Iminochloromethanesulfenyl chlorides *(9)* [a].

R	B.p. (°C/torr) (M.p. (°C))	Ref.	Yield (%) [b]
CH_3	38/12	[10]	31
i-C_3H_7	63–65/22	[10]	54
n-C_4H_9	80–81.5/11	[10]	54
C_6H_{11}	76–78/0.2	[10]	61
C_6H_5	84–86/0.15	[3, 11]	97
p-Cl–C_6H_4	109–112/0.25	[10]	73
C_6H_5CO	(91–92)	[12]	12
p-Cl–C_6H_4CO	(115–116)	[13]	70
C_6H_5–C(=NC_6H_5)	(189–190)	[14]	
$(CH_3)_2NSO_2$	104–105/0.075	[3]	
p-Cl–$C_6H_4SO_2$	[c]	[3]	

[a] Arylenedi(iminochloromethanesulfenyl chlorides) ClS–C(Cl)=N–R–N=C(Cl)–SCl: R = *p*-C_6H_4 m.p. 82–83 °C [11]; R = 4-CH_3-1,3-C_6H_3, m.p. 75–75.5 °C [11]; R = *p*-C_6H_4–N=N–C_6H_4(*p*), m.p. 158–160 °C [3].
[b] Yields not optimized. [c] Characterized as a derivative.

[4] Formerly known as "mustard oil chlorides".

[5] *P. Klason*, Ber. dtsch. chem. Ges. *20*, 2376 (1887).

[6] *H. M. Pitt* and *H. Bender*, US-Pat. 3331872 (April 13, 1964), Stauffer Chem. Comp.

[7] *B. Freedman*, DAS 1203742 (Oct. 26, 1963), California Res. Comp.

[8] *I. B. Douglass* and *C. E. Osborne*, J. Amer. chem. Soc. *75* 4582 (1953).

[9] *W. Weiss*, German Pat. 1224720 (Nov. 11, 1964), Farbenfabriken Bayer AG.

[10] *G. Zumach*, unpublished.

[11] *G. Ottmann* and *H. Hooks jr.*, Angew. Chem. *77*, 427 (1965); Angew. Chem. internat. Edit. *4*, 432 (1965).

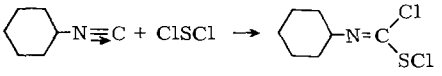
[12] *Z. M. Ivanova*, *N. A. Kirsanova*, and *G. I. Derkač*, Ž. org. Chim. *1*, 2186 (1965).

[13] *R. Neidlein* and *W. Haussmann*, Arch. Pharmaz. *300*, 609 (1967).

[14] *G. I. Derkač* and *N. A. Kirsanova*, Ž. org. Chim. *3*, 1144 (1967).

tillation under nitrogen), the aromatic and acylated compounds are fairly stable (Table 1).

Proof of the structure of the compounds *(9)* is provided by their synthesis from sulfur dichloride and from isocyanides, *e.g.* from cyclohexyl isocyanide.



3. Reactions of Chlorocarbonylsulfenyl Chloride

3.1. Open-Chain Reaction Products

Both the chlorosulfenyl and the chlorocarbonyl grouping of chlorocarbonylsulfenyl chloride *(7)* are available for nucleophilic substitutions *e.g.* with alcohols, thiols, and amines. These reactions can also be carried out selectively in some cases. The action of alcohols on chlorocarbonylsulfenyl chloride *(7)* in a molar ratio of 1 : 1 leads to alkoxycarbonylsulfenyl chlorides *(11)* [15] (Table 2).

$$\underset{}{ROH} + \underset{\underset{O}{\|}}{ClC-SCl} \xrightarrow{30-60\,^{\circ}C} \underset{\underset{O}{\|}}{RO-C-SCl} + HCl$$

(7) *(11)*

Very good yields are obtained in this reaction if the alcohol is added to the chlorocarbonylsulfenyl chloride at 30–60 °C, care being taken to ensure that a little chlorocarbonylsulfenyl chloride is still present at the end of the reaction.

Table 2. Alkoxycarbonylsulfenyl chlorides *(11)*.

R	B.p. (°C/torr)	Yield (%) [a]	R	B.p. (°C/torr)	Yield (%) [a]
CH_3	73–74/100	74	$ClCH_2CH_2$	99–104/19	69
C_2H_5	45–47/15–16	78	$C_6H_5-CH_2CH_2$	155–159/14	63
n-C_3H_7	99/100	95.5	$CH_3OCH_2CH_2$	93–96/20	56
n-C_8H_{17}	89–93/0.3	78			

[a] Yields not optimized.

In contrast with the alcohols, aliphatic thiols react with chlorocarbonylsulfenyl chloride in equimolar quantities on the chlorosulfenyl residue with formation of the alkyl chlorocarbonyl disulfides *(12)* [16]. This

$$\underset{}{RSH} + \underset{(7)\ \underset{O}{\|}}{ClS-CCl} \xrightarrow{0-30\,^{\circ}C} \underset{(12)\ \underset{O}{\|}}{R-S-S-CCl} + HCl$$

reaction is so selective that it stops at the disulfide stage *(12)* even when the thiol is used in excess (Table 3).

[15] *E. Mühlbauer* and *W. Weiss*, German Pat. Appl. P 1 568 633.5 (Dec. 2, 1966), Farbenfabriken Bayer AG.

[16] *E. Mühlbauer* and *W. Weiss*, German Pat. 1219925 (March 20, 1965), Farbenfabriken Bayer AG.

[17] Studies by Dr. *W. Meise*, Leverkusen

Table 3. Chlorocarbonyl alkyl disulfides *(12)*.

R	B.p. (°C/torr)	Yield (%) [a]
CH_3	55/22	42
C_2H_5	59–60/11	92
n-C_4H_9	54–55/0.2	76

[a] Yields not optimized.

The structure of the compounds *(12)* is shown by the carbonyl band, which occurs at a relatively low wavelength (5.6 μm), and from the reaction with an amine *e.g.*

$$\underset{(12a)\ \underset{O}{\|}}{C_4H_9-S-S-CCl} + HN(C_2H_5)_2 \rightarrow \underset{(13)\ \underset{O}{\|}}{C_4H_9-S-S-C-N(C_2H_5)_2}$$

Butyl *N,N*-diethylcarbamoyl disulfide *(13)* gives a carbonyl band (at 6.0 μm) and yields tetraethylurea, dibutyl disulfide and dibutyl trisulfide in the mass spectrometer [17].

Some other reactions of the alkoxycarbonylsulfenyl chlorides *(11)* and alkyl chlorocarbonyl disulfides *(12)* are shown in Scheme 1.

$C_2H_5OC(O)SCl + KSC(S)OC_2H_5 \xrightarrow{-KCl}$

(11a) $C_2H_5OC(O)-S-S-C(S)OC_2H_5$

b.p. = 95 °C/0.3 torr [20]

$CH_3OC(O)SCl + (CH_3)_2N-C(S)OC_4H_9 \xrightarrow{-C_4H_9Cl}$

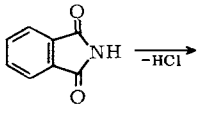
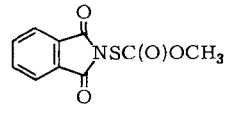
(11b) $CH_3OC(O)-S-S-C(O)N(CH_3)_2$

b.p. = 120–122 °C/0.3 torr

$CH_3OC(O)SCl + CH_3SC(S)OCH_3 \xrightarrow{-CH_3Cl}$

(11b) $CH_3OC(O)-S-S-C(O)SCH_3$

b.p. = 86–88 °C/0.2 torr

$CH_3OC(O)SCl$ *(11b)* +  $\xrightarrow{-HCl}$ 

m.p. = 137–138 °C

$C_2H_5-S-S-C(O)Cl + NaOC_2H_5 \xrightarrow{-NaCl}$

(12b) $C_2H_5-S-S-C(O)OC_2H_5$

b.p. = 94–98 °C/14–19 torr

$C_2H_5-S-S-C(O)Cl + NaOC_6H_5 \xrightarrow{-NaCl}$

(12b) $C_2H_5-S-S-C(O)OC_6H_5$

b.p. = 120 °C/1.9 torr

$C_2H_5-S-S-C(O)Cl + NaSC_2H_5 \xrightarrow{-NaCl}$

(12b) $C_2H_5-S-S-C(O)SC_2H_5$

b.p. = 69 °C/0.12 torr

$C_4H_9-S-S-C(O)Cl + HN(C_3H_7)_2 \xrightarrow{-HCl}$

(12a) $C_4H_9-S-S-C(O)N(C_3H_7)_2$

b.p. = 125–127 °C/0.1 torr

$C_2H_5-S-S-C(O)Cl + HSC_6H_5 \xrightarrow{-HCl}$

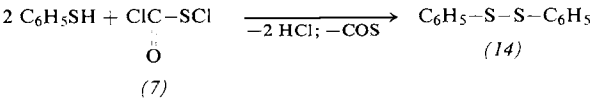
(12b)

$[C_2H_5-S-S-C(O)SC_6H_5] \xrightarrow{-COS} C_2H_5-S-S-C_6H_5$

b.p. = 82–84 °C/0.9 torr

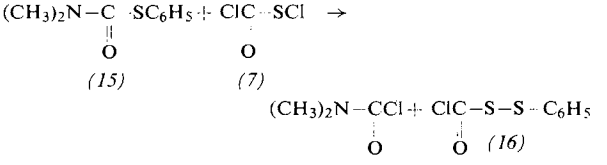
Scheme 1.

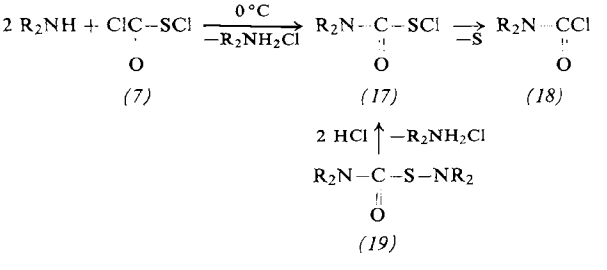
Thiophenols are oxidized by chlorocarbonylsulfenyl chloride *(7)* to diaryl disulfides *(14)*.



Aryl chlorocarbonyl disulfides can also be prepared by another route. The action of chlorocarbonylsulfenyl chloride *(7)* on an *S*-aryl ester of thiocarbamic acid, *e.g. (15)*, leads to elimination of carbamoyl chloride and formation of an aryl chlorocarbonyl disulfide *e.g. (16)* [18], b.p. = 86–88 °C/0.7 torr.

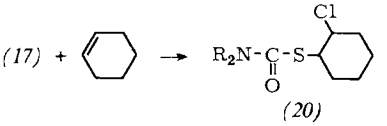
Chlorocarbonylsulfenyl chloride *(7)* reacts in the cold with aliphatic amines, as with alcohols, on the chlorocarbonyl residue at first, but the resulting carbamoylsulfenyl chlorides *(17)* readily decompose with elimination of sulfur to form the carbamoyl chlorides *(18)*. Even the mild cleavage of the carbamoylsulfenylamides *(19)* with hydrogen chloride yields the same products [19].



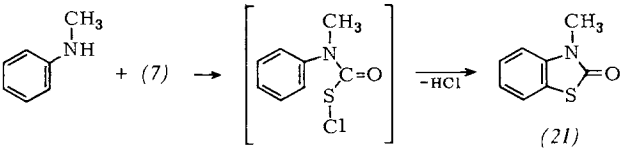


The unstable carbamoylsulfenyl chloride *(17)* can however be intercepted with cyclohexene *e.g.* to form the compound *(20)* (R = CH_3, n_D^{20} = 1.5329).

With aromatic amines, this "interception reaction" takes place intramolecularly with cyclization. Thus



chlorocarbonylsulfenyl chloride *(7)* reacts practically quantitatively with *N*-methylaniline to give *N*-methylbenzothiazolone *(21)* [20], b.p. = 140 °C/2 torr.



Primary and secondary amines react smoothly with chlorocarbonylsulfenyl chloride *(7)* in a molar ratio of 2 : 1 to give the stable carbamoylsulfenylamides *(19)* (Table 4).

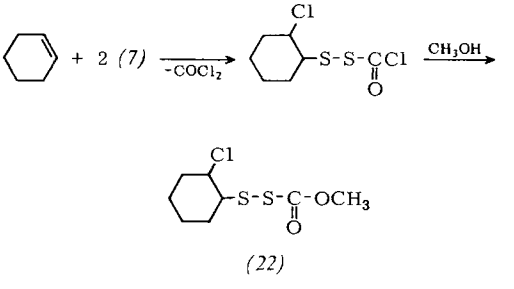
Table 4. Carbamoylsulfenylamides R–C(=O)–SR *(19)*.

R	B.p. (°C/torr) (M.p. (°C))	Yield (%) [a]	R	B.p. (°C/torr) (M.p. (°C))	Yield (%) [a]
$(CH_3)_2N$	85–86/14	65	*i*-C_3H_7–NH	(113)	23.5
$(n\text{-}C_3H_7)_2N$	122–124/0.13	60	$(CH_3)_3C$–NH	(decomp. at 200)	100
morpholino	(119)	70	anilino	(133–134)	86

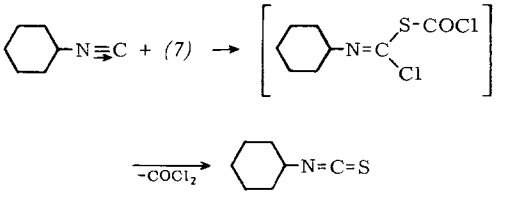
[a] Yields not optimized.

As well as substitutions, chlorocarbonylsulfenyl chloride *(7)* can also undergo additions, of which two types will be described.

The addition of compound *(7)* to olefins in a molar ratio of 2 : 1 leads to elimination of phosgene and formation of 2-chloroalkyl chlorocarbonyl disulfides. Chlorocarbonyl 2-chlorocyclohexyl disulfide reacts with methanol to form the compound *(22)*, b.p. = 143 to 145 °C/1.8 torr.



Isothiocyanates are formed by addition of chlorocarbonylsulfenyl chloride *(7)* to isocyanides, again with elimination of phosgene.



In the reaction of chlorocarbonylsulfenyl chloride *(7)* with an *O*-alkyl *N*,*N*-dialkylthiocarbamate, chloroalkane is eliminated as in a reaction described by *Harris* [21]. The expected chlorocarbonyl *N*,*N*-dialkylcarbamoyl disulfide, *e.g. (23)*, decomposes even at 0 °C

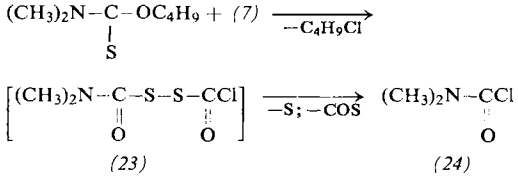
[18] *G. Zumach* and *E. Kühle*, German Pat. Appl. P 1947952.8 (Sept. 23, 1969), Farbenfabriken Bayer AG.

[19] The dimethylthiocarbamidosulfenyl chloride formed as an intermediate in the chlorolysis of tetramethylthiuram disulfide also immediately loses sulfur to form dimethylthiocarbamoyl chloride; cf. *E. J. Ritter*, US-Pat. 2466276 (Feb. 2, 1946), Sharples Chem. Inc.

[20] *E. Mühlbauer*, Leverkusen, unpublished.

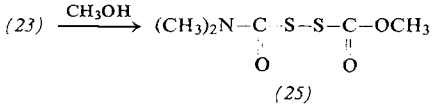
[21] *J. F. Harris*, J. Amer. chem. Soc. *82*, 155 (1960).

with liberation of sulfur and carbon oxide sulfide to give the *N,N*-dialkylcarbamoyl chloride, in this case *(24)*.



(23) *(24)*

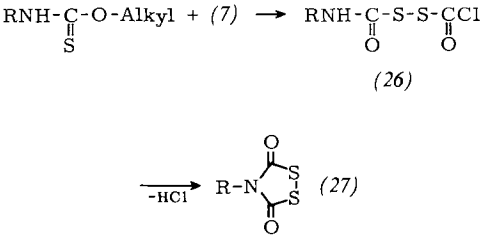
It is sometimes possible to intercept the unstable intermediate *(23)* as an ester or amide, *e.g.* as the ester *(25)* (b.p. = 120–122 °C/0.3 torr).



(25)

3.2. Ring Closure Reactions

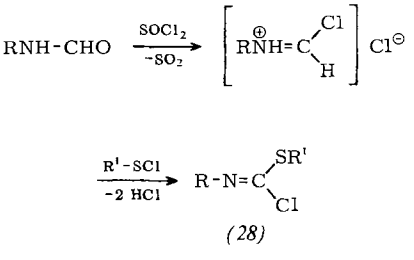
In contrast with the reaction of chlorocarbonylsulfenyl chloride *(7)* with *O*-esters of *N,N*-dialkylthiocarbamic acids, in which the unstable intermediate *(23)* changes into dialkylcarbamoyl chloride *(24)*, the carbamoyl chlorocarbonyl disulfides *(26)* formed in the reaction of compound *(7)* with *O*-alkyl esters of *N*-monosubstituted thiocarbamic acids can achieve stability by cyclization to form 1,2,4-dithiazolidine-3,5-diones *(27)* (method a in Table 5)[22].



(26) *(27)*

This reaction proceeds particularly smoothly with *O*-alkyl esters of *N*-arylthiocarbamic acids in the presence of a tertiary amine as a hydrogen chloride acceptor.

N-monosubstituted formamides react with sulfenyl chlorides in the presence of thionyl chloride to give the iminocarbonic acid derivatives *(28)*[23].



(28)

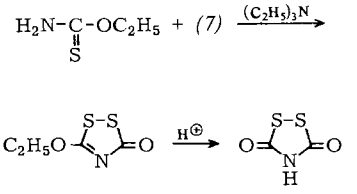
Chlorocarbonylsulfenyl chloride *(7)*, however, does not give *(28)* with R′ = COCl; two moles of *(7)* react instead with one mole of the monosubstituted formamide to give the heterocycle *(27)* (method b in Table 5)[24].

Table 5. 1,2,4-dithiazolidine-3,5-diones *(27)*. For methods a and b see text.

R	M.p. (°C) (B.p. (°C/torr))	Yield (%) [a] Method a	Method b
CH_3	38–39 (80/0.2)	67	40
n-C_4H_9	(90–92/0.15)	83	—
C_6H_{11}	87–88	41	42
C_6H_5–CH_2	93–94	35	—
C_6H_5	168	75.5	28
p-Br–C_6H_4	109–110	41	—
3,4-Cl_2–C_6H_3	166–168	79	35
3-Cl-4-CH_3O–C_6H_3	183–184	70	39

[a] Yields not optimized.

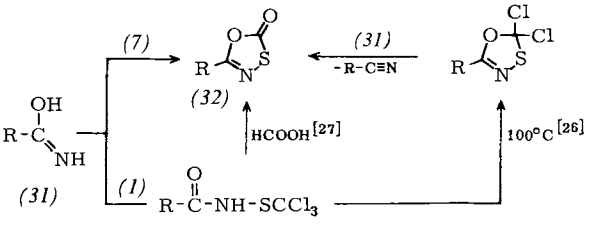
The unsubstituted 1,2,4-dithiazolidine-3,5-dione *(30)*, m.p. = 142–144 °C cannot be obtained by the two methods described. It is obtained by reaction of *O*-ethyl thiocarbamate with *(7)* in the presence of triethylamine followed by hydrolysis of the intermediate *(29)* with concentrated hydrochloric acid.



(29) *(30)*

As a bifunctional compound, chlorocarbonylsulfenyl chloride *(7)* can be used with other bifunctional reactants for the synthesis of heterocycles containing sulfur. Thus primary carbonamides *(31)* undergo *N*-sulfenylation and simultaneous ring closure with *(7)* to form 5-substituted 2-oxo-1,3,4-oxathiazoles *(32)*[25]. These can also be obtained from the amides *(31)* with trichloromethanesulfenyl chloride *(1)*[26,27].

When primary thioamides are used, the sulfenylation with *(7)* takes place not on the nitrogen but on the



[22] *G. Zumach, W. Weiss*, and *E. Kühle*, Belgian Pat. 682991 (June 23, 1966), Farbenfabriken Bayer AG.

[23] *E. Kühle*, Angew. Chem. *74*, 861 (1962); Angew. Chem. internat. Edit. *1*, 647 (1962).

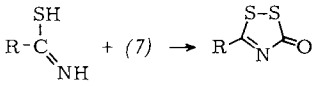
[24] *G. Zumach, W. Weiss*, and *E. Kühle*, Belgian Pat. 682820 (June 20, 1966), Farbenfabriken Bayer AG.

[25] *E. Mühlbauer* and *W. Weiss*, Belgian Pat. 680644 (May 6, 1966), Farbenfabriken Bayer AG.

[26] a) *E. Kühle*, unpublished; b) *A. Sennig* and *P. Kelly*, Acta chem. scand. *21*, 1871 (1967).

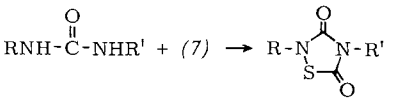
[27] Belgian Pat. 710988 (Aug. 19, 1968), Badische Anilin- und Soda-Fabrik.

sulfur, with formation of 5-substituted 3-oxo-1,2,4-dithiazoles *(33)* [10,28].



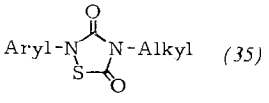
(33)

N,N'-Disubstituted ureas react with compound *(7)* not in the enol form but in the keto form with "*N,N'*-bridging" to form 2,4-disubstituted 1,2,4-thiadiazolidine-3,5-diones *(34)* [29].



(34)

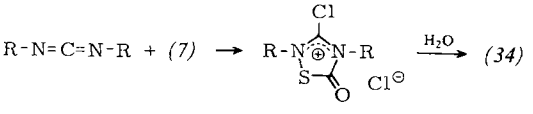
As is shown by NMR spectroscopic studies and independent synthesis (see Section 4.2.3), the reaction of *N*-alkyl-*N'*-arylureas with compound *(7)* leads exclusively to 4-alkyl-2-aryl-1,2,4-thiadiazolidine-3,5-diones *(35)*. No isomers are formed.



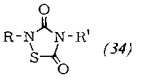
(35)

Another synthesis for (preferably symmetrically substituted) compounds *(34)* is the addition of *(7)* to carbodiimides followed by hydrolysis of the intermediate 3-chloro-5-oxothiadiazolinium chlorides *(36)* [30]. A number of 1,2,4-thiadiazolidine-3,5-diones *(34)* are listed in Table 6.

The IR spectra of the compounds *(36)* contain a split absorption band between 1650 and 1750 cm^{-1}, the stronger component, situated around 1730 cm^{-1}, being due to the CO group, and the weaker component, situated around 1680 cm^{-1}, to a C=N double bond.



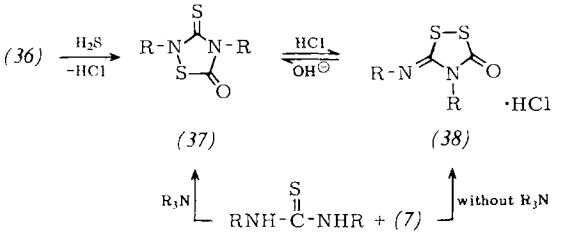
(36)

Table 6. 1,2,4-Thiadiazolidine-3,5-diones  *(34)*

R	R'	M.p. (°C)	Yield (%) [a]
CH_3	CH_3	65	44
CH_3OCH_2	CH_3	52–54	47
CH_3	CH_2–$COOCH_3$	90–91	15
C_6H_{11}	C_6H_{11}	48–49	24
C_6H_5	CH_3	107	52
C_6H_5	C_6H_5	114–115	36
p-CF_3–C_6H_4	CH_3	154	35
3,4-Cl_2–C_6H_3	CH_3	158–159	67
3-Cl-4-CH_3O–C_6H_3	CH_3	179–180	44.5

[a] Yield not optimized.

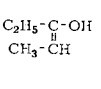
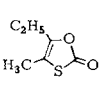
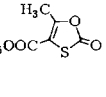
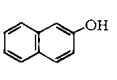
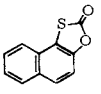
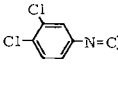
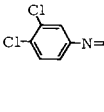
The reaction of *(36)* with hydrogen sulfide in aprotic solvents leads to 3-imino-5-oxo-1,2,4-dithiazolidine hydrochlorides *(38)* and the thiadiazolidines *(37)*. The reaction probably proceeds *via* the 5-oxo-3-thioxo-1,2,4-thiadiazolidines *(37)*, which rearrange in the presence of hydrogen chloride into *(38)*. The salts *(38)* can also be obtained by the reaction of *N,N'*-disubstituted thioureas with chlorocarbonylsulfenyl chloride *(7)* in the absence of a hydrogen chloride acceptor, whereas compound *(37)* is formed in the presence of a tertiary amine. The bases of the salts *(38)* are unstable and change back into *(37)* [31].



The reversible rearrangement *(37)*⇌*(38)* can be followed IR-spectroscopically by observation of the appearance and disappearance of an absorption band at 1620 cm^{-1}, which must be assigned to the C=N double bond in *(38)* [32].

In contrast with the reaction of *N*-alkyl-*N'*-alkylureas with the compound *(7)*, the reaction of *N*-alkyl-*N'*-arylthioureas with *(7)* leads to isomer mixtures in which the component *(39)* generally predominates strongly. Other examples of ring closure reactions with *(7)* are listed in Table 7.

Table 7. Cyclizations with chlorocarbonylsulfenyl chloride *(7)*

Reaction partner	Reaction product	B.p. (°C/torr) (m.p. (°C))	Yield (%) [a]
		68/0.9 [33]	75
		116/3.5 [33]	40
		170–173/0.15 [20] (102)	68
		(51) [10]	72

[a] Yields not optimized.

[28] *P. M. Hell*, Dissertation, Universität Hamburg 1968.

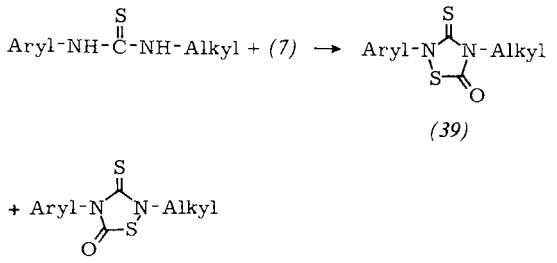
[29] *G. Zumach, L. Eue, W. Weiss, E. Kühle*, and *H. Hack*, Belgian Pat. 698601 (May 17, 1967); Belgian Pat. 709916 (Jan. 26, 1968), both Farbenfabriken Bayer AG.

[30] *P. Fischer* and *W. Weiss*, German Pat. Appl. P 1670917.4 (Sept. 4, 1967), Farbenfabriken Bayer AG.

[31] The bisaromatic compounds, for which the form of the thiadiazolidine *(37)* is unknown, represent an exception.

[32] *C. K. Bradsher, F. C. Brown, E. F. Sinclair*, and *S. T. Webster*, J. Amer. chem. Soc. *80*, 414 (1958).

[33] *E. Mühlbauer* and *W. Weiss*, German Pat. 1233882 (March 18, 1965), Farbenfabriken Bayer AG.



(39)

4. Reactions of Iminochloromethanesulfenyl Chlorides

4.1. Open-Chain Reaction Products

The principal reactants for reactions of iminochloromethanesulfenyl chlorides *(9)* to give open-chain products are primary and secondary aliphatic and aromatic amines. The reaction with two moles of amine yields *S*-aminoisothioureas *(40)*, the stability of which depends on the substituents (Table 8).

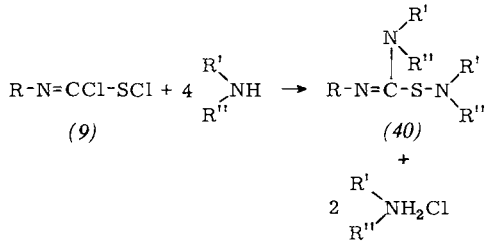


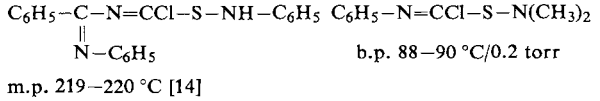
Table 8. *S*-Aminoisothioureas *(40)* [35].

R	R′	R″	M.p. (°C) (B.p. (°C/torr))	Ref.	Yield [a] (%)
C_6H_5	H	C_6H_5	150–150.5	[34]	71
C_6H_5	CH_3	CH_3	(88/0.015)	[10]	45
C_6H_5–CO	H	C_6H_5	102–103	[12]	63
p-Cl–C_6H_4–CO	H	*p*-CH_3–C_6H_4	215–216	[13]	90

[a] Yields optimized.

Delocalization of the double bond in *(40)* can be detected in certain cases by NMR spectroscopy [34].

Selective reaction of iminochloromethanesulfenyl chlorides *(9)* with only one mole of amine is also possible; the products are sulfenylamide derivatives.

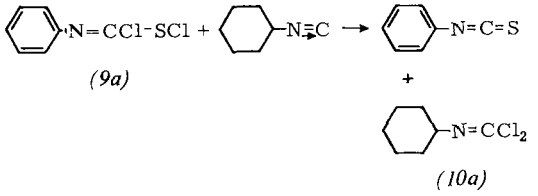


m.p. 219–220 °C [14]

b.p. 88–90 °C/0.2 torr

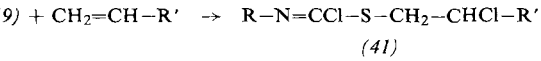
The reaction of the compounds *(9)* with alkoxides leads to elimination of sulfur [14], whereas with sodium thiolates they give isothiocyanates and diaryl disulfides [34].

In the presence of isocyanides, the iminochloromethanesulfenyl chlorides, *e.g. (9a)*, lose chlorine with regeneration of the isothiocyanates from which they are derived, while the isocyanides are converted into isocyanide dichlorides *e.g. (10a)*.



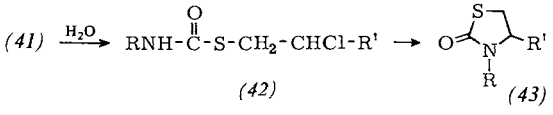
(9a) *(10a)*

As sulfenyl chlorides, the compounds *(9)* also add to olefinic double bonds [3,36].



(41)

Hydrolysis of the adducts *(41)* leads to the *S*-esters of thiocarbamic acids *(42)*, which, when R′ is an electronegative residue (*e.g.* phenyl), can sometimes cyclize to give 2-oxo-1,3-thiazolidines *(43)* [36].

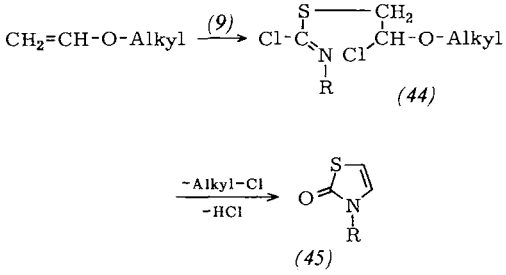


(42) *(43)*

4.2. Ring Closure Reactions

4.2.1. Reaction with Vinyl Ethers

A special case of the reaction of iminochloromethanesulfenyl chlorides *(9)* with olefins is the addition of *(9)* to vinyl alkyl ethers. The resulting adducts *(44)* lose chloroalkane and hydrogen chloride even at room temperature to give 2-oxo-1,3-thiazolines *(45)* (Table 9) [10, 37].



(44) *(45)*

Table 9. 2-Oxo-1,3-thiazolines *(45)*.

R	M.p. (°C) (B.p. (°C/torr))	Ref.	Yield (%) [a]
CH_3	46–47 (65–67/0.15)	[10]	51
C_4H_9	(81–83/0.15)	[10]	49
C_6H_5	70–71	[37]	81

[a] Yields not optimized.

[34] *G. Ottmann* and *H. Hooks jr.*, Angew. Chem. *79*, 1062 (1967); Angew. Chem. internat. Edit. *6*, 1072 (1967).

[35] Cf. also *K. Ley* and *U. Eholzer*, Angew. Chem. *78*, 672 (1966); Angew. Chem. internat. Edit. *5*, 674 (1966).

[36] *G. Ottmann* and *H. Hooksjr.*, Angew. Chem. *78*, 210 (1966); Angew. Chem. internat. Edit. *5*, 250 (1966).

[37] *G. Ottmann*, *H. Hoberecht*, and *H. Hooksjr.*, Angew. Chem. *79*, 1063 (1967); Angew. Chem. internat. Edit. *6*, 1073 (1967).

4.2.2. Reaction with Ketones and Aldehydes

The first step in the reaction of compounds *(9)* with ketones is probably the addition of the SCl grouping to the enolized form of the ketone[38]. The hypothetical intermediate *(46)* is stabilized by ring closure and intramolecular neutralization of the hydrogen chloride to form the salt *(47)*, from which the base *(49)* can be liberated with tertiary amines even below 0 °C. With another mole of tertiary amine, *(49)* can be converted into the oxathiole *(50)* (Table 10). The compounds *(47)* and *(49)* rearrange instantaneously on contact with water or alcohol into the 4,5-disubstituted 2-oxo-1,3-thiazolines *(48)* (Table 11).

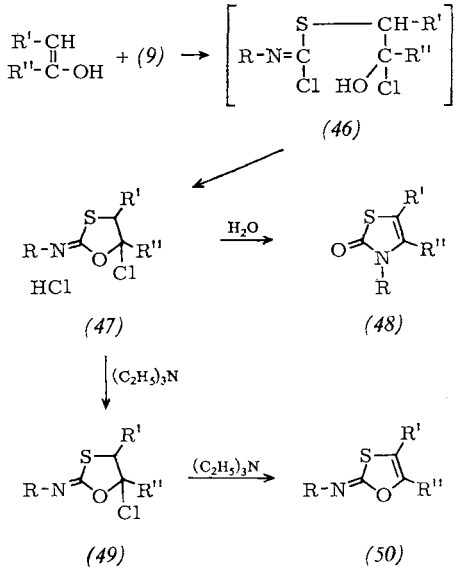


Table 10. 2-Imino-1,3-oxathioles *(50)*.

R	R'	R''	M.p. (°C) (B.p. (°C/torr))	Yield (%) [a]
C_4H_9	H	CH_3	28–28.5	43
C_4H_9	$-(CH_2)_4-$		(117–119/0.3)	32.5
C_6H_5	C_4H_9	CH_3	(152/0.2)	33

[a] Yields not optimized.

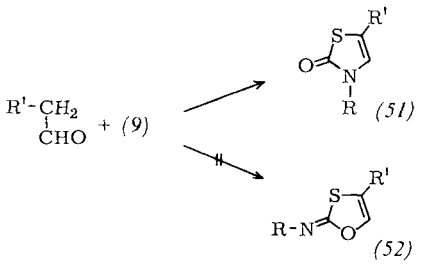


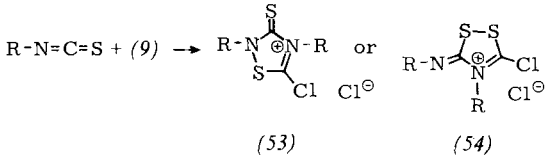
Table 11. 2-Oxo-1,3-thiazolines *(48)* and *(51)* from ketones and aldehydes.

	R	R'	R''	M.p. (°C) (B.p. (°C torr))	Yield (%) [a]
(48a)	C_6H_5	H	CH_3	147.5–148	52
(48b)	C_6H_5	CH_3	CH_3	103–103.5	39
(48c)	C_6H_5	$COOC_2H_5$	CH_3	103.5–104.5	32.5
(48d)	*p*-Cl–C_6H_4	$-(CH_2)_4-$		115–116	52
(51a)	C_6H_5	CH_3		83.5–84.5	87
(51b)	*n*-C_4H_9	CH_3		(94/0.4)	26

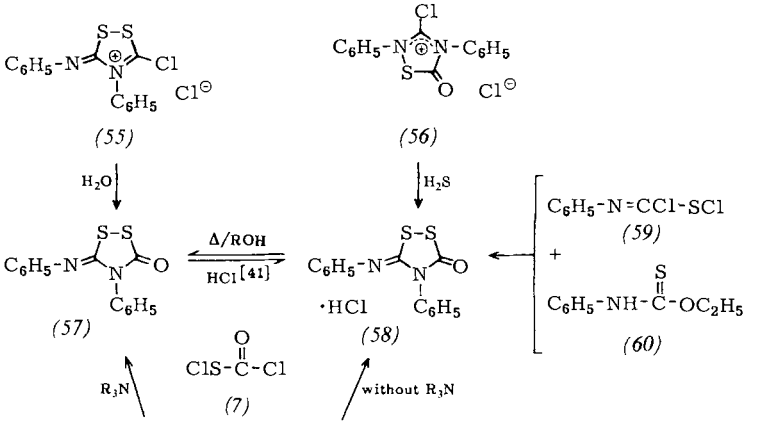
[a] Yields not optimized.

4.2.3. Reaction with Compounds Containing C–N Multiple Bonds

Possibly the most interesting property of the iminochloromethanesulfenyl chlorides *(9)* is their ability to react with certain compounds containing C–N multiple bonds. With isothiocyanates, for example, they form sparingly soluble unstable products that



have been known for a long time as "mustard oil monochlorides", and for which we[3] have proposed the polar structures *(53)* and *(54)*[38a].



Reaction of *(9)* with aliphatic primary aldehydes yields 2-oxo-1,3-thiazolines *(51)* [≡ *(48)*, R'' = H] that are monosubstituted in position 5 (Table 11). The isomeric iminooxathioles *(52)* are not formed[37].

Scheme 2.

[38] *G. Ottmann, G. D. Vickers*, and *H. Hooks jr.*, J. heterocyclic Chem. *4*, 527 (1967).

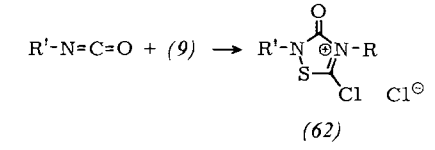
[38a] In view of the differences in the nucleophilic strengths of N, O, and S, we favor type *(54)* in the case of the isothiocyanate adducts and type *(53)* for the isocyanate adducts.

The salt character of the compounds explains their sparing solubility in organic solvents. The hydrolysis of the "mustard oil monochlorides", *e.g. (55)*, to give the "mustard oil oxides" *e.g. (57)*, can be similarly explained [39].

The structure of *(57)* can be proved by degradation with amines to form *N,N',N''*-trisubstituted monothiobiurets [40,41] as well as by independent synthesis (see Scheme 2).

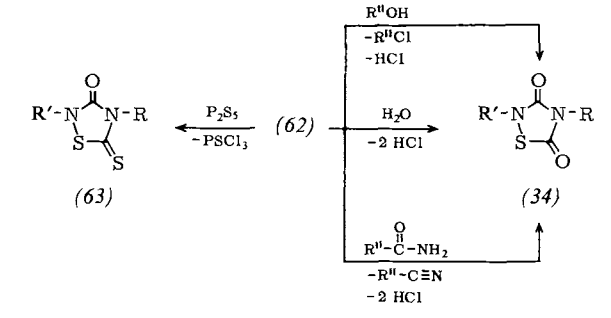
We have obtained similar results in the hydrolysis of *(55)*, with CH_3 instead of C_6H_5. In principle, mixed aromatic-aliphatic compounds *(57)* can also be prepared by the methods described, but the products are usually mixtures of isomers that are difficult to separate.

Isocyanates, like isothiocyanates, can also react with the compounds *(9)* [42], and the products are again sparingly soluble, salt-like substances, which we believe to be 3-oxothiadiazolinium chlorides *(62)* [38a]. The synthesis described proceeds particularly easily and in high yields when the chlorination of isothiocyanates is carried out in the presence of isocyanates [43].



(62)

Hydrolysis of the very reactive compounds *(62)* with water [42,44] yields 1,2,4-thiadiazolidine-3,5-diones *(34)*, which are also obtained from *N,N'*-disubstituted ureas with chlorocarbonylsulfenyl chloride *(7)* or from carbodiimides with *(7)* (see Table 6). *(34)* is also obtained in the reaction of *(62)* with alcohols, which is accompanied by elimination of chloroalkane, or with primary amides, which is accompanied by the formation of the nitriles. *(62)* reacts with hydrogen sulfide, or preferably with phosphorus pentasulfide, to give 3-oxo-5-thioxo-1,2,4-thiadiazolidines *(63)* (Table 12).



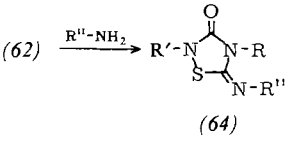
(63) *(34)*

Table 12. 3-Oxo-5-thioxo-1,2,4-thiadiazolidines *(63)*.

R'	R	M.p. (°C)	Yield (%) [a]
CH_3	CH_3	60	60
C_6H_5	CH_3	142–143	56
3,4-Cl_2–C_6H_3	CH_3	170	63

[a] Yields not optimized.

The aminolysis of *(62)* with primary aliphatic and aromatic amines leads to 5-imino-3-oxo-1,2,4-thiadiazolidines *(64)* (Table 13) [45,46].



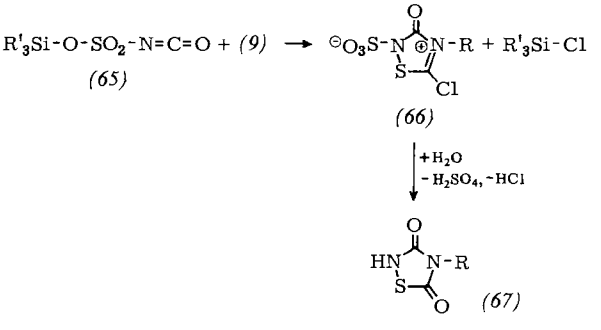
(64)

Table 13. 5-Imino-3-oxo-1,2,4-thiadiazolidines *(64)*.

R'	R	R''	M.p. (°C) (B.p. (°C/torr))	Yield (%) [a]
C_4H_9	CH_3	C_4H_9	(110/0.05)	76.5
i-C_3H_7	C_6H_5	C_6H_{11}	101–102	81
C_6H_5	C_2H_5	C_6H_5	55–56	51
p-Cl–C_6H_4	C_6H_5	C_6H_5	134–135	6

[a] Yields not optimized.

A special case of the addition of iminochloromethanesulfenyl chlorides *(9)* to isocyanates is the addition to silyloxysulfonyl isocyanates *(65)* or the corresponding chlorination of isothiocyanates in the presence of *(65)*. These reactions lead to elimination of the chlorosilanes, again with formation of sparingly soluble products, for which we propose the structure of inner salts *(66)*. Their hydrolysis yields 1,2,4-thiadiazolidine-3,5-diones *(67)* with no substituent in position 2 (Table 14) [47].



(65) *(66)* *(67)*

Table 14. 1,2,4-Thiadiazolidine-3,5-diones *(67)*.

R	M.p. (°C)	Yield (%) [a]	R	M.p. (°C)	Yield (%) [a]
CH_3	149–150	46.5	c-C_6H_{11}	128–130	73.5
C_4H_9	64–65	74	C_6H_5	218–220	79.5
C_6H_5–CH_2	67–68	45	3,4-Cl_2–C_6H_3	225–227	61.5

[a] Yields not optimized.

The reaction of alkyloxymethyliminochloromethanesulfenyl chlorides *(68)* with isocyanates follows an unexpected course. It is possible that the expected but

[39] *E. Fromm* and *R. Heyder*, Ber. dtsch. chem. Ges. *42*, 3800 (1909).

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[43] *H. Holtschmidt*, *G. Zumach*, *F. Döring*, and *E. Kühle*, Belgian Pat. 712734 (March 25, 1968), Farbenfabriken Bayer AG.

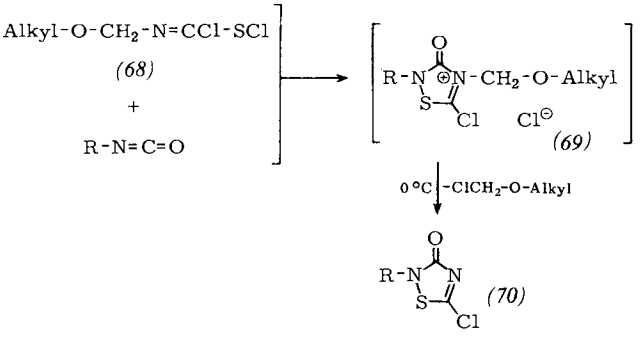
[44] *G. Ottmann* and *H. Hooks jr.*, US-Pat. 3374240 (June 29, 1965), Olin Mathieson Chem. Corp.

[45] *G. Ottmann* and *H. Hooks jr.*, J. heterocyclic Chem. *4*, 365 (1967).

[46] According to *G. Ottmann* and *H. Hooks jr.* [45], the aminolysis of the compounds *(62)*, which they formulate as R–N=CCl–S–NR'–COCl, yields an isomer mixture. However, they describe only one type of compound in their patent (US-Pat. 3282950 (Jan. 21, 1965), Olin Mathieson Chem. Corp.).

[47] *G. Zumach*, *H. Holtschmidt*, *E. Kühle*, and *J. Pedain*, Belgian Pat. 728853 (Feb. 24, 1969), Farbenfabriken Bayer AG.

unisolable salts *(69)* lose the chloromethyl ether to give the 2-substituted 5-chloro-3-oxo-1,2,4-thiadiazolines *(70)* (Table 15)[48], whose chlorine on C-5 is accessible to the usual nucleophilic substitution reactions.



It is even possible in some cases to obtain compounds *(70)* by chlorination of carbamoyl isothiocyanates and cyclization of the intermediate, unisolated carbamoyliminochloromethanesulfenyl chlorides with tertiary amines, *e.g.*:

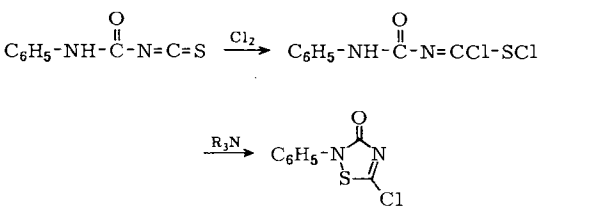
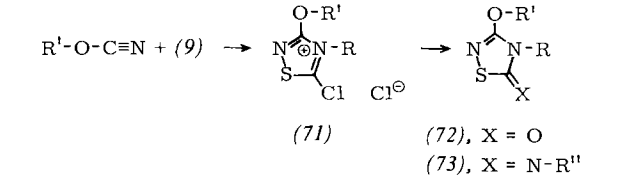


Table 15. 5-Chloro-3-oxo-1,2,4-thiadiazolines *(70)*.

R	M.p. (°C)	Yield (%) [a]	R	M.p. (°C)	Yield (%) [a]
CH_3	99–100	40	3,4-Cl_2–C_6H_3	187–188	66
i-C_3H_7	71–72				
C_6H_5	132–133	72	*p*-C_2H_5O–C_6H_4	118–119	37.5
p-Br–C_6H_4	204–206	53			

[a] Yields not optimized.

Another example of the addition of compounds *(9)* to C–N multiple bonds is their reaction with cyanates. The products are again sparingly soluble, very reactive substances, which probably have the structure *(71)* [49]. Hydrolysis of these products yields 5-oxo-1,2,4-thiadiazolines *(72)* with an aryloxy or alkoxy residue on



(71) *(72)*, X = O; *(73)*, X = N-R''

[48] *G. Zumach, H. Holtschmidt*, and *E. Kühle*, German Pat. App. P 1907116.0 (Feb. 13, 1969), Farbenfabriken Bayer AG.

[49] *G. Zumach, H. Holtschmidt*, and *E. Kühle*, Belgian Pat. 725054 (Dec. 6, 1968), Farbenfabriken Bayer AG.

Table 16. 1,2,4-Thiadiazoline derivatives *(72)* and *(73)*.

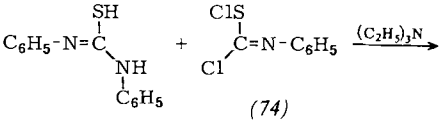
	R	R'	X	M.p. (°C)	Yield (%) [a]
(72a)	CH_3	Cl_3C–CH_2	O	69	69
(72b)	CH_3	C_6H_5	O	109–110	48.5
(72c)	C_6H_5	2,4-Cl_2–C_6H_3	O	93–94	26
(73a)	CH_3	*m*-NO_2–C_6H_4	CH_3–N	128–130	46
(73b)	CH_3	Cl_3C–CH_2	*p*-Cl–C_6H_4–N	95	37

[a] Yields not optimized.

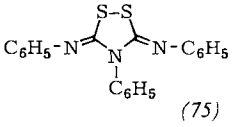
C-3. On aminolysis of *(71)* with primary aliphatic or aromatic amines, imino derivatives *(73)* are formed (Table 16).

4.2.4. Other Reactions

Thioureas react smoothly with the compounds *(9)* in the presence of a tertiary amine to form diiminodithiazolidines. For example, *N,N'*-diphenylthiourea reacts with *N*-phenyliminochloromethanesulfenyl chloride *(74)* to form 3,5-bis(phenylimino)-4-phenyl-1,2,4-dithiazolidine *(75)*.

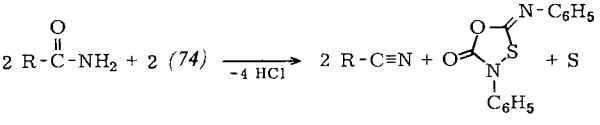


(74)



(75)

The reaction of chlorocarbonylsulfenyl chloride *(7)* with primary amides (Section 3.2) cannot be applied to the compounds *(9)*. Whereas aliphatic compounds *(9)* give compounds such as *(58)* with primary amides (cf. Section 4.2.3), the aromatic compounds, *e.g. (74)*, give the 2-imino-5-oxo-1,3,4-oxothiazolidines, *e.g. (76)*, m.p. = 112 °C.



(76)

We are grateful to Prof. Dr. Holtschmidt for his valuable suggestions. Dr. Heitzer kindly recorded a large number of IR and NMR spectra and contributed to the progress of the investigations by discussion, while we are indebted to Dr. Weiss, Inorganic Section of Farbenfabriken Bayer AG, for providing the chlorocarbonylsulfenyl chloride.

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The Stereochemistry of the α-Ferrocenylethyl Carbonium Ion

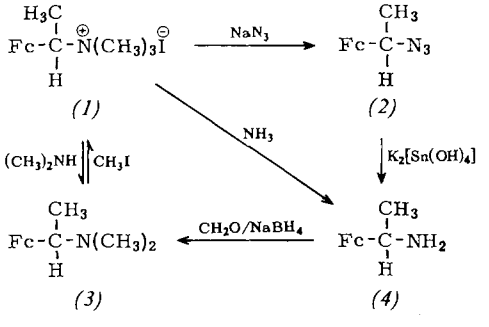
By *G. Gokel, P. Hoffmann, H. Klusacek, D. Marquarding, E. Ruch*, and *I. Ugi* [*]

Dedicated to Professor K. Hansen on the occasion of his 60th birthday

Recent investigations of the solvolytic reactions of α-ferrocenylalkyl compounds have demonstrated a pronounced stability of ferrocenylalkyl cations [1–8]. This is explained by assuming metal participation [1–3,6] or iron hyperconjugation [4,7,8].

Both interpretations imply stereoselective nucleophilic substitutions of α-ferrocenylalkyl compounds. There is some evidence for the stereoselectivity of the above reactions [2,4,6,7] but to our knowledge no studies on the retention of optical activity during nucleophilic substitutions on non-cyclic centers of chirality having a ferrocenyl ligand have been performed.

With regard to the use of optically active 1-ferrocenylaminoalkanes as regenerable amine components in four-component peptide syntheses [9,10], we were interested in investigating the reactions depicted in Scheme 1, which involves several nucleophilic substitutions at a center of chirality bearing a ferrocenyl ligand.



Scheme 1. Fc = Ferrocenyl.

We observed complete retention of the configuration of the chiral center during the nucleophilic substitutions in this cycle. This is further relevant evidence for the unique influence of an α-ferrocenyl group upon the mechanism of nucleophilic substitution.

Reaction of (*R*)-α-ferrocenylethylamine *(4)* [10,11], ($[\alpha]_D^{20}$ = −20.8 °, *c* = 4.0 in ethanol) with formaldehyde (5 moles) and $NaBH_4$ (3 moles) in methanol at 0 °C yields 90% of *(3)* [b.p. 81 °C/0.035 torr; $[\alpha]_D^{20}$ = +14.0 °, *c* = 1.0 in ethanol; NMR in CCl_4 (rel. to TMS as internal std.): τ = 8.65 (d), *J* = 6.9 Hz, $-CH(CH_3)-N$, I_{rel} = 3; τ = 8.01 (s), $-N(CH_3)_2$, I_{rel} = 6; τ = 6.48 (q), *J* = 6.9 Hz, $-CH(CH_3)-$, I_{rel} = 1; τ = 6.00 (s), ferrocene protons, I_{rel} = 9; IR, film on KBr: 3092 cm^{-1}, 1108 cm^{-1}, 1000 cm^{-1}].

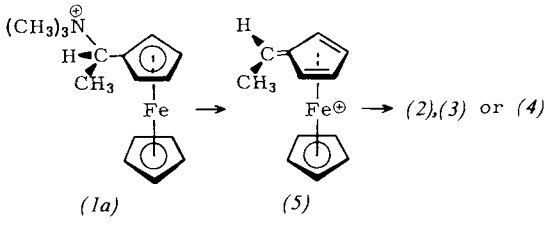
Methyl iodide (4.5 moles) in acetone alkylates *(3)* at 0 °C to form 95% of *(1)* [m.p. 126–127 °C; $[\alpha]_D^{20}$ = +41.6, *c* = 0.64 in methyl cellosolve].

In ethylene glycol-water (1 : 1) or diglyme-water (3 : 2) at 50 °C *(1)* (0.1 moles/kg) and sodium azide (0.6 moles/kg) react to form 88% of *(2)* [3] (b.p. 80 °C/0.02 torr; $[\alpha]_D^{20}$ = −66.1 °, *c* = 1.36 in benzene; NMR (CCl_4): τ = 8.52 (d), *J* = 6.8 Hz, $-CH(CH_3)-N$, I_{rel} = 3; τ = 5.90 (s), ferrocene protons; and τ = 5.72 (q), *J* = 6.8 Hz, $-CH(CH_3)$, I_{rel} (for ferrocene protons $+CH(CH_3)$) = 10. IR (film on KBr): 3090, 2095, 1105, 998 cm^{-1}.

The conversions of *(1)* into *(4)* (by conc. aqueous ammonia) and *(3)* (by dimethylamine in water or acetonitrile) at 20 °C also occur with retention.

The reduction of *(2)* with $K_2[Sn(OH)_4]$ [12] at 25 °C in methyl cellosolve-water (1 : 1) leads back to 90% of *(4)* [$[\alpha]_D^{20}$ = −20.8 °, *c* = 4.0 in ethanol; all data identical with those of an authentic sample].

We interpret the observed facts by assuming that *(1)* reacts from the conformation *(1a)* with concerted cleavage of the anti-periplanar Fe—C and C—N bonds, forming the cation *(5)* as an intermediate, which subsequently reacts with the nucleophilic azide anion; this is analogous to olefin-forming β-eliminations [13]. During the latter step, an N—C bond is formed by a process which resembles, sterically and electronically, a reversal of the elimination *(1a)* → *(5)*.



Nucleophilic substitutions of analogous α-ferrocenylalkyl systems bearing substituents on C-2 of the ferrocene also occur with retention with nucleophilic anions. Partial epimerization occurs with weaker nucleophiles. Recently, we found that (1*S*)-(*R*)-1-(2-trimethylsilylferrocenyl)-1-ethyltrimethylammonium iodide reacts with sodium methoxide in methanol to form (1*S*)-(*R*)-1-(2-trimethylsilylferrocenyl)-1-methoxyethane; with methanol alone a mixture of the latter and a minor amount of its (1*S*)-(*S*)-diastereomer results [14].

The steric peculiarities of α-ferrocenyl carbonium ions such as *(5)* are easily understood from the qualitative results of theoretical analyses of the bond systems of sandwich complexes [15].

This treatment indicates that the complex is stabilized by six bonding pairs of electrons which occupy hybrid orbitals of the rings and the central atom. These ring orbitals are the occupied π-orbitals of the isolated quasi-aromatic rings, and the central atom orbitals are of the d^2sp^3 configuration.

The relevant point for our problem is that the occupied bonding orbitals are linear combinations in which the ring orbitals participate with large coefficients and the central atom orbitals participate with small coefficients. This leads to the following qualitative description:

The essential difference between the π-electron distribution of the isolated rings carrying unit negative charge and that of the two complexed rings is a slight deformation of π-electron density toward the central atom in the latter case. The electron polarizability parallel to the plane of the rings is not appreciably affected. We can therefore draw conclusions about the present system from the electron distribution in fulvene and thus arrive at formula *(5)*.

Since there is an appreciable rotational barrier around the ferrocenyl-C_α bond (with a slightly weakened ring-metal bond), stereoisomeric α-ferrocenyl alkyl ions, such as *(5)* and its optical antipode, behave differently in chemical reactions (see also ref. [14]).

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Thermal Cyclization of *o*-Chloroaryl Isothiocyanates

By *E. Degener, G. Beck*, and *H. Holtschmidt*[*]

Dedicated to Professor K. Hansen on the occasion of his 60th birthday

The observation that numerous polychloro amine derivatives undergo stabilization by ring closure when heated, induced us to study the thermal behavior of polychloroaryl isothiocyanates. We found that *o*-chloroaryl isothiocyanates *(1)* cyclize to 2-chlorobenzothiazoles *(2)* in preparatively satisfactory yields at 330–380 °C, which are unusually high temperatures for organic reactions.



(1) *(2)*

	R¹	R²	R³	R⁴	(2) Yield (%)	M.p. (°C)
(a)	Cl	Cl	Cl	Cl	90	162–164
(b)	Cl	H	Cl	H	50	105–107
(c)	Cl	Cl	H	Cl	50	108–109
(d)	Cl	H	Cl	Cl	50	115–116
(e)	Cl	Cl	CN	Cl	50	185–189
(f)	—CCl=CCl—CCl=CCl—		Cl	Cl	90	260

Ring closure is particularly smooth and uniform for the polychlorinated isothiocyanates *(1a)* and *(1f)*; the less highly chlorinated isothiocyanates *(1b)–(1d)* give nitriles as well as *(2)*.

This cyclization is related to the isomerization of cyano-*N*-(pentachlorophenyl)formimidoyl chloride to hexachloroquinoxaline previously observed by us[1]; this also occurs only at high temperatures (*ca.* 400 °C) and similarly involves migration of an *o*-chlorine atom.

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[1] *H. Holtschmidt, E. Degener, H.-G. Schmelzer, H. Tarnow*, and *W. Zecher*, Angew. Chem. *80*, 942 (1968); Angew. Chem. internat. Edit. *7*, 856 (1968).

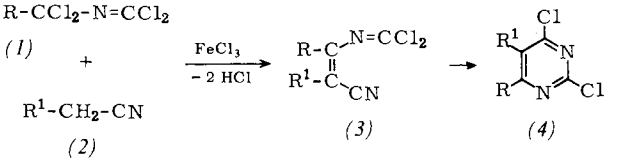
Direct Synthesis of Chlorinated Pyrimidines

By *R. Braden, K. Findeisen*, and *H. Holtschmidt*[*]

Dedicated to Professor K. Hansen on the occasion of his 60th birthday

In recent years isocyanide dichlorides have become a readily accessible class of compounds[1]; their high chemical reactivity has led to a wide variety of new compounds[2]. On reaction with bifunctional nucleophiles, various kinds of ring closures can be accomplished[2,3]. α-Chlorinated aliphatic isocyanide dichlorides, whose α-chlorine atoms generally react first on nucleophilic substitution[4], occupy a special position. Compounds having mobile halogen atoms add readily to nitriles[5,6].

We have found that in the presence of Lewis acids at elevated temperatures α-dihalogenated isocyanide dichlorides *(1)* react with nitriles *(2)* bearing two hydrogen atoms in the α-position to give chlorinated pyrimidines *(4)*. The reaction takes place in two stages, the rate-determining step being the elimination of hydrogen chloride. In a number of cases, however, it was possible to stop the reaction at the first stage and to detect the primary product *(3)*.



R	(4) R¹	Yield (%)	M.p. (°C)
Cl	H	88	89–93
Cl	Cl	94	68
Cl	CH_3	61	68
Cl	$ClCH_2$	74	112
Cl	C_6H_5	57	159
Cl	p-O_2N–C_6H_4	72	188
Cl	3,4-$Cl_2C_6H_3$	75	141
Cl	2,3,4-$Cl_3C_6H_2$	65	200
Cl	$NC-CH_2$	14	125
Cl	2-(2,4,6-trichloro-5-pyrimidinyl)ethyl	32	200
CCl_3	H	5	[a]
C_6H_5	H	58	88

[a] B.p. 140–155 °C/0.5 torr.

If the α-chlorine atoms of the isocyanide dichloride are replaced by hydrogen and the α-hydrogen atoms of the nitrile by chlorine the reaction proceeds in an analogous fashion. Of particular interest is the reaction of trichloroacetonitrile *(2')*, R^1 = Cl, with trichloromethyl isocyanide dichloride *(1)*, R = Cl; chlorine is evolved leaving a 30% yield of tetrachloropyrimidine (m.p. 67 °C).

$$R{-}CH_2{-}N{=}CCl_2 + R^1{-}CCl_2{-}CN \rightarrow (3) \rightarrow (4)$$
(1') *(2')*

R	R^1	*(4)* yield (%)	m.p. (°C)	b.p. (°C/torr)
Cl	Cl	46	67	
$ClCH_2$	Cl	5		130–145/0.5

The reaction is carried out in the following manner: The starting materials are mixed together, then mixed with about 0.1% of a Lewis acid (preferably iron(III) chloride) and heated to 200 °C. The process may be performed in low-boiling polar solvents in an autoclave or in high-boiling solvents under normal pressure.

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Synthesis of Disulfonimides, *N*-Sulfonyl Carboxamides, and α-Oxo *N*-Sulfonyl Carboxamides

By *F. Bentz* and *G.-E. Nischk* [*]

Dedicated to Professor K. Hansen on the occasion of his 60th birthday

Starting from *N*-sulfinyl sulfonamides *(1)* and sulfonic acids *(2)* we have prepared disulfonimides *(3)* in excellent yield [1] (see Table for examples).

The *N*-sulfinyl sulfonamides *(1)* can usually be obtained by boiling the sulfonamides with an excess of thionyl chloride,

$$R^1{-}SO_2{-}NSO + R^2{-}SO_3H \xrightarrow{40-150\,^\circ C} R^1{-}SO_2{-}NH{-}SO_2{-}R^2 + SO_2$$
(1) *(2)* *(3)*

R^1	R^2	*(3)* Yield (%)	M.p. (°C)
m-NO_2–C_6H_4	*p*-CH_3–C_6H_4	85	Isolated as K salt
C_6H_5	*p*-CH_3–C_6H_4	82	160
CH_3	*p*-CH_3–C_6H_4	92	116

usually without a solvent. Aliphatic or aromatic sulfonic acids may be used in the reaction, *e.g.*, methane-, chloroethane-, or benzene-sulfonic acid or their substitution products such as toluene- or chlorobenzene-sulfonic acid.

The components *(1)* and *(2)* are usually allowed to react in the molar ratio 1 : 1 in a melt or in the presence of a solvent. Solvents used were inert organic solvents such as toluene, chlorobenzene, and dichlorobenzene. Aliphatic and aromatic *N*-sulfinyl sulfonamides *(1)* also react with aromatic or aliphatic monocarboxylic acids, giving *N*-sulfonyl carboxamides [2].

$$R^1{-}SO_2{-}NSO + R^3{-}COOH \rightarrow R^1{-}SO_2{-}NH{-}COR^3 + SO_2$$
(1) *(4)*

R^1	R^3	*(4)* Yield (%)	M.p. (°C)
m-NO_2–C_6H_4	C_6H_5	73	173 (glacial acetic acid)
m-NO_2–C_6H_4	C_2H_5	84	115 (benzene)
C_6H_5	$ClCH_2$	67	104 (benzene)
m-NO_2–C_6H_4	Cl_2CH	63	137 (benzene)
C_6H_5	Cl_3C	61	92 (benzene)

The reactions, which are sometimes violent, are carried out in a melt or in an inert solvent (for examples see the Table).

N-Sulfinyl sulfonamides react with dicarboxylic acids, giving bis(substituted amides), *e.g.* *m*-nitrobenzene-*N*-sulfinylsulfonamide and adipic acid give an 82% yield of a product having m.p. 252 °C.

With oxamic esters or oxalic esters, sulfonamides give α-oxo *N*-sulfonyl carboxamides *(5)* in very high yield [3,4].

$$R^4{-}SO_2{-}NH_2 + \underset{\displaystyle COR^5}{\overset{\displaystyle |}{COOC_2H_5}} \xrightarrow{60-140\,^\circ C} R^4{-}SO_2{-}NH{-}COCOR^5 + C_2H_5OH$$
(5)

R^4	R^5	*(5)* Yield (%)	M.p. (°C)
m-NO_2–C_6H_4	$NHCH_3$	100	245
m-NO_2–C_6H_4	OC_2H_5	100	195
p-CH_3–C_6H_4	$NHCH_3$	100	156
m-NO_2–C_6H_4	NH_2	96	247
m-NO_2–C_6H_4	$N(CH_3)_2$	100	230
CH_3	$CH_2{=}C(CH_3){-}CONHCH_2NH$	100	208 (water)
C_6H_5	$(CH_2{=}CHCH_2)_2N$	87	95
m-NO_2–C_6H_4	$CH_2{=}CHCH_2NH$	100	178
C_6H_5	$CH_2{=}C(CH_3){-}CONHCH_2NH$	100	217

The sulfonamide is caused to react with an alkali hydroxide in an alcohol, preferably methanol, with addition of an aromatic hydrocarbon that boils higher than the alcohol. The alcohol and part of the aromatic hydrocarbon are distilled off at atmospheric pressure, then the oxamic ester or oxalic ester is added and the mixture is warmed (for examples see the Table).

The strongly acidic properties of these products *(3)*, *(4)*, and *(5)* give compounds of high molecular weight having very good dyeing properties towards basic dyestuffs.

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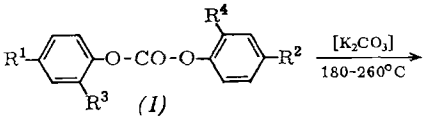
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A New Synthesis of Substituted Diphenyl Ethers

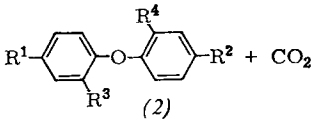
By *H. Witt*, *H. Holtschmidt*, and *E. Müller*[*]

Dedicated to Professor K. Hansen on the occasion of his 60th birthday

It has already been reported[1] that phenyl *o*-phenoxybenzoate can be prepared in high yields by heating a melt of diphenyl carbonate in the presence of small amounts of K_2CO_3 at 230—270 °C. We have now found that the diphenyl ethers *(2)* can be prepared from *o*- and/or *p*-substituted diphenyl carbonates *(1)* when subjected to similar reaction conditions.



(1)



(2)

R¹	R²	R³	R⁴	Catalyst wt.-% calc. w. r. t. *(1)*	Temp. (°C)	Yield of *(2)* (%)[a]
NO_2	H	H	H	1 K_2CO_3	210—250	17
NO_2	NO_2	H	H	0.5 $KOCOCH_3$	180—205	>90
H	H	NO_2	NO_2	1 $KOCOCH_3$	190—220	41
NO_2	NO_2	NO_2	NO_2	1 $KOCOCH_3$	156—186	89
NO_2	NO_2	Cl	Cl	1 K_2CO_3	186—226	31
CN	CN	H	H	1 K_2CO_3	200—242	65
$SO_2C_6H_5$	$SO_2C_6H_5$	H	H	1 K_2CO_3	240—260	66
$COOCH_3$	$COOCH_3$	H	H	1 K_2CO_3	200—214	22

[a] Not optimized.

A prerequisite for this reaction is that at least one of the groups R¹—R⁴ is a second order substituent; preparatively useful yields, however, are obtainable only from symmetrically substituted, particularly *p,p'*-disubstituted, diphenyl carbonates. Numerous other alkali metal compounds may be used as catalysts (in amounts of 0.5—2 wt.-%) instead of potassium carbonate.

4,4'-Dinitrodiphenyl ether (2), $R^1=R^2=NO_2$, $R^3=R^4=H$[2]

4,4'-Dinitrodiphenyl carbonate (1000 g) (crude phosgenation product, m.p. 140 °C)[3] is melted (silicone oil bath) in a 2 l three-necked flask fitted with stirrer, internal thermometer, and a delivery tube connected *via* a bubble counter. Potassium acetate (5 g) is added slowly, with stirring, to the melt at a temperature of 150 °C. Decarboxylation (180—205 °C, bath temperature 190—215 °C) is complete after 4—5 hours. The temperature of the mixture is then allowed to drop to 150 °C, and, after the apparatus has been fitted with a reflux condenser, toluene (580 g) is added slowly. The solution is filtered hot from insoluble residue (*ca.* 8 g). The filtrate is then cooled and the 4,4'-dinitrodiphenyl ether which crystallizes out is recovered by filtration, washed with a little methanol, and finally dried in a vacuum (yield 749 g (88 %), m.p. 144 °C). A further 28 g can be recovered by concentration of the mother liquor, m.p. 142 °C, total yield 91 %. If recrystallized starting material is used, yields of more than 93 % of the ether can be obtained.

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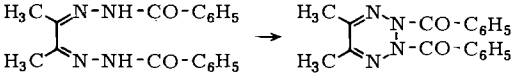
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Mesoionic 2-Benzoyl-1-benzoylimino-4,5-dimethyl-1,2,3-triazole

By *S. Petersen* and *H. Heitzer*[*]

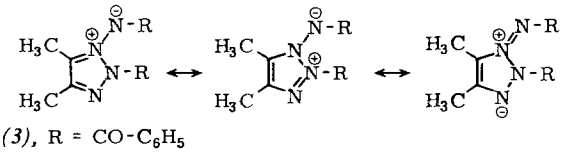
Dedicated to Professor K. Hansen on the occasion of his 60th birthday

The oxidation product first prepared by *H. v. Pechmann* and *W. Bauer* by reaction of 2,3-butanedione bis(benzoylhydrazone) *(1)*[1] with potassium hexacyanoferrate(III) was formulated[2] as 2,3-dibenzoyl-5,6-dimethyl-2,3-dihydrotetraazine *(2)*.



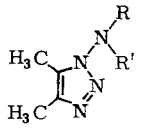
(1) *(2)*

The ^{1}H-NMR spectra (in $CDCl_3$) of the oxidation product at 60 and 220 MHz[3] show that the compound does not have a symmetrical structure. Two methyl-group signals appear in the 60 MHz spectrum at 2.23 ppm and 2.36 ppm in addition to a multiplet (signal width *ca.* 20 Hz) centered at 8.1 ppm which is due to the protons of both aromatic rings that are *ortho* to the carbonyl groups. In the 220 MHz spectrum the multiplet is resolved into two pseudo doublets at 8.116 ppm and 8.236 ppm (J = 7.8 to 8.0 Hz). The remaining six aromatic protons absorb between 7.4 and 7.8 ppm. On the basis of these findings, therefore, we suggest that the oxidation product has the structure of a mesoionic triazole *(3)*,



(3), R = $CO-C_6H_5$

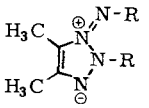
which is in agreement with the chemical properties of this compound. The ready hydrolytic and thermal loss of a benzoyl group is now understandable since the compound is being considered as an azolide[4]. As is already known, compound *(3)* affords 1-(dibenzoylamino)-4,5-dimethyl-1,2,3-triazole *(4)*[5] when heated and 1-benzoylamino-1,2,3-triazole *(5)* when treated with hydrochloric acid. Hydrolysis of *(3)* with concentrated hydrochloric acid at higher temperatures leads to formation of the free 1-amino-4,5-dimethyl-1,2,3-triazole *(6)*[2]. We have obtained 4-chlorobenzoic anhydride as reaction product by recrystallizing compound *(7)*



(4), R = R' = COC_6H_5

(5), R = COC_6H_5, R' = H

(6), R = R' = H



(7), R = $COC_6H_4Cl(p)$

from aqueous dimethylformamide. All these secondary reactions can now be adequately explained without recourse, as previously, to complicated assumptions of rearrangement and ring contraction.

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Direct Conversion of Cyclic Carboxylic Acid Anhydrides into Carboximide Derivatives

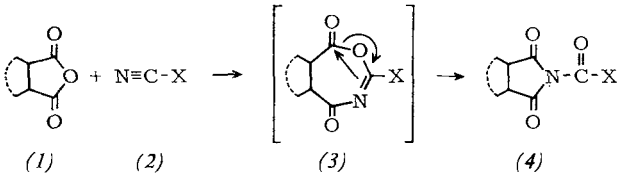
By *E. Grigat* [*]

Dedicated to Professor K. Hansen on the occasion of his 60th birthday.

Although cyanates *(2)*, X = OR, react with carbonyl halides to give *N*-acyliminocarbonic halides [1], attempted reactions with carboxylic anhydrides have so far been unsuccessful [2, 3].

Cyclic anhydrides of aromatic and cycloaliphatic dicarboxylic acids *(1)* are exceptions. They react exothermally with cyanates *(2)*, X = OR, at 150 °C in the presence of catalytic amounts of triethylamine to give *N*-acylated cyclic dicarboximides *(4)*, X = OR. Cyanamides react analogously, even without addition of triethylamine, to give *(4)*, X = NR_2 (see Table). The reaction probably proceeds, like reaction of *(2)* with acid halides, *via* a primary *N*-acylation of the CN group. The non-isolable primary addition product *(3)* is stabilized by intramolecular transacylation to *(4)*.

The compounds *(4)*, X = OR, can be converted into compounds *(4)*, X = NR_2, by reaction with amines.

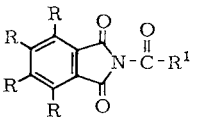


(1) *(2)* *(3)* *(4)*

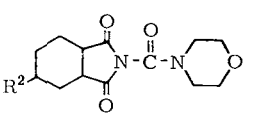
N-(2,4-Dimethylphenoxycarbonyl)phthalimide (4a)

A mixture of phthalic anhydride (29.6 g, 0.20 mole) and 2,4-dimethylphenyl cyanate (32.5 g, 0.22 mole) is heated and stirred at 180 °C. On adding a few drops of triethylamine the temperature of the mixture rises to 230 °C. After 15 minutes' stirring, the reaction mixture is cooled, mixed with about 50–80 ml alcohol, and the compound *(4a)* which separates is recovered by filtration (48 g = 81% yield).

Table. Representative carboximide derivatives.



(4a)-(4l)



(4m), *(4n)*

(4)	R	R^1	R^2	M.p. (°C)	Yield (%)
(a)	H	2,4-$(CH_3)_2$–C_6H_3–O		174–176	81
(b)	H	4-CH_3–C_6H_4–O		152–154	—
(c)	H	C_6H_5–O		148–150	—
(d)	H	Cl_3C–CH_2–O		138–139	35
(e)	Cl	2,4-$(CH_3)_2$–C_6H_3–O		197–198	46
(f)	H	Morpholino		205–207	78
(g)	H	$(C_2H_5)_2N$		119–120	53
(h)	H	$(CH_2{=}CH{-}CH_2)_2N$		77–78	76
(i)	H	Piperidino		158–159	80
(j)	H	C_6H_5–CH_2–$N(CH_3)$		112–114	65
(k)	Cl	Morpholino		249–250	62
(l)	Br	Morpholino		287–288 (decomp.)	49
(m)			H	163–165	25
(n)			CH_3	122–124	—

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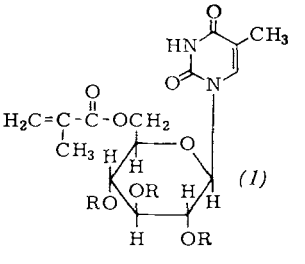
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Separation of Nucleosides on Polymer Gels Containing Thymine or Cytidine

By *G. Greber* and *H. Schott* [*]

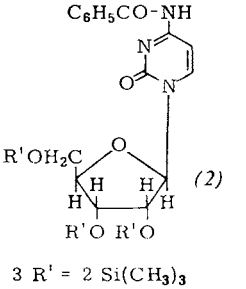
By using Amberlite ion exchangers, which contained covalent built-in nucleoside species, *Tuppy* and *Küchler* [1] were able to separate *via* the base-pairing reaction of *Watson* and *Crick* [2] the corresponding nucleoside from an aqueous solution of two nucleosides. These experiments were carried out with extremely small amounts of substance (0.04 mg/0.04 ml).

In the meantime it has been established [3,4] that measurable base pairing of nucleosides takes place only in chloroform or



(1)

R = $Si(CH_3)_3$



(2)

3 R' = 2 $Si(CH_3)_3$

dimethyl sulfoxide (DMSO) and not in water. Separation of nucleosides on a preparative scale ought to be possible, therefore, on organic polymer gels which swell in these solvents and which contain covalent nucleoside residues.

We have prepared such gels and tested their separation efficiency regarding the nucleosides thymidine (T), adenosine (A), cytidine (C), and guanosine (G). 1-[2,3,4-*O*-tris(trimethylsilyl)-6-methacryloyl-β-D-glucopyranosyl]thymine *(1)* and N^4-benzoyl-$O^{x'}$,$O^{y'}$-bis(trimethylsilyl)-$O^{z'}$-methacryloylcytidine *(2)* [5] were copolymerized radically with tetramethylene dimethacrylate to give insoluble thymine- and cytidine-containing polymer gels that swell in organic solvents. Cleavage of the trimethylsilyl groups with HCl/acetone and of the trimethylsilyl- and benzoyl groups with NH_3/methanol afforded T gels and G gels, which swell in DMSO or DMSO/$CHCl_3$ and exhibit very good flow rates.

With T gels it was not possible to separate the 1 : 1 complex of the two corresponding nucleosides formed from equimolar amounts of T and A in DMSO. On the other hand it was possible to separate the excess amounts of A from the 1 : 1 complex formed from a mixture of T and an excess of A. In experiments with an analogous sample gel that did not contain T species, no interactions took place and consequently there was no separation effect.

In separation experiments carried out with CG mixtures on C gels similar results were obtained as with TA mixtures on T gels. With C gels, however, it was found that not only good separation of the 1 : 1 TA complex could be accomplished but also that the separation could be improved by lengthening the column. The two non-classical 1 : 1 complexes between A and G and between T and G can be completely separated on C gels. These results confirm indirectly the interaction energies [6] calculated for vacuum for the classical and non-classical base pairs. Accordingly, the value for the base pair CG (—19.2 kcal/mole) is almost three times higher than that for the other combinations (AT = —7.0, AC = —7.8, AG = —7.5, TG = —7.4, and TC = —6.5 kcal/mole).

Chromatographic procedure:

Glass columns, 48 cm in length and 1 cm in diameter, were filled with 18 g of swollen T- or C-gel — a mixture of DMSO/$CHCl_3$ (2 : 3) being used as swelling agent. For separation, up to 100 mg of mixed nucleosides was dissolved in DMSO (*ca.* 20 mg/ml), transferred to the column, and then developed at room temperature with a mixture of DMSO/$CHCl_3$ (2 : 3), the flow rate being about 38 ml/h. The separation process was monitored in a measuring cell using a Uvicord-Ultraviolet absorptiometer and recorded in the form of a UV absorption diagram by an LKB pen recorder. Samples of the eluate were collected at regular intervals and the separation of the nucleosides examined by UV absorption measurements using a Zeiss spectrophotometer PMQ 11 at E_{280}/E_{260} nm.

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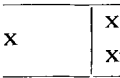
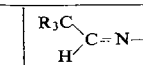
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The Color of Trimethylsilyl Derivatives of Diimine [1]

By *H. Seidl*, *H. Bock* [*], *N. Wiberg*, and *M. Veith* [**]

The n→π* excitation energies of hetero atom chromophores are lowered drastically by trimethylsilyl substituents (Table 1); for instance bis(triphenylsilyl) ketone [2,3] is violet in contrast to the colorless dialkyl ketones, and bis(trimethylsilyl)diimine [5] is blue in contrast to the colorless dialkyldiimines [6].

Table 1. n→π* excitation energies (cm^{-1}) of silyl- and alkyl-substituted hetero atom chromophores [R = C_6H_5 in $(R_3Si)_2CO$, otherwise CH_3].

X	 [3]	 [4]	X—N=N—X [5, 6]
CR_3	35800	40200	27200
CR_3/SiR_3	26800		20000
SiR_3	18500	33400	12750

On the basis of experimental data [7] the color of the silyl ketones has to be ascribed to the strong inductive rise of the highest occupied n-orbital of the oxygen atom due to the R_3Si group in the β-position and to the lowering of the π*-orbital by $Si \leftarrow C_\pi$ interaction with unoccupied atomic orbitals of silicon in α-position to the C=O π-system. The long-wavelength shift of the n→π* absorption band of bis(trimethylsilyl)diimine whose R_3Si groups are in α-position to both the N=N π-system and to the nitrogen lone pairs n_N is, however, still unexplained.

For a study of the substituent effects on the azo chromophore [8] we selected the more stable phenyl derivatives *(1)* [9] and *(2)* [10], for which additional experimental data can be obtained. Their ionization energies (determined by mass spectroscopy [11]), electron-spectroscopic excitation energies, and half-wave reduction potentials [12] are collected in Table 2.

Table 2. Experimental data for *tert*-butyl- *(1)* and (trimethylsilyl)-phenyldiimine *(2)*.

	C_6H_5—N=N—$C(CH_3)_3$ *(1)*	C_6H_5—N=N—$Si(CH_3)_3$ *(2)*
$IE(n_N)$ (eV)	7.75	7.05
$\tilde{\nu}_m^{n\to\pi^*}$ (cm^{-1}) [13]	24400	17250
$\tilde{\nu}_m^{\pi\to\pi^*}$ (cm^{-1}) [13]	38400	37500
$E_{1/2}^{Red}$ (V)	—1.35	—1.13

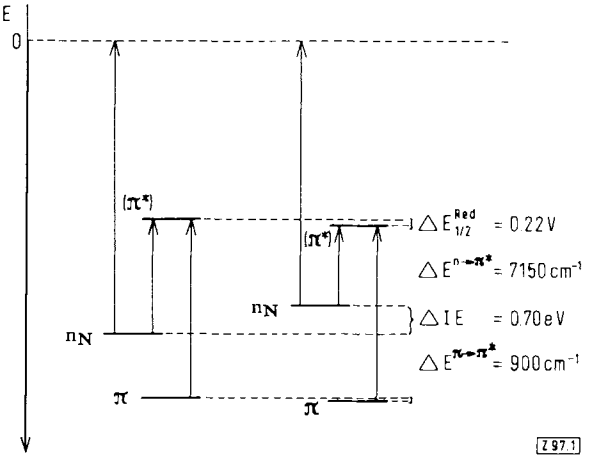


Fig. 1. Experimental energy level schemes for *tert*-butyl- *(1)* and trimethylsilyl-phenyldiimine *(2)*.

Comparison of the energy level schemes for the inner molecular orbitals of *(1)* and *(2)* drawn up from the data in Table 2 shows that the R_3Si substituent in phenyldiimine derivatives also increases the energy of the nitrogen lone pair n_N whilst lowering the π-molecular orbitals. The decreased $n\rightarrow\pi^*$ excitation energy of *(2)*, and thence also of bis(trimethylsilyl) diimine, is then to be explained as in the case of the silyl ketones[7]. However, as the rise in the n_O level of the oxygen due to silicon in the β-position amounts to 0.9 eV relative to the standard *tert*-butyl phenyl ketone[7], a difference in the ionization potential $\Delta IE > 1$ eV would be expected between the alkyl- and the silyl-substituted phenyldiimine derivatives, because the inductive effect of substituents in the α-position should be enhanced by a factor $I_\alpha/I_\beta \approx 1.6$[14].

The observed difference of only 0.7 eV can be accounted for by an additional $Si\leftarrow n_N$ interaction (in the direction opposite to the inductive increase) of the n_N lone pair with unoccupied atomic orbitals of the silicon in α-position to the nitrogen[15]. The interaction should lead to an increase in the NNSi angle since a wider angle favors the overlap[16].

Neither the NNSi angles[13] in the trimethylsilyldiimine derivatives nor the interaction between the two n_N electron pairs discussed for azo compounds[6,8] is known. Since, however, the whole visible and ultraviolet region of the electronic spectrum of bis(trimethylsilyl)diimine shows only the $n\rightarrow\pi^*$ absorption at 12750 cm^{-1}, the n_a/n_s splitting must exceed 4.7 eV[17].

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[12] Measured in a 0.1 M *N,N*-dimethylformamide solution of tetrabutylammonium iodide against the mercury pool at 25 °C.

[13] The corresponding extinction values $\varepsilon_m^{n\rightarrow\pi^*}$ and $\varepsilon_m^{\pi\rightarrow\pi^*}$ ($l \cdot mole^{-1} \cdot cm^{-1}$) are for *(1)* 100 and 7100, respectively, and for *(2)* 29 and 16350, respectively. As for the (trimethylsilyl)styrenes, the differences in the $\pi\rightarrow\pi^*$ transitions are explained by expansion of the π-system in *(2)*; for the $n\rightarrow\pi^*$ transitions they possibly can be interpreted on the basis of increased p hybridization of the lone pair due to widening of the angle and the thus more strongly overlap-forbidden transition in the case of the silicon compound.

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[15] Experimental results for silyl- and alkyl-substituted aldimine derivatives RHC=NX, whose $n\rightarrow\pi^*$ excitation energies (Table 1) also differ by more than 0.8 eV, prove also that $Si\rightarrow n_N$ interaction occurs between the n_N elctron pair and unoccupied orbitals of the silicon atom in the α-position [4].

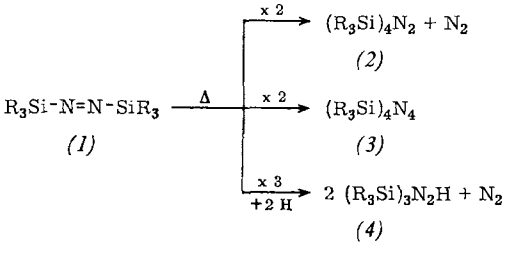
[16] Cf. the ESR data for the radical anion of *N,N'*-bis(trimethylsilyl)benzoquinone diimine [*F. Gerson, U. Krynitz*, and *H. Bock*, Helv. chim. Acta, in press].

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1,1,4,4-Tetrakis(trimethylsilyl)tetrazene[1]

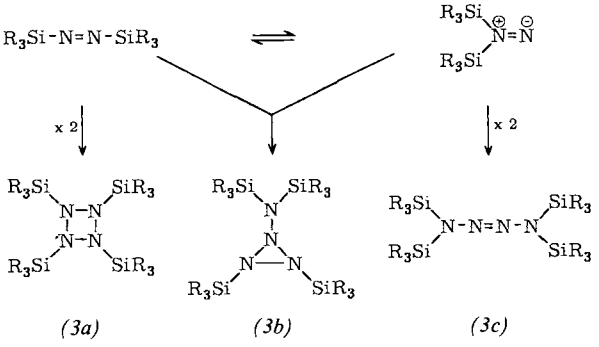
By *N. Wiberg* and *W. Uhlenbrock*[*]

Thermal decomposition of bis(trimethylsilyl)diimine *(1)* below 0 °C affords almost exclusively tetrakis(trimethylsilyl)-hydrazine *(2)* and nitrogen[2]. We have now found that an increase in thermolysis temperature reduces the yield of these two products; instead, other thermolysis products are formed, and in particular a compound having the composition $(R_3Si)_4N_4$ *(3)* (R = CH_3; elemental analysis, mass spectrum) as well as tris(trimethylsilyl)hydrazine *(4)*.



The hydrogen required for formation of *(4)* comes from methyl groups; those molecules affected by hydrogen abstraction react further to give various products that have not yet been examined in detail.

The ^1H—NMR spectrum of compound *(3)* contains only one signal in the $(CH_3)_3Si$ region [δ = —16.7 Hz, measured against TMS as internal standard in benzene[3]]. Thus, of the isomers *(3a)*, *(3b)*, and *(3c)* that are *formally* possible according to



(3a) *(3b)* *(3c)*

(3b) can be ruled out (the same applies to the compound $(R_3Si)_2N{-}N(SiR_3){-}N{=}N(SiR_3)$). The IR and Raman spectra indicate the presence of *(3c)* rather than *(3a)*; unequivocal evidence for an atomic skeleton containing an N=N bond comes, in particular, from the position, intensity, and polarization of a band at 1444 cm^{-1} that is absent from the Raman spectrum of *(2)*[4]. The electronic spectrum of the compound also lends support to the 2-tetrazene structure: as in the case of organic tetrazenes[5] an $n\rightarrow\pi^*$ transition of medium intensity is observed at about 280 nm, λ_{max} = 293 nm, (ε = 5820).

The exclusion rule apparent from the vibrational spectra and the small dipole moment of $\mu = 0.45$ D[3] also indicate that *(3c)* is present in the *trans* configuration (C_{2h}).

The colorless, crystalline tetrakis(trimethylsilyl)tetrazene, which melts at 38—39 °C[3] and sublimes at about 70 °C[3], is the first silyl-nitrogen compound known to contain a four-membered nitrogen chain. It decomposes very slowly above about 160 °C, yielding mainly hexamethyldisilazane and nitrogen

$$(3c) \xrightarrow[+\,2H]{>160\,^\circ C} 2\,(R_3Si)_2NH + N_2$$

As in the case of thermolysis of *(1)*, hydrogen transfer leads to by-products that have not been investigated further. Under normal conditions *(3c)* does not react with oxygen and is not attacked by water below 130 °C. Acids catalyze the hydrolysis of *(3c)* to ammonium azide and hexamethyldisiloxane

$$(3c) \xrightarrow[-\,2R_3SiOSiR_3]{+\,2\,HOH} (H_2N{-}N{=}N{-}NH_2) \longrightarrow [NH_4]N_3$$

Procedure:

A pure sample of *(1)*[2] (36.17 g, 207.5 mmoles) in benzene (200 g) is heated to 150—160 °C for 1 h in an extremely dry, sealed bomb tube; 32.3 % of the nitrogen in the compound is liberated during thermolysis. Fractional distillation of the reaction mixture at 65—75 °C/*ca.* 10^{-3} torr yields a colorless mixture of *(2)* and *(3)*, from which pure *(3)* (5.10 g, 14.63 mmoles; yield 14.1 %) can be isolated by repeated recrystallization from pentane at —78 °C.

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[1] Derivatives of Diimine, Part 5. This work was supported by the Deutsche Forschungsgemeinschaft. — Part 4: *H. Seidl, H. Bock, N. Wiberg*, and *M. Veith*, Angew. Chem. *82*, 42 (1970); Angew. Chem. internat. Edit. *9*, 69 (1970). Also Part 8 of Silicon Compounds. -- Part 7: ref. [2].

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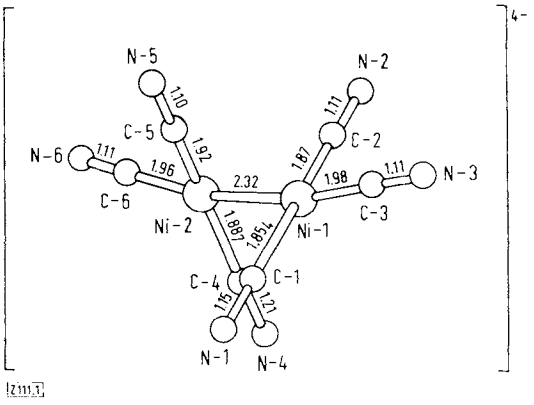
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Structure of the Anion in Solid $K_4[Ni_2(CN)_6]$

By *O. Jarchow*[*], *H. Schulz*, and *R. Nast*[**]

"Bellucci's salt" $K_4[Ni_2(CN)_6]$ has already been subjected to preliminary X-ray structure analysis[1,2] and been investigated in a series of IR and Raman studies[3–6], the results of which, however, have so far failed to provide an unequivocal answer to the long-discussed question of the structure of the $[Ni_2(CN)_6]^{4-}$ ion. A recent X-ray study of the compound[7] has now yielded the structure shown in the Figure for the hexacyanodiniccolate(I) ion. The dinuclear anion is seen to contain two almost planar tricyanoniccolate(I) units that are linked *via* an Ni—Ni bond about which they are twisted by 82 ° with respect to each other. The mean deviation of the cyano ligands from the respective $Ni(CN)_3$ planes is 0.04 Å and thus approaches the limits of experimental accuracy. The somewhat greater deviation of the Ni atoms from these planes — 0.18 Å for Ni-1 and 0.16 Å for Ni-2 — is interpreted as a steric effect of the potassium ions (not shown in the Figure).



[Z 111 3]

The Ni—Ni bond of 2.32 Å is remarkably short; the Ni^I radius (1.16 Å) calculated from this figure is of the same order of magnitude as the value given by *Pauling* for the Ni radius in purely metallic bonding. The mean length of the Ni—C bond is 1.91 ± 0.02 Å, that of the C—N bond 1.13 ± 0.02 Å. The angles Ni-2—Ni-1—C-3 and Ni-1—Ni-2—C-6 not shown in the Figure are each equal to 169 ° and thus deviate considerably from 180 °.

The possibility of additional linkage of the Ni atoms *via* cyano bridges[1,3,5] can now be ruled out since the distances Ni-2—C-1 (2.90 Å) and Ni-1—C-4 (2.96 Å) are far too great for such bonding.

The symmetry of the complex anion in the solid approaches 2 (C_2); the slight deviations observed are attributed to the low overall symmetry $P\bar{1}$ of the structure. The twofold axis is vertical in the plane of the Figure and passes through the center of gravity of the Ni—Ni dumbell.

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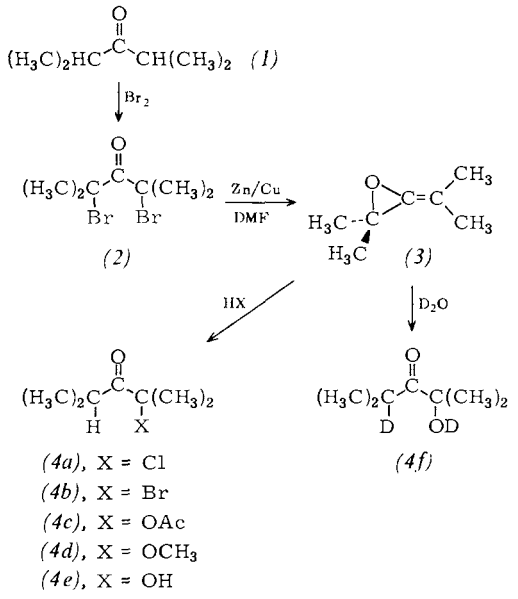
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3-Isopropylidene-2,2-dimethyloxirane (Tetramethylallene Oxide)[1,2]

By *H. M. R. Hoffmann* and *R. H. Smithers*[*]

Allene oxides show promise as versatile intermediates in numerous reactions, for instance as precursors of allylic cations in (4 + 3) cycloadditions[3]. We have obtained 3-isopropylidene-2,2-dimethyloxirane (tetramethylallene oxide) *(3)* in two simple stages starting from readily available diisopropyl ketone *(1)*, which on PBr_3-catalyzed bromination gives the known 1,3-dibromoketone *(2)*[4]. Debromination of *(2)* with a zinc-copper couple in dimethylformamide affords a *ca.* 5 % solution of compound *(3)*[5]. To our surprise tetramethylcyclopropanone[7] was *not* formed under these conditions. Solutions of *(3)* in dimethylformamide are stable at —78 °C and also for one hour at 35 °C, provided that $ZnBr_2$ is absent.



(4a), X = Cl
(4b), X = Br
(4c), X = OAc
(4d), X = OCH_3
(4e), X = OH

(3) reacts with a variety of compounds containing acidic hydrogen to form the ring-opened keto derivatives *(4)*. For instance, passage of gaseous hydrogen chloride into a solution of *(3)* immediately gives rise to *(4a)* [8], while gaseous hydrogen bromide affords *(4b)* [9]. A solution of *(3)* and acetic acid form the acetate *(4c)* [6a]. *(3)* and methanol react to *(4d)* [9], which interestingly can also be prepared from *(2)* by debromination with a zinc-copper couple in methanol. *(3)* and water form *(4e)* [9], also obtainable in high yield directly from *(2)* by treatment with a zinc-copper couple in tetrahydrofuran-water (4 : 1 v/v) at room temperature. *(3)* and D_2O give rise to *(4f)*; ^{1}H-NMR in dimethylformamide: τ = 8.95 (6H/br. s), τ = 8.7 (6H/s). Generally, ring-opening of *(3)* is markedly accelerated by $ZnBr_2$. The compounds *(4)* were identified by NMR spectroscopy and, when known, by comparison with authentic material.

3-Isopropylidene-2,2-dimethyloxirane (3)

A solution of 2,4-dimethyl-2,4-dibromo-3-pentanone *(2)* [4] (5 g) in dimethylformamide (DMF) (7 ml) is added dropwise to a stirred suspension of a zinc-copper couple (3.6 g) in DMF at −10 °C under nitrogen. Debromination ensues immediately as shown by the rise in temperature to *ca.* −5 °C. After completed addition of *(2)* the reaction mixture is stirred for a further 30 min and the excess of the metal removed by rapid filtration under nitrogen. In order to remove the $ZnBr_2$ the mother liquor (*ca.* 25 ml) is diluted with formamide (25 ml) and distilled at −10 °C/0.002 torr into a trap kept at −78 °C. A *ca.* 5% solution of *(3)* in DMF results, the formamide remaining behind together with $ZnBr_2$. ^{1}H-NMR in DMF: τ = 8.44 (6H/s), τ = 8.55 (3H/s), τ = 8.65 (3H/s). IR (in DMF): 1145 cm^{-1}; other region obscured by bands of DMF. Mass spectrum: *m/e* = 112 and fragmentation peaks consistent with a partial rearrangement into tetramethylcyclopropanone (cf. also [6b,9]).

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[1] Allene Oxides, Part 1.

[2] Work supported by the Science Research Council (London) and the Petroleum Research Fund, administered by the American Chemical Society.

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Transfer of Methoxyphenylcarbene Ligands from Molybdenum to Iron and Nickel [1]

By *E. O. Fischer* and *H.-J. Beck* [*]

Earlier experiments had shown that in the thermal decomposition of methoxyphenylcarbenepentacarbonylchromium(0) [2] the ligand $:C(OCH_3)C_6H_5$ undergoes dimerization with formation of *cis*- and *trans*-α,α′-dimethoxystilbene [3]. Meanwhile we have succeeded for the first time in transferring a carbene ligand from one metal to another. When subjected to UV irradiation methoxyphenylcarbenecarbonylcyclopentadienylnitrosylmolybdenum(I) *(1)* [4] reacts with pentacarbonyliron in benzene to give methoxyphenylcarbenetetracarbonyliron(0) *(2)*, which could not be prepared [6] by conventional methods [2, 5].

$$C_6H_5Mo(NO)(CO)C(OCH_3)C_6H_5 + Fe(CO)_5 \xrightarrow[C_6H_6]{h\nu}$$
(1)

$$(CO)_4FeC(OCH_3)C_6H_5 + C_5H_5Mo(NO)(CO)_2 + \ldots$$
(2)

Characterization of the iron complex *(2)*, which is red-brown, sensitive to air, readily volatile, and diamagnetic, follows from the mode of preparation, total analysis, and spectroscopic findings.

The ^{1}H-NMR spectrum of *(2)* in deuterioacetone contains two singlets of relative intensities 5 : 3 at $\tau_{C_6H_5}$ = 2.54 and τ_{OCH_3} = 5.15. Four ν_{CO} bands occur in the IR spectrum (*n*-hexane; LiF optics) at 2055 m (A_1), 1990 m (A_1), 1964 s, and 1947 cm^{-1} s (both resulting from E), which are to be expected for a molecule of symmetry C_{3v} containing an asymmetric ligand such as $:C(OCH_3)C_6H_5$ in an axial position [7,8].

The mass spectrum [9] (50 eV), which provides independent confirmation of the composition of *(2)*, shows the molecular ion at *m/e* = 288, the fragmentation pattern $[(CO)_nFeL]^+$, *n* = 4, 3 . . . 0, expected for the $(CO)_4Fe$ residue, and the typical mass line *m/e* = 240 for the dimerized carbene ligand. A dipole moment measurement in cyclohexane at 20 °C yielded a value of μ = 3.19 ± 0.1 D.

At present the question whether the transfer reaction proceeds *via* a phenylmethoxycarbene formed as intermediate or whether *(2)* occurs by direct reaction of molecules *(1)* with $Fe(CO)_4$ fragments cannot be answered. A further similar transfer reaction should also be mentioned in which tetracarbonylnickel reacts with *(1)* immediately on stirring in tetrahydrofuran without UV irradiation to give a violet diamagnetic product that is very sensitive to air. On the basis of current spectroscopic findings (IR, ^{1}H-NMR), partial analysis, and a mass spectroscopically determined

molecular weight $m/e = 620$, we would expect a trimeric structure with empirical formula $[Ni(CO)C(OCH_3)C_6H_5]_3$ having terminal CO ligands and $C(OCH_3)C_6H_5$ groups.

Experimental:

All operations must be carried out in an inert gas and in a fume cupboard since metalcarbonyls are extremely poisonous. A solution of *(1)* (1.65 g, 4.8 mmole) and $Fe(CO)_5$ (6.47 ml, 48 mmole) in benzene (100 ml) is vigorously stirred and subjected to UV irradiation (water-cooled, high-pressure lamp Q 81, Quarzlampen GmbH, Hanau) for a period of 5 hours. The reaction mixture is filtered through a G4 frit and the solvent removed at reduced pressure. The brown-yellow residue is taken up in 5 ml of an hexane/benzene mixture and then purified by column chromatography (silica gel, Merck) with hexane and benzene.

The first dark-red zone contains *(2)* as a red-brown, analytically pure oil (yield *ca.* 20% w.r.t. *(1)*), which is readily soluble in organic solvents.

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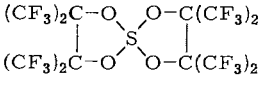
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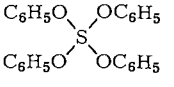
Tetraphenyl Orthosulfite

By *J. I. Darragh* and *D. W. A. Sharp* [*]

Previously the only known orthosulfite was the perfluoropinacol derivative *(1)*, which can be prepared [1] by the action of disodium perfluoropinacolate on sulfur tetrachloride. We have now found, however, that phenyl orthosulfite *(2)* can be prepared by reaction of more than 3 moles



(1)



(2)

of phenoxytrimethylsilane with one mole of sulfur tetrafluoride. The action of smaller ratios of phenoxytrimethylsilane on sulfur tetrafluoride leads to formation of phenoxytrifluorosulfur *(3)* and diphenoxydifluorosulfur *(4)*, along with traces of triphenoxyfluorosulfur *(5)*. Full analytical data are available for compounds *(2)*, *(3)*, and *(4)*; compound *(5)* has been characterized by spectroscopic data only. The ester *(2)* is a white hygroscopic solid which is hydrolyzed to phenol and diphenyl sulfite.

The coordination arrangement about the S^{IV} atom in *(2)* when it is surrounded by four oxygens is of interest since the lone pair of electrons on the sulfur should be stereochemically active and the structure derived either from a trigonal bipyramid or a square pyramid. The ^{1}H-NMR spectrum of *(2)* is complex and cannot be used to obtain definitive information on the stereochemistry of the molecule; the ^{19}F-NMR spectra (see Table) of compounds *(3)*, *(4)*, and *(5)*, on the other hand, are closely analogous to that of SF_4 [2], which has been shown by microwave spectroscopy to have a structure derived from a trigonal bipyramid [3]. It is noteworthy that the ^{19}F-NMR spectrum of *(3)* shows non-equivalence of the fluorine atoms at room temperature; previous studies of mono-substituted derivatives of SF_4 have shown equivalence of the fluorine atoms at room temperature [4]. The spectra of *(4)* and *(5)* are consistent with fluorine atoms in the apical positions of the trigonal bipyramid. All of this evidence strongly favors a coordination arrangement in *(2)* in which the oxygens are arranged at four apices of a trigonal bipyramid with the lone pair of the sulfur occupying an equatorial position.

Table: ^{19}F-NMR data of sulfur tetrafluoride and its phenoxy-substituted derivatives (measured in CD_3CN; external standard CCl_3F).

Compound	F_{axial} (ppm)	$F_{equatorial}$ (ppm)	J_{F-F} (Hz)
SF_4	−116.4 [2]	−69.4 [2]	78 [2]
$C_6H_5OSF_3$ *(3)*	− 79.1 d	−30.5 t	67.7
$(C_6H_5O)_2SF_2$ *(4)*	− 67.4 s, broad		
$(C_6H_5O)_3SF$ *(5)*	− 70.8 s, broad		
$(C_6H_5O)_4S$ *(2)*			

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A Reinterpretation of the ESR Spectrum Ascribed to a Non-degenerate State of the Benzene Radical Anion [***]

By *J. Kelm* and *K. Möbius* [*]

Köhnlein, Böddeker, and *Schindewolf* [1] observed a 15-line ESR spectrum for solutions of benzene(−) at 0 °C produced by reduction of benzene by a Na—K alloy in dimethoxyethane/tetrahydrofuran (DME/THF); they interpreted this finding on the basis of the assumption that the unpaired electron occupies the symmetrical benzene orbital. This observation is of particular interest because it indicates that counter ions can remove the orbital degeneracy and stabilize the symmetrical MO.

In our attempts to reproduce the 15-line spectrum we found that it occurs only when the solvent DME/THF is dried with $LiAlH_4$; the spectrum is not obtained when the solvent is dried only with Na—K alloy under high vacuum (cf. ref. [1b, 2]).

Like *Wormington* and *Bolton* [3], we succeeded in resolving each of the 15 lines into more than 13 components. Attempts to simulate this substructure by hyperfine structure (HFS) splitting of four equivalent alkali metal ions failed to reproduce the gradual decrease in intensity of the outermost lines. *Wormington* and *Bolton* [3] simulated the substructure on the

assumption of an additional HFS splitting with at least seven further protons.

We therefore agree with these authors that the radical in question, hereafter designated X, is not benzene(—) whose degeneracy has been lifted but a product of its reaction with the solvent. In order to substantiate this hypothesis, we have measured the g factors of benzene(—) and of X (relative error ±2.5 ppm) at various temperatures (see ref. [4] for measuring technique): The values show a weak but significant temperature dependence (Table); comparison of the two radicals was on the basis of the values recorded at −30 °C (Fig. 1).

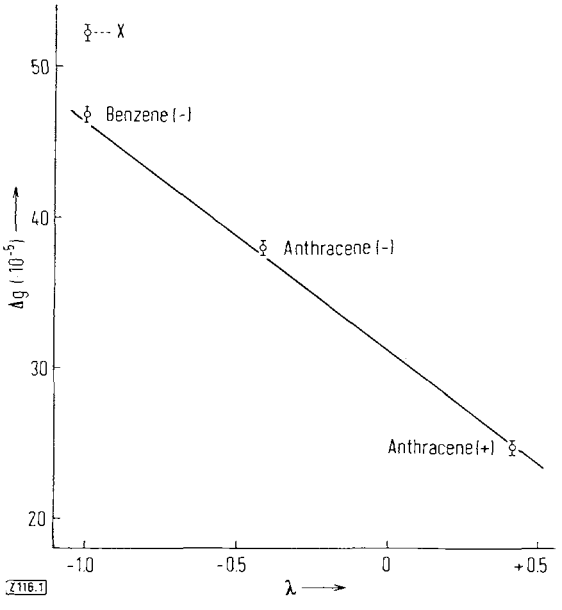


Fig. 1. Stone plot, $\Delta g = f(\lambda)$.

Table 1. Variation of g factors (not corrected for second-order effects) of benzene(—) and in X with temperature.

T (°C)	Benzene(—)	T (°C)	X
−32	2.002787	+25	2.002829
−64	2.002810	−30	2.002841
−84	2.002828	−70	2.002838

According to *Stone* [5], the deviation of the g factor from the value for the free electron $g_0 = 2.002319$ is a linear function of the Hückel energy coefficient λ of the lowest half-filled π orbital. With our instrumentation, the Stone line has the analytical form $\Delta g = [(31.2 \pm 0.4) - (15.1 \pm 0.7)\ \lambda] \times 10^{-5}$ [6], which we were able to verify by subsequent measurements of the g factors of anthracene(—) (2.002699) and anthracene(+) (2.002566).

If the X spectrum is assigned to a nondegenerate state of benzene(—), then $|\lambda|$ should decrease by about 0.07 (this estimate is based on an energy drop of 500 cm^{-1} for the symmetrical MO [7] and a resonance integral of −20 kcal/mole [8]). Accordingly, the g factor of the X spectrum should be about 5 ppm *smaller* than the g factor of benzene(—). The opposite effect is observed (Table and Fig. 1). If an alkali metal ion pair is present the g factor should be even smaller [9]. Not only the experimental findings (cf. ref. [3]) but also the fact that addition of LiCl to solvents that have been treated with with K—Na fails to give the X spectrum (although the HFS then observed suggests "contact") [10] appear to refute the assumption that X is an isolated benzene(—)/counter ion whose degeneracy has been lifted. Like the unsuccessful simulation attempts, the large g factor of X contradicts the assumption of an ion pair but rather suggests a reaction product. If the radical X were a pure hydrocarbon then $|\lambda|$ should also be smaller than 1; according to *Stone*'s theory a product of this kind should have a smaller g factor than benzene(—).

We therefore believe that the X spectrum arises from an unknown product of benzene(—) with the solvent, whose formation is favored by the presence of $LiAlH_4$, and in which the unpaired electron can delocalize to a fractional extent into the p orbitals of the oxygen. It is conceivable that the Al nuclei ($I = 5/2$, $\mu = 3.64\ \mu_N$) also contribute to the HFS interaction in this product since, according to *Paddock* [11], the equilibrium

$$[AlH_4]^- \rightleftarrows H^- + AlH_3$$

is set up in ethereal solvents, the ether coordinating with AlH_3 and thus shifting the equilibrium to the right; on distillation AlH_3 is found in the distillate [10, 11].

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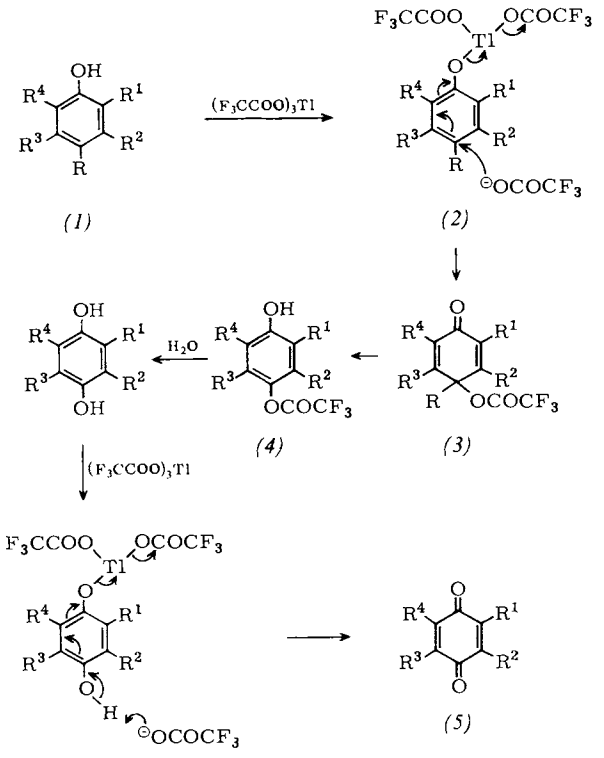
Synthesis of *p*-Quinones with Thallium(III) Trifluoroacetate[1]

By *A. McKillop, B. P. Swann, M. J. Zelesko*, and *E. C. Taylor* [*]

Much of the present interest in the chemistry of 4-*tert*-butylphenols has been centered upon the ease with which they may be converted, by treatment with nucleophiles in the presence of one-electron oxidizing agents [2], into 4,4-disubstituted cyclohexadienones which then, by acid-catalyzed loss of isobutylene [3], yield 4-substituted phenols. We describe a useful extension of this general principle which permits the direct conversion of 2,6-disubstituted 4-*tert*-butylphenols into the corresponding 2,6-disubstituted *p*-quinones.

We have found that thallium(III) trifluoroacetate [4] is an extremely effective oxidizing agent for *p*-quinone synthesis. Thus, a 2,6-disubstituted 4-*tert*-butylphenol (0.05 mole) is stirred for 1—2 h with a standard solution of thallium(III) trifluoroacetate (0.11 mole) in trifluoroacetic acid (TFA), excess TFA evaporated under reduced pressure, the residue poured into 50 ml of ice-water, and the *p*-quinone *(5)* isolated by extraction with chloroform and evaporation of the dried extracts. Typical *p*-quinones prepared in this manner are given in the Table.

We suggest that these oxidations proceed as shown in the above Scheme [for the formation of intermediates analogous to *(2)* and *(3)* see [5] and [6]].



In principle, such oxidations of 2,4,6-trisubstituted phenols should also be possible in those cases where the substituent on C-4 is capable of departing with its bonding electron pair. The reactions take place at room temperature and require 6—10 hours. Representative conversions are given in the following Table:

Table. Examples of the oxidation of phenols *(1)* to *p*-quinones *(5)* by thallium(III) trifluoroacetate.

R	R^1	R^2	R^3	R^4	Yield (%)
$(CH_3)_3C$	$(CH_3)_3C$	H	H	$(CH_3)_3C$	73
$(CH_3)_3C$	Br	H	H	Br	57
$(CH_3)_3C$	Br	H	H	CH_3	89
$(CH_3)_3C$	Br	CH_3	H	$(CH_3)_3C$	70
$(CH_3)_3C$	CH_3	H	H	CH_3	88
$(CH_3)_3C$	$(CH_3)_3C$	H	H	C_6H_5	62
Br	Br	H	H	Br	77
Br	Br	H	H	$(CH_3)_3C$	81
Cl	Cl	H	H	CH_3	82
I	I	H	H	I	62
CH_3COO	$(CH_3)_3C$	H	H	$(CH_3)_3C$	97
OH	$(CH_3)_3C$	H	H	H	91
OH	CH_3	H	H	H	77
OH	CH_3	CH_3	H	CH_3	82
OH	Cl	Cl	Cl	Cl	73

Hydroquinones can also be oxidized to *p*-quinones by this method (see Table); in this instance reaction is complete within a few minutes at room temperature.

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The Preparation of Solutions of Anhydrous Perchloric Acid in Methylene Chloride: A Cautionary Note

By *H. Musso* and *B. Bock* [*]

During an attempt to prepare a solution of anhydrous perchloric acid in methylene chloride according to a published procedure [1] a violent explosion occurred which completely destroyed a fume hood. A mixture of 25% oleum and 70% perchloric acid was prepared exactly according to the instructions given, allowed to stand overnight, and then extracted with dry methylene chloride. After the extraction apparatus had been working for about one hour and the methylene chloride was boiling gently the mixture in the non-heated part of the apparatus at the methylene chloride interface suddenly began to boil vigorously and immediately exploded. The methylene chloride had been freshly-distilled over P_4O_{10} and did not contain any impurities that could be detected by gas chromatography.

It is strongly recommended that this procedure be carried out with extreme care and that only small amounts of reagents be used; furthermore, the extraction flask should be kept adequately cooled.

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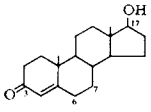
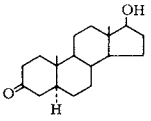
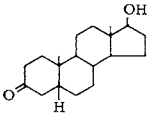
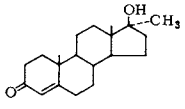
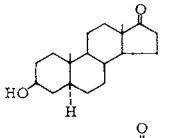
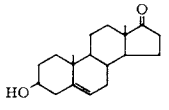
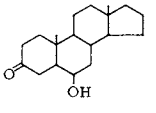
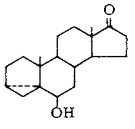
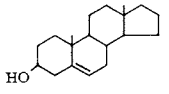
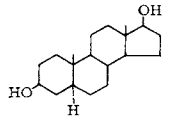
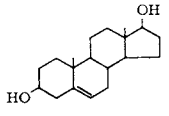
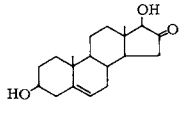
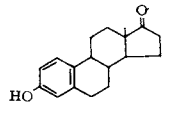
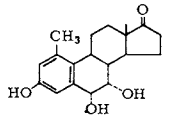
A New Method for Structure Determination of Hydroxy Steroids [**]

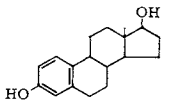
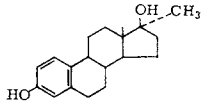
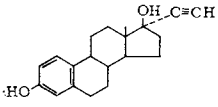
By *E. Breitmaier, W. Voelter, G. Jung*, and *E. Bayer* [*]

Determination of the position and conformation of the OH group in steroids by common chemical and molecular-spectroscopic techniques often runs into considerable difficulties. Since ^{19}F-NMR spectroscopy of *O*-trifluoroacetylated steroids only detects the OH group, the ^{19}F-NMR spectra of these compounds are readily interpretable singlet systems; moreover, the amount of sample required for recording the 56.4-MHz ^{19}F-NMR spectra is reduced to about 10 μmoles, which is much smaller than that required for ^{1}H-NMR spectra and is a realistic amount for a natural product. Recent measurements on a 94.1-MHz instrument have shown that the amounts required can be reduced by a further factor of ten, and even by several orders of magnitude if the CAT technique and Fourier transformation are applied [1].

Comparison of the CF_3 signals of the *O*-trifluoroacetyl group (abbreviation: *O*-TFA) attached to C-17 in 5α- and 5β-dihydrotestosterone (see Table) shows that the linkage of rings A and B, which are relatively far removed from C-17, gives rise to a distinct signal shift in the ^{19}F-NMR spectrum. The ^{19}F-NMR spectra of 17β-estradiol and 17α-methyl- and 17α-ethynylestradiol, on the other hand, reflect the effect of the substituents attached to C-17 in ring D on the position of the CF_3 signal of the *O*-TFA group on C-3 in ring A.

Chemical shifts of the CF_3 signals of *O*-TFA-androstanes and -estranes.

	O-TFA derivative of	δ (ppm) C-3	δ (ppm) C-17
	Testosterone		0.162
	5α-Dihydro-testosterone		0.181
	5β-Dihydro-testosterone		0.156
	17α-Methyl-testosterone		0.0
	Epiandro-sterone	0.385	
	5,6-Didehydro-epiandro-sterone	0.347	
	6β-Hydroxy-5ξ-andro-stan-3-one	[a]	
	6β-Hydroxy-3α,5-cyclo-androstan-17-one	[b]	
	5-Androsten-3β-ol	0.361	
	5α-Androstan-3β,17β-diol	0.353	0.169
	5-Androstene-3β,17β-diol	0.344	0.168
	3β, 17β-Di-hydroxy-5-androsten-16-one	0.326	−0.308
	Estrone	−0.116	
	6α,7α-Di-hydroxy-1-methyl-estrone	−0.175	[c]

	O-TFA derivative of	δ (ppm) C-3	δ (ppm) C-17
	17β-Estradiol	−0.125	0.142
	17α-Methyl-estradiol	−0.115	−0.08
	17α-Ethynyl estradiol	−0.135	0.247

[a] δ (C-6) = 0.453 ppm; [b] δ (C-6) = 0.343 ppm; [c] δ (C-6) = −0.11 ppm; δ (C-7) = −0.03 ppm.

Further relationships between the chemical shift and the position of the *O*-TFA groups may be summarized as follows:

1. The CF_3 signal of the *O*-TFA group on C-3 in androstane derivatives is between 0.33 and 0.38 ppm.

2. In the case of estrane derivatives, the CF_3 signal of the phenolic *O*-TFA group is shifted downfield owing to the ring current effect, occurring between −0.11 and −0.17 ppm.

3. The CF_3 signal of the secondary *O*-TFA group on C-17 is between 0.14 and 0.18 ppm.

4. If C-17 is a tertiary carbon atom bearing only saturated alkyl groups, the CF_3 signal of the *O*-TFA group attached to this atom is shifted downfield.

5. Neighboring electron-withdrawing substituents such as *O*-TFA or carbonyl groups shift the CF_3 signals of an *O*-TFA group downfield.

6. The ethynyl group on C-17 in 17α-ethynylestradiol shifts the CF_3 signal of the 17β-*O*-TFA group upfield.

The *O*-TFA derivatives can be prepared by reacting the steroids with trifluoroacetic anhydride[1]. Prior to the ^{19}F-NMR measurements the reaction products only have to be kept for 10 h at 25 °C and 0.5 torr over potassium hydroxide in order to remove moisture and trifluoroacetic acid. The 56.4-MHz ^{19}F-NMR spectra were recorded at 25 °C on a Varian HA-60 instrument using 0.1 M solutions of *O*-TFA steroids in carbon tetrachloride containing 2 % of methyl trifluoroacetate as internal standard. The chemical shifts of the CF_3 signals can be measured with an accuracy of ± 1 %, and do not depend on concentration within these limits.

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[**] W. V. is grateful to the Deutsche Forschungsgemeinschaft for a Habilitation Stipendium.

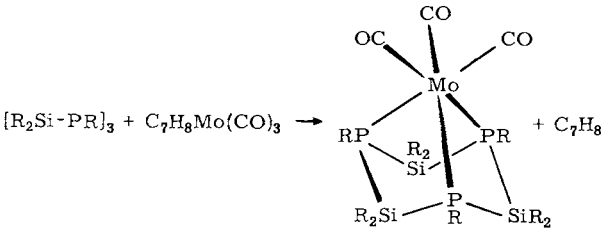
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Nonaphenylcyclotrisilaphosphanetricarbonylmolybdenum(0)[**][1]

By *H. Schumann* and *H. Benda*[*]

Hexamethylcyclotrisilazanetrichlorotitanium(III) and -vanadium(III) are well known[2]. Attempts to couple cyclotrisilazanes or analogous cyclic compounds containing elements

of Groups IVb and Vb as tridentate ligands to transition metal carbonyls have hitherto failed. We have now been able to prepare the first representative of this class of compounds, nonaphenylcyclotrisilaphosphanetricarbonylmolybdenum(0) *(1)*, by reaction of nonaphenylcyclotrisilaphosphane[3] with cycloheptatrienetricarbonylmolybdenum.



R = C_6H_5 *(1)*

Compound *(1)* can be prepared in yields of up to 52% as brilliant yellow crystals which are readily soluble in tetrahydrofuran and hot benzene, are sensitive to air, and decompose slowly with charring at temperatures above 165 °C. The IR spectrum[4] shows two sharp νCO bands at 1931 and 1838 cm^{-1} and three νSiP bands at 393, 333, and 305 cm^{-1}, corresponding to a molybdenum complex having an octahedral structure (C_{3v}) with silylphosphine in the chair configuration as tridentate ligand. A complete elemental analysis and cryoscopically determined molecular weight were also in agreement with such a structure.

Attempts to prepare analogous germyl- and stannyl-tricarbonylmolybdenum complexes as well as the corresponding chromium and tungsten compounds resulted in the formation of complex mixtures only.

Experimental:

A solution of nonaphenylcyclotrisilaphosphane[**] (3 mmole) in tetrahydrofuran (20 ml) is added to a solution of cycloheptatrienetricarbonylmolybdenum (3 mmole) in methylcyclohexane (30 ml) with exclusion of oxygen. The initially dark red reaction mixture turns pale in color on stirring for 25 hours at 50 °C and a yellow precipitate of *(1)* is formed which can be purified by recrystallization from warm benzene.

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[**] By analogy with the terms "cyclosiloxane, -silathiane, and -silazane" used in the Nomenclature Recommendations of the IUPAC, the name nonaphenylcyclotrisilaphosphane is used for nonaphenyl-1,3,5-triphospha-2,4,6-trisilacyclohexane.

[1] Part 6 of Organometallophosphine-substituted Transition Metal Complexes. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. – Part 5: *H. Schumann, L. Rosch*, and *O. Stelzer*, J. organometallic Chem., in press.

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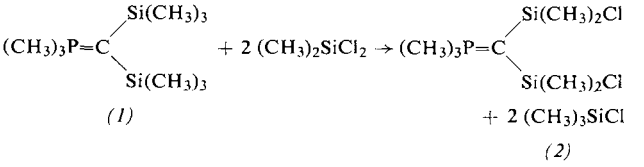
[4] Perkin-Elmer 221 and 337; nujol mull, capillary.

Trans-Silylation – A New Method for the Synthesis of Silylated Phosphorus Ylides[1]

By *H. Schmidbaur* and *W. Malisch*[*]

The possibility of synthesizing cyclic silylalkylenephosphoranes[1] has hitherto been seriously limited because of the inavailability of silylated phosphorus ylides with reactive substituents on the Si atom. We have now found that trialkylsilyl groups on an ylide C-atom can be exchanged smoothly for halogenosilyl groups. As a rule this "trans-silylation" proceeds sufficiently rapidly even at room temperature to give pure products in high yields; the only by-product formed in the reaction is the readily separable trialkylchlorosilane.

Bis(trimethylsilyl)methylenetrimethylphosphorane *(1)*[2,3] can be readily converted into bis(dimethylchlorosilyl)methylenetrimethylphosphorane *(2)* by reaction with an excess of dimethyldichlorosilane:



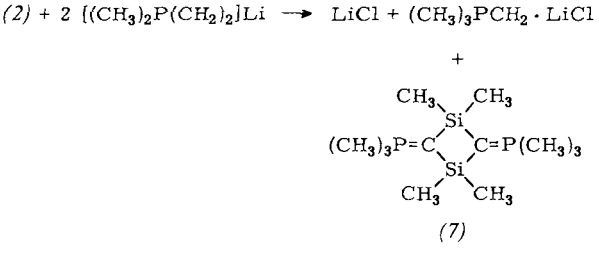
(1) *(2)*

Correspondingly, reaction of *(1)* with methyltrichlorosilane leads to formation of bis(methyldichlorosilyl)methylenetrimethylphosphorane *(3)*, and with silicon tetrachloride to bis(trichlorosilyl)methylenetrimethylphosphorane *(4)*.

Even mixed halogen- and halogenoalkyl-substituted silyl groups can be readily introduced on the ylide C-atom in this way; reaction of *(1)* with $ClCH_2(CH_3)SiCl_2$ yields $(CH_3)_3P{=}C[Si(CH_3)(CH_2Cl)Cl]_2$ *(5)*.

Sometimes, intermediates are formed in these trans-silylation reactions; thus, in the reaction of *(1)* with $SiCl_4$ in equimolar quantities the unsymmetrically silylated ylide *(6)* is obtained as the main product.

The ylides *(2)*–*(5)* open a new route to cyclic silylalkylenephosphoranes[1]; compound *(2)* reacts with metalated methylenetrimethylphosphorane[4] leading directly to the four-membered heterocycle *(7)*, which was recently prepared for the first time by another route[1].



(7)

(2) + $[CH_3P(CH_2)_3]Li_2$ → 2 LiCl + *(7)*

These reactions clearly illustrate the mobility of the substituents on the methylene C-atom situated in an α-position to the phosphorus atom[5,6].

Compound *(8)* (see Table) was prepared as the first siloxane having an ylide function by reaction of *(2)* with $LiOSi(CH_3)_3$ in the molar ratio 1 : 2.

Table. Properties of the ylides *(2)*–*(8)* [a].

	M.p. (°C)	B.p. (°C/torr)
(2) $(CH_3)_3P{=}C[Si(CH_3)_2Cl]_2$	30–31	80–81/0.1
(3) $(CH_3)_3P{=}C(SiCH_3Cl_2)_2$	47–48	90–92/0.1
(4) $(CH_3)_3P{=}C(SiCl_3)_2$	122	113/0.1 [b]
(5) $(CH_3)_3P{=}C[Si(CH_3)(CH_2Cl)Cl]_2$	–3–0	[c]
(6) $(CH_3)_3P{=}C(SiCl_3)Si(CH_3)_3$ [d]	–	–
(7) $[(CH_3)_3P{=}CSi(CH_3)_2]_2$	70–71	68/0.01 [b]
(8) $(CH_3)_3P{=}C[Si(CH_3)_2OSi(CH_3)_3]_2$	–6 to –4	75.5/0.1
$(CH_3)_3P{=}C[SiH(CH_3)Cl]_2$	–	88/0.1

[a] The composition and structure of the new compounds were established by elemental analysis, molecular weight determination, and NMR and IR spectroscopy. [b] Sublimes. [c] Non-distillable.
[d] Detected NMR-spectroscopically in admixture with *(4)*.

The ylides *(1)*–*(8)* do not react with trimethylchlorosilane. Trimethyliodosilane, on the other hand, reacts with *(1)* to give tris(trimethylsilyl)methyltrimethylphosphonium iodide

as a stable, colorless adduct. The cation of this salt is of particular interest on account of its isosteric relation to tetrakis(trimethylsilyl)methane[7].

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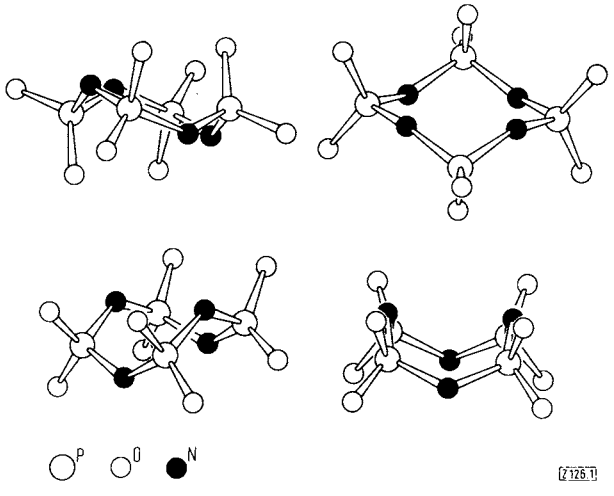
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On the Conformational Isomerism of the Eight-membered P–N Ring in Octaoxocyclotetraphosphazanates

By *Dietrich Mootz* and *Bernhard Berking*[*]

The conformational isomerism of the P–N skeleton of alkali-metal octaoxocyclotetraphosphazanates (salts of tetrametaphosphimic acid), deduced from the vibration spectra, was described by *Steger* and *Lunkwitz*[1] and less completely by *Griffith* and *Rutt*[2]. We have investigated this by X-ray analysis of the selected examples $K_4[PO_2NH]_4 \cdot 4H_2O$ *(1)* and $Cs_4[PO_2NH]_4 \cdot 6H_2O$ *(2)*. The conformations and symmetries of the structures thus determined for the anion are shown in the Figure.



Steger and *Lunkwitz*[1] determined the point group of the anion in crystals of *(1)* as C_{2h}-2/m with the mirror plane through two opposing phosphorus atoms. The chair conformation resulting from this was confirmed by the crystal structure analysis (see left and right upper Figs.), in which minor deviations of the atomic positions from C_{2h} (exact symmetry only C_i-$\bar{1}$) have no significance.

Steger and *Lunkwitz*[1] assigned S_4-$\bar{4}$ as the point group of the anion from the crystal spectra of *(2)*. However, our crystal structure analysis results in the higher precise symmetry (required by the space group) of D_{2d}-$\bar{4}$2m with the mirror planes through opposing nitrogen atoms (see lower left and right Figs.). This particular saddle conformation was ascribed by *Griffith* and *Rutt*[2] to the anion in aqueous solution, whereas *Steger* and *Lunkwitz*[1] found only symmetry S_4 in this case also.

Mean values of the bond lengths and angles found by us for the anions are given in the Table, which includes for comparison the corresponding values from an X-ray structure analysis[3] of the crystalline dihydrate of free tetrametaphosphimic acid, $H_4[PO_2NH]_4 \cdot 2H_2O$ (molecular symmetry S_4, tub conformation):

		(1)	*(2)*	*(3)*
d (Å)	P–O	1.500	1.498	1.501
	P–N	1.673	1.676	1.661
∢(°)	O–P–O	117.8	117.7	116.1
	O–P–N	107.9	107.5	108.3
	N–P–N	108.1	106.9	107.4
	P–N–P	131.9	128.9	125.6

Both the salts studied contain a complex system of hydrogen bonds: whereas in *(1)* both anion-water bridges (NH · · · O and O · · · HO) and anion-anion bridges (NH · · · O) contribute to bonding of the structure, there are no bridges of the latter type in *(2)* owing to its greater water content. Coordination of the cations by oxygen is six-fold in *(1)* (an octahedron and a trigonal prism, both distorted), but *(2)* with its eleven Cs–O distances between 3.0 and 4.5 Å cannot by given a simple description in terms of a characteristic polyhedron.

(1) forms monoclinic crystals in space group $P2_1/c$ with two formula units in the unit cell; *(2)* forms tetragonal crystals in $P4_2/nmc$ also with $Z = 2$. An automatic diffractometer (AED from *W. Hoppe* of Siemens AG) was used for collection of the data. Determination and refinement of the structures was by the usual methods. Final *R*-factors were 0.039 for *(1)* with 1579 reflections and 0.055 for *(2)* with 569 reflections.

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Crystal Growth from the Vapor Phase

By *R. Nitsche* [*]

Successful solid-state research requires the production of single crystals of high purity with defined doping and few structural imperfections. Most crystal growth methods are based on the solid-liquid phase transition, *i.e.* they involve the use of melts or solutions. These methods cannot be used for substances whose melting points are difficult to reach experimentally, that decompose or sublime prior to melting, or for which no suitable solvents exist.

To close these gaps, increasing use has recently been made of vapor-phase methods. Whereas sublimation is confined to a relatively small number of volatile substances, gas reaction methods are very widely applicable. In these methods a gaseous mixture yielding the solid phase reacts under controlled conditions in a growth chamber in the presence of seeds. The gas mixture is transported to the seed by:

a) Blowing separate gas streams into the growth chamber (flow transport).

b) Reaction of the polycrystalline feed material from which crystals are to be grown with a gas at temperature T_1 to give one (or several) volatile compound(s), transport of the gas mixture, whose composition corresponds to the heterogeneous equilibrium at T_1, to the seed (at T_2) by diffusion, convection, or flow, and reversal of the reaction with deposition of the solid phase according to the equilibrium conditions at T_2 (chemical transport).

c) Combination of a and b.

With skilful control (low supersaturation, good temperature stability), gas reactions can yield crystals of considerable size having high purity and structural perfection. Crystals of elements and binary compounds (oxides, sulfides, phosphides, *etc.*), as well as of many ternary and quaternary compounds have been grown.

Two types of apparatus are used:

1) Closed systems (mostly sealed quartz tubes) for automatic chemical transport in the temperature gradient between the solution chamber (T_1) and the growth chamber (T_2).

2) Open systems for chemical transport in flowing gases between T_1 and T_2 or for direct combination of separate gas streams.

(1) Is particularly suitable for the growth of large crystals over long periods, and (2) for the growth of monocrystalline layers on oriented substrates (epitaxy), for which less time is required. Continuous or abrupt modification of the crystal composition (*i.e.* formation of solid solutions or doping) is possible during growth.

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Structure and Function of Cell Receptors

By *R. Drzeniek* [*]

Cell receptors play a decisive role in many interesting biological phenomena, *e.g.* in the action of drugs, toxins, hormones, antibodies, and viruses on living cells. Although the best-known receptor theory, that proposed by *Paul Ehrlich* who regarded cell receptors as having defined chemical structures, dates back to about 1900, first attempts to isolate these receptors and to characterize them chemically were not made until comparatively recently.

There has been no lack of experiments designed to modify the mode of action of biologically active substances by chemical changes. However, such an approach becomes all the more difficult to justify the more complicated the mode of action of a substance is.It would therefore appear advisable to limit primary studies on the reactions between substances and their cell receptors to *in-vitro* systems that are as simple and comprehensible as possible. Such systems are currently being developed.

In this way the action of digitalis glycosides on cell membrane components that are designated transport adenosine triphosphatase can be tested [1]. Studies in which the action of receptors on artificial lipid membranes can be measured appear particularly promising. The effect of transport adenosine triphosphatase and digitalis compounds on the permeability of black lipid membranes may be cited as a model [2].

Considerable interest attaches to the analysis of cell receptors in virology too. It is a known fact that a virus infection can only occur when the infectious agent becomes bound to a corresponding cell surface. Virus-binding cell receptors have been isolated and some of them characterized for a number of different viruses. The best-known receptors include those for certain phages and for myxoviruses.

The components isolated primarily by *Weidel et al.* [3] from cell walls of *E. coli* are lipoproteins and/or lipopolysaccharides that react specifically with certain T-phages. Cell receptors for myxoviruses (influenza and parainfluenza viruses) contain acylated neuraminic acid [4], whose structure has been completely elucidated [5], as receptor-dominant sugar. The component of the myxoviruses which reacts specifically with the neuraminic acid of the cell, *i.e.* the enzyme neuraminidase, has been isolated in highly pure form [6] and rendered visible under an electron microscope [7]. The substrate specificity [8] and the function of neuraminidase [9] are particularly interesting. Studies on the *in-vitro* interactions between cell receptor and virus neuraminidase represent the starting point for the elucidation of the mechanism of infection by myxoviruses.

Lecture at Giessen on October 21, 1969 [VB 215 IE]
German version: Angew. Chem. *82*, 48 (1970)

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[1] *K. Repke*, Der Internist *7*, 418 (1966).

[2] *M. K. Jain, A. Strickholm*, and *E. H. Cordes*, Nature (London) *222*, 871 (1969).

[3] *W. Weidel*, Annu. Rev. Microbiol. *12*, 27 (1958).

[4] *E. Klenk*, Hoppe-Seylers Z. physiol. Chem. *268*, 50 (1941).

[5] *A. Gottschalk*: Glycoproteins. Their Composition, Structure and Function. Elsevier, Amsterdam 1966.

[6] *R. Drzeniek, J. T. Seto*, and *R. Rott*, Biochim. biophysica Acta *128*, 547 (1966).

[7] *R. Drzeniek, H. Frank*, and *R. Rott*, Virology *36*, 703 (1968).

[8] *R. Drzeniek*, Biochem. biophysic. Res. Commun. *26*, 631 (1967).

[9] *J. T. Seto* and *R. Rott*, Virology *30*, 731 (1966).

Organometal Pseudohalides [1]

By *K. Dehnicke* [*]

Lewis acids and alkyl- and arylmetal compounds react with gaseous ClN_3 to form organometal azides in accordance with equation (1).

$$R_nM + ClN_3 \rightarrow R_{n-1}M{-}N_3 + RCl \qquad (1)$$

New azides of the type $RHgN_3$, with R = cyclopentadienyl, cyclopropyl, and cyclopentyl, can be synthesized in this way, as can also the compound $(CH_3)_2BiN_3$. $As(CH_3)_3$, on the other hand, like the tetraalkyl compounds of the elements of Group IV A, is inert towards ClN_3; $(CH_3)_2AsN_3$, however, can be obtained by reaction (2).

$$(CH_3)_2AsI + AgN_3 \rightarrow (CH_3)_2As{-}N_3 + AgI \quad (2)$$

All the above mentioned organometal azides are monomeric and nonexplosive. IR and laser-Raman spectra afford information concerning their structures; thus, it is found that the N_3 group is covalently bound and distorted at the α—N atom. Cyclopropylmercury azide occurs as a mixture of the *cis*- and *trans* isomers, whereas the cyclopropyl ring in liquid dicyclopropylmercury rotates freely (pseudosymmetry $D_{\infty h}$). In many cases, organometal thiocyanates are accessible from alkyl- or arylmetal compounds and dithiocyanogen in accordance with eq. (3).

$$R_nM + (SCN)_2 \rightarrow R_{n-1}M{-}SCN + RSCN \quad (3)$$

They differ considerably in their physical and chemical properties from the corresponding well-known isothiocyanates. We have prepared the previously unknown compounds $(C_6H_5)_2BSCN$ (monomer), $(CH_3CdSCN)_\infty$, $(C_2H_5CdSCN)_\infty$, $(C_2H_5OCdSCN)_\infty$, and $(CH_3)_2BiSCN$ (degree of association unknown) by the method shown in reaction (3). In contrast to the substitution reaction (3), addition of $(SCN)_2$ in accordance with eq. (4) leads exclusively to organometal isothiocyanates.

$$R_3M + (SCN)_2 \rightarrow R_3M(NCS)_2 \quad (4)$$

$As(CH_3)_3$, $As(C_6H_5)_3$, $Sb(CH_3)_3$, and $Sb(C_6H_5)_3$ react with $(SCN)_2$ in this manner (4). In a few cases organometal azides can be converted into thiocyanates as shown in eq. (5).

$$2\ CH_3Hg{-}N_3 + (SCN)_2 \rightarrow 2\ CH_3Hg{-}SCN + 3\ N_2 \quad (5)$$

Lecture at Aachen, October 28, 1969 [VB 216 IE]
German version: Angew. Chem. *82*, 48 (1970)

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[1] Including work carried out in collaboration with *T. Wizemann, D. Seybold, H. Müller, J. Müller, F. Weller, A. Shihada,* and *R. Schmitt.*

Stereo- and Polymerization Chemistry of Tellurites and Tellurates in the Solid State

By *J. Zemann* [*]

The following common features for the coordination and polymerization chemistry of tellurium can be inferred from the previously reported crystal structures of tellurites and tellurates:

With oxygen, tetravalent tellurium forms either a trigonal pyramid with dTe—O ≈ 1.95 Å and $\sphericalangle$ OTeO $\approx 95°$ (*e.g.* $CuTeO_3 \cdot 2\,H_2O$ and $ZnTeO_3$) or a trigonal bipyramid in which an equatorial corner is unoccupied; the deformation can be explained, therefore, as being due to occupation of this "free" corner by a lone pair of electrons having large spatial demands (*e.g.* tetragonal TeO_2). Coupling of TeO_3 pyramids, to Te_2O_5 units in $(Ca,Mn,Zn)[Te_2O_5]$ and $Fe(OH)[Te_2O_5]$, to Te_6O_{12} rings in the mineral cliffordite (whose chemical composition corresponds approximately to $U_2O_4[Te_6O_{12}]$), and to a two-dimensional infinite layer in $Te_2O_3[SO_4]$, is well known. In $Zn_2[Te_3O_8]$ one TeO_4 group is bonded to two TeO_3 groups *via* oxygen atoms. In tetragonal TeO_2, TeO_4 groups are coupled *via* Te—O—Te bonds to form a three-dimensional framework and in rhombic TeO_2 to form a layer structure; in the latter case the four Te—O bond lengths vary from 1.88 to 2.19 Å.

That the following coordination occurs rather often in the oxygen compounds of tetravalent tellurium appears to be important: a fourth oxygen atom coordinates to a TeO_3 pyramid having three short Te—O bonds to form a bond whose length is about 20% longer than those in the pyramid. This results in a coordination very close to that which has been described for the TeO_4 group. These "long" Te—O bonds, which are obviously much weaker than the short ones, vary greatly in length and it is difficult to give an upper limit. Examples are $(Ca,Mn,Zn)[Te_2O_5]$, $Fe(OH)[Te_2O_5]$, and cliffordite.

Compounds of oxygen and hexavalent tellurium exhibit predominantly octahedral coordination and can undergo polymerization to double octahedra (in $K_4[Te_2O_6(OH_4)] \cdot 7.3\,H_2O$) or to infinite chains (as in $K[TeO_3OH]$). A coupling *via* corners to form infinite chains has been detected in $K[TeO_2(OH)_3]$.

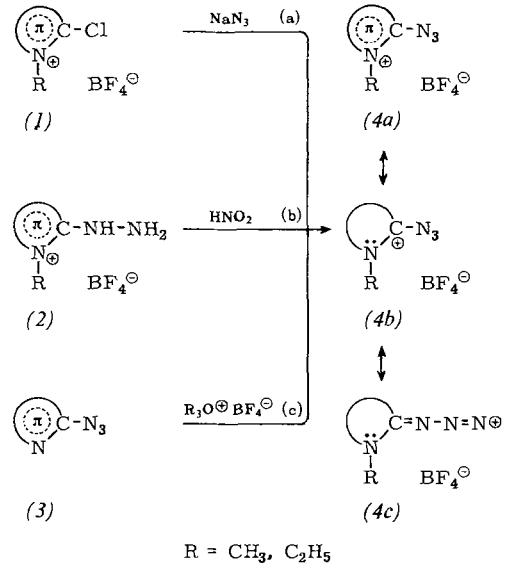
Lecture at Göttingen, October 30, 1969 [VB 217 IE]
German version: Angew. Chem. *82*, 49 (1970)

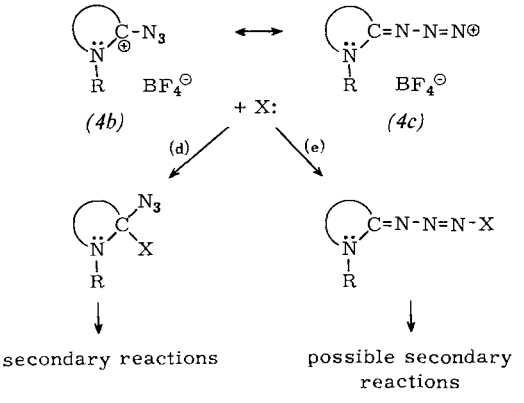
[*] Prof. Dr. J. Zemann
Institut für Mineralogie and Kristallographie
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Heterocyclic Azidinium Salts in Preparative Chemistry

By *H. Balli* [*]

Heterocyclic azidinium salts *(4)* [1] have previously been prepared *via* the routes (a), (b), and (c) [1,2]. The N-heteroaromatic compounds pyridine, thiazole, 1,2,4-triazole,



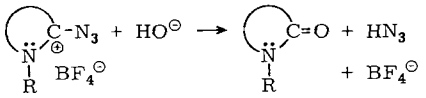


quinoline, isoquinoline, benzimidazole, benzothiazole, benzoxazole, benzoselenazole, and their substitution products could be used in the syntheses.

The salts *(4)* react as electrophiles having ambidentate reactivity in the routes (d) or (e).

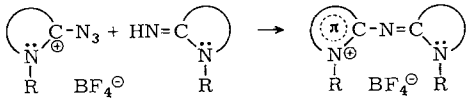
Hard bases, X, react according to route (d) with substitution of the azido group on the hard carbonium ion of *(4b)*.

1. Hydrolysis of azidinium salts.



(4b)

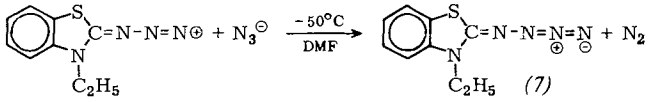
2. Synthesis of azamonomethinecyanines *(6)* with the bases *(5)*.



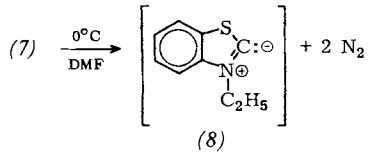
(4b) *(5)* *(6)*

Soft bases, X, react according to route (e) with addition at the terminal nitrogen atom of the azido group of *(4c)*, secondary reactions often occurring at the same time.

1. Addition of azide ions.

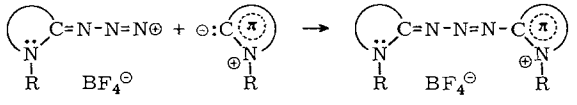


(7)



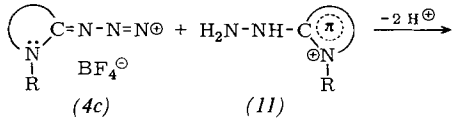
(8)

2. Addition of heterocyclic ylides such as *(8)* or *(9)*; synthesis of triazatrimethinecyanines *(10)* [3].

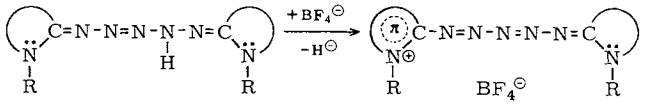


(4c) *(9)* *(10)*

3. Addition of heterocyclic hydrazines *(11)* with subsequent oxidation to pentaazapentamethinecyanines *(12)* [4].

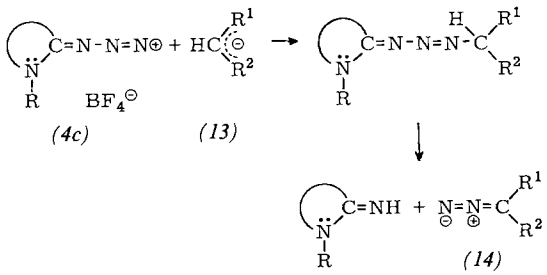


(4c) *(11)*



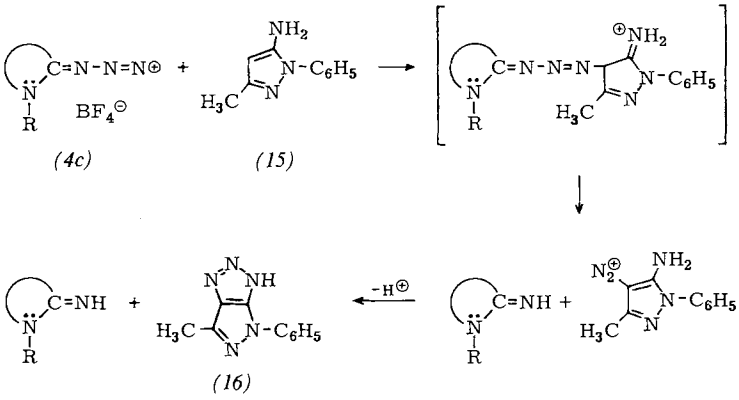
(12)

4. Addition of anions of reactive methylene compounds *(13)* or hydroxyaromatic compounds involving diazo group or azo group transfer (synthesis of diazo compounds and azo dyes) [5]. Examples for *(14)* are diazomeldrum acid (yield 46 %), 4-diazo-3-methyl-1-phenyl-5-pyrazolone (96 %), 2,4,6-tris(diazo)-1,3,5-cyclohexanetrione (95 %).



(4c) *(13)* *(14)*

5. Addition of heteroaromatic amines such as *(15)* with formation of condensed triazoles (16).



(4c) *(15)* *(16)*

Lecture at Freiburg, November 13, 1969 [VB 218 IE]
German version: Angew. Chem. *82*, 86 (1970)

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[1] *H. Balli* and *F. Kersting*, Liebigs Ann. Chem. *647*, 1 (1961).

[2] *G. Henseke* and *G Hanisch*, Liebigs Ann. Chem. *643*, 184 (1961); *H. Quast*, Dissertation, Universität Marburg 1963.

[3] *H. Balli* and *F. Kersting*, Liebigs Ann. Chem. *663*, 96 (1963).

[4] *S. Hünig*, *H. Balli*, and *H. Quast*, Angew. Chem. *74*, 28 (1962); Angew. Chem. internat. Edit. *1*, 47 (1962).

[5] *H. Balli* and *V. Müller*, Angew. Chem. *76*, 573 (1964); Angew. Chem. internat. Edit. *3*, 644 (1964); *H. Balli* and *R. Gipp*, Liebigs Ann. Chem. *699*, 133 (1966).

Dissolution of Bituminous Coals at Temperatures below 200 °C

By *G. Kölling* [*]

Bituminous coals are scarcely soluble in most solvents at temperatures below 200 °C; however, in "specific" solvents such as phenols, pyridine bases, and a few amines, their solubility can be as high as 40 %.

After alkylation with alkyl chlorides and $AlCl_3$ at 50 °C, or with olefins, HF, and BF_3 at 80 °C the solubility increases still further. Even more efficient is acylation with higher fatty acids and $AlCl_3$ at 50 °C, a treatment which makes medium-rank coals soluble but for their inert constituents.

The carbon matter pretreated in this way can easily be further investigated. The average molecular weight is found to be about 3000 after deduction of the alkyl groups introduced. Similar values have been reported by *van Krevelen* [1] and his co-workers as a result of an extrapolation of the average molecular weights which they had found by studies on partial extracts.

Lecture at Mülheim/Ruhr, November 27, 1969 [VB 219 IE]
German version: Angew. Chem. *82*, 87 (1970)

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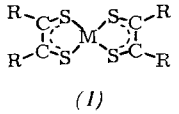
[1] *H. N. M. Dormans* and *D. W. van Krevelen*, Fuel *39*, 273 (1960).

The kinetics of the oxidation of plutonium have been studied by *D. T. Larson* and *D. L. Cash*. The plutonium was stabilized by alloying with 1 wt.-% of Ga in the Δ-phase; the surface to be oxidized was cleaned by bombardment with argon ions in a high vacuum. Oxidation was then carried out at 28–90 °C under 5×10^{-2} torr of oxygen. The growth of the oxide layer was followed by optical methods: linearly polarized, monochromatic light appears elliptically polarized after reflection at the surface. Analysis of the ellipticity affords the complex refractive index of the system (metal + oxide layer). If the complex refractive indices of the metal and oxide are known it is possible to calculate the thickness of the oxide layer. The results obtained after a short induction period can be represented by the equation

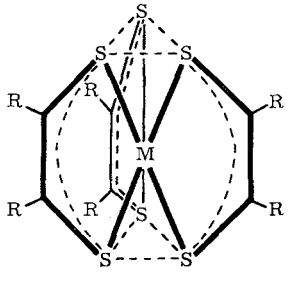
$$d^2 = kt + C$$

where d is the thickness of the oxide layer, k is the rate constant, and t is the reaction time. This form of rate equation would indicate a diffusion-controlled process. The activation energy is 30 kcal/mole. X-ray diffraction studies have shown that PuO_2 is the main product. / J. physic. Chem. *73*, 2814 (1969) / —Hz. [Rd 118 IE]

Semiconductor properties of transition metal chelates that are derived from α-dithiones have been described by *E. J. Rosa* and *G. N. Schrauzer*. The specific resistances (at 25 °C) of the compounds investigated lie between 10^3 and 10^{15} Ω cm (organic substances with extended aromatic bonding systems and charge-transfer complexes have conductivities in the same range). In the case of the square-planar complexes $M(S_2C_2R_2)_2$ *(1)* with M = Ni, Pd, Pt; R = *e.g.* CH_3, C_6H_5, a linear relationship was found between the logarithm of the specific resistance and the first polarographic half-wave potential, indicating that charge transport takes place in the lowest unoccupied π MO's of the complexes. The charge carrier was characterized as predominantly negatively charged by measurements of the Hall effect. In the series of trigonal-prismatic complexes $M(S_2C_2R_2)_3$ *(2)*, R = *e.g.* CH_3, C_6H_5, the Re complexes have a conductivity six orders of magnitude better than the complexes of V, Cr, Mo, and W.



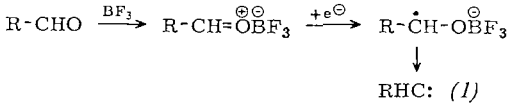
(1)



(2)

This suggests that the single electron of the Re complex is to be found in an orbital that is delocalized over the whole molecule. / J. physic. Chem. *73*, 3132 (1969) / —Hz. [Rd 116 IE]

A new route to phenylcyclopropanes has been described by *I. Elphimoff-Felkin* and *P. Sarda*. On reduction of benzaldehyde with amalgamated zinc powder in ether and in the presence of BF_3, phenylcarbene *(1a)* or possibly a carbenoid of type *(1)* is formed as intermediate. In the presence of olefins or enol acetates, phenylcyclopropanes or phenylcyclopropyl



(1a) *(2)* *(3)*

R = C_6H_5

acetates are formed respectively. Examples: Cyclohexene → 7-phenylnorcarane, 35% yield (calculated with respect to benzaldehyde); 1-cyclopentenyl acetate → *(2)*, 24% (*endo* : *exo* = 3 : 2); 1-methylvinyl acetate → *(3)*, 26% (*cis* : *trans* = 1 : 2); allyl methyl ether → 1-methoxy-2-phenylcyclopropane, 25% (*cis* : *trans* = 1 : 1). / Chem. Commun. *1969*, 1065 / —Ma. [Rd 110 IE]

Phosphorus oxide fluorides of high molecular weight occur in the products formed on reacting P_4O_{10} with PtF_4, according to mass spectrometric investigations carried out by *D. W. Muenow*, *O. M. Uy*, and *J. L. Margrave*. The components react rapidly at room temperature with considerable evolution of heat. Mass lines having *m/e* values up to *ca.* 1000, which can be ascribed to the molecular ions $P_nO_{2n-1}F_{n+2}^+$ (n = 1—13), $P_nO_{2n}F_{n+2}^+$ (n = 2—11), and $P_nO_{2n+1}F_{n+2}^+$ (n = 2—10), occur in the spectra produced by 15 V electrons on the products vaporized from a Knudsen cell. It is assumed that the ions of the first type originate from linear polymeric molecules having the structure $F_2P(O)—O[—PF(O)—O]_m—P(O)F_2$; the oxide fluorides POF_3 and $P_2O_3F_4$ are the first members of this homologous series. No suggestions are made regarding the structures of the parent molecules of the other two types of ions. / J. inorg. nuclear Chem. *31*, 3417 (1969) / —Bl. [Rd 124 IE]

A simple method for the preparation of methylphosphines, $H_nP(CH_3)_{3-n}$ (n = 0—2), is described by *K. D. Crosbie* and *G. M. Sheldrick*. Reduction of dimethyl methylphosphonate, $CH_3PO(OCH_3)_2$, with $LiAlH_4$ in monoglyme leads to methylphosphine in 87% yield. Methylphosphine is quaternized within 24 hours by methyl iodide in methanolic solution, the following equilibria being established:

$$\begin{aligned}
CH_3PH_2 + CH_3I &\rightleftharpoons (CH_3)_2PH_2^+ + I^- \\
(CH_3)_2PH_2^+ + CH_3OH &\rightleftharpoons (CH_3)_2PH + CH_3OH_2^+ \\
CH_3PH_2 + CH_3OH_2^+ &\rightleftharpoons CH_3PH_3^+ + CH_3OH \\
CH_3OH_2^+ + I^- &\rightleftharpoons H_2O + CH_3I \\
(CH_3)_2PH + CH_3I &\rightleftharpoons (CH_3)_3PH^+ + I^- \quad \textit{etc.}
\end{aligned}$$

Under suitable reaction conditions these systems prove useful for the preparation of dimethyl- and trimethyl-phosphine in 70% yield. / J. inorg. nuclear Chem. *31*, 3684 (1969) / —Bl. [Rd 125 IE]

α-Ag_3NSeO_3 is not salt-like but built up of Ag_3NSeO_3 molecular units, which possess a three-fold symmetry axis and are arranged as a double helix in the rhombohedral space group R3c (a_r = 6.184 ± 0.003 Å, α = 86.35 ± 0.01 °; $d_{exp.}$ = 6.63, $d_{calc.}$ = 6.56 g cm^{-3}). NAg_3 and SeO_3 groups having an approximately tetrahedral configuration are arranged in an eclipsed conformation with a dihedral angle of 11.1 °; the

interatomic distances are: AgN 2.178 ± 0.018, SeN 1.667 ± 0.050, and SeO 1.670 ± 0.015 Å. The double helix structure of the Ag_3NSeO_3, which has been determined with an automatic diffractometer by *J. K. Fawcett, V. Kocman, S. C. Nyburg*, and *R. J. O'Brien*, results from the short intermolecular AgO distance of 2.217 ± 0.015 Å and an NAgO angle of 173.8 ± 1.5 °. / Chem. Commun. *1969*, 1198 / —HB.

[Rd 126 IE]

Compounds containing the sulfur cations S_8^{2+} and S_{16}^{2+} have been obtained by *R. J. Gillespie* and *J. Passmore*. The substances were prepared as crystalline hexafluoroarsenates according to

$$S_8 + 3\,AsF_5 \rightarrow \underset{(1)}{S_8[AsF_6]_2} + AsF_3$$

and

$$2\,S_8 + 3\,AsF_5 \rightarrow \underset{(2)}{S_{16}[AsF_6]_2} + AsF_3$$

in HF at 0 °C. Both salts show the IR and ^{19}F-NMR spectra of $[AsF_6]^-$. *(1)* is blue (λ_{max} at 599 nm) and crystallizes in the space group $P2_1/c$ with $Z = 16$ S_4AsF_6; since the asymmetric unit contains 4 S_4AsF_6 and the substance is diamagnetic at room temperature, only S_8^{2+} and S_{16}^{4+} come into question as possible cations: by analogy with Se_8^{2+}, preference is given to S_8^{2+}. *(1)* and *(2)* (red) become reversibly paramagnetic on heating to *ca.* 100 °C, probably owing to the dissociation $S_{2n}^{2+} \rightleftarrows 2\,S_n^+$. / Chem. Commun. *1969*, 1333 / —HB.

[Rd 134 IE]

Compounds having the 1,2,4,3,5-trithiadiborolane skeleton, a new 6π system has been prepared by *Max Schmidt* and *W. Siebert* in a variety of ways. Thus, 2,3-dibromo-1,2,4,3,5-trithiaborolane *(1)* is formed according to

$$2\,BBr_3 + 2\,H_2S_{n>1} \rightarrow \underset{(1)}{Br\text{-}B\langle S\text{-}S\rangle B\text{-}Br} + 4\,HBr + (2n\text{-}3)/8\,S_8$$

in 90% yield as a water-clear, extremely hygroscopic liquid instead of the expected perhydro-1,2,4,5,3,6-tetrathiadiborin derivative. Compound *(1)* remains undecomposed even after six hours' heating at 200 °C. It can also be prepared in 50 to 60% yield according to

$$H_2S + H_2S_2 + 2\,BBr_3 \rightarrow (1) + 4\,HBr$$

The bromine atoms in *(1)* can be replaced, *inter alia*, by diethylamino, diphenylamino, alkyl, phenyl, and alkylthio groups. The ring in *(1)* is cleaved on treatment with alcohols and thiols. / Chem. Ber. *102*, 2752 (1969) / —Kr. [Rd 113 IE]

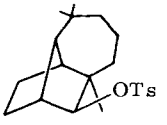
The electrochemical reduction of rhodium(I)- to rhodium(0) compounds has been accomplished by *D. C. Olson* and *W. Keim*. For the reaction $[(C_6H_5)_3P]_3RhCl$ in acetonitrile/toluene was treated with a large excess of $(C_6H_5)_3P$ as well as with $(C_2H_5)_4ClO_4$ and electrolyzed at −2.3 V to a conversion of 98%. $[(C_6H_5)_3P]_4Rh$, light-green crystals that decompose at 175—179 °C, was formed in 70% yield. Under similar conditions in acetonitrile $[(C_6H_5)_2PCH_3]_3RhCl$ affords the solid black compound $[(C_6H_5)_2PCH_3]_4Rh$ (74% yield). Having a d^9 electron configuration, Rh^0 should form paramagnetic complexes. However, $[(C_6H_5)_3P]_4Rh$ is diamagnetic, and the magnetic moment of the paramagnetic compound $[(C_6H_5)_2PCH_3]_4Rh$ (1.16 BM) is much lower than expected. The authors assume that a metal-metal interaction takes place

$$\underset{\text{diamagnetic}}{L_4Rh\text{–}RhL_4} \rightleftarrows \underset{\text{paramagnetic}}{2\,L_4Rh}$$

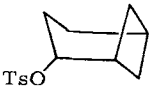
similar to that in $[Co(CO)_4]_2$. / Inorg. Chem. *8*, 2028 (1969) / —Kr.

[Rd 114 IE]

Tosylates of low stability have been prepared by *R. M. Coates* and *J. P. Chen*, who have developed a simple method entailing conversion of the alcohols into the sulfinates by treatment with *p*-toluenesulfinyl chloride as first step[1]. Subsequent mild oxidation with *m*-chloroperbenzoic acid at



(1)



(2)

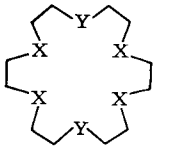
0 °C still yields tosylates in those cases where the oxidizing agents used previously (*e.g.* $KMnO_4$ in aqueous acetone and H_2O_2 in protonic solvents) are too strong. Examples: *(1)*, yield 84% (calculated with respect to the *p*-toluenesulfinate); *(2)*, 82%; cyclohexyl tosylate, 88%. / Tetrahedron Letters *1969*, 2705 / —Kr.

[Rd 115 IE]

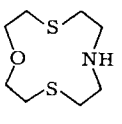
Syntheses involving perfluoroalkyl radicals from perfluoroalkyl iodides are reported by *N. O. Brace*. Alkenecarboxylic acids afford adducts of the type $RCH_2\text{—}CHI\text{—}(CH_2)_n\text{-}COOH$ (n = 1—16) (R = perfluoroalkyl) in high yields. Dehydrohalogenation of $CF_3\text{—}(CF_2)_3\text{—}CH_2\text{—}CHI\text{—}CH_2\text{—}COOH$ *(1)* with 2 mol. equiv. of base gives $CF_3\text{—}(CF_2)_2\text{—}CF\text{=}CH\text{—}CH\text{=}CH\text{—}COOH$ *(2)*, and with 1 mol. equiv. a mixture of $CF_3\text{—}(CF_2)_3\text{—}CH_2\text{—}CH\text{=}CH\text{—}COOH$ and *(1)* is formed. On hydrolysis of $RCH_2\text{—}CHI\text{—}CH_2\text{—}CH_2\text{—}COOH$, however, only $RCH\text{=}CH\text{—}CH_2\text{—}CH_2\text{—}COOH$ is formed, as is typical for such compounds. / 158th ACS Meeting 1969, Abstracts of Papers, FLUO 42 / —Ma.

[Rd 119 IE]

The synthesis of macrocyclic polythioethers has been reported on by *D. St. C. Black* and *I. A. McLean*. The hexathioether *(1)* and the tetrathioetherdiether *(2)* were prepared by reaction of 1,2-dibromoethane with the disodium salts of 3-thiapentane-1,5-dithiol and 3-oxapentane-1,5-dithiol, respectively, in ethanol in high dilution (yields 31% and 7% resp.). *(1)* behaves as a sexidentate ligand and yields complexes of the type [M (ligand)] (picrate)$_2$, M = Ni, Co. Compound *(2)* does not form complexes. The twelve-membered macrocyclic compound *(3)*, which can be prepared from the disodium salt of 3-oxapentane-1,5-dithiol and bis(2-bromoethyl)amine (yield 18%), readily forms the metal complexes Ni(ligand)Cl_2 and Co(ligand)X_2, X = Br, Cl.



(1), X = Y = S
(2), X = S, Y = O



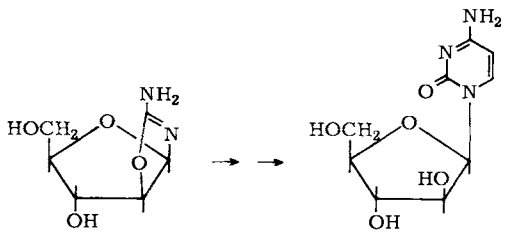
(3)

/ Tetrahedron Letters *1969*, 3961 / —Ma.

[Rd 120 IE]

[1] *J. T. Wilt, R. G. Stein*, and *W. J. Wagner*, J. org. Chemistry *32*, 2097 (1967).

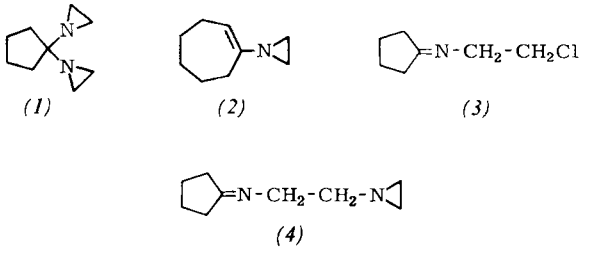
A new simple synthesis of β-cytosine arabinoside *(2)*, which is effective in a few forms of acute lukemia in adults (remission rate *in vivo ca.* 30%), has been developed by *L. E. Orgel* and *R. A. Sanchez*. Reaction of arabinose, cyanamide, and NH_3 in aqueous methanol yields an aminooxazoline derivative *(1)* (80%), which, on reaction with cyanoacetylene in dimethylacetamide and subsequent hydrolysis, affords *(2)* in 90% yield. Like 6-mercaptopurine or 5-fluorouracil, compound *(2)* is an effective chemotherapeutic antimetabolite towards rapidly growing cells.



(1) *(2)*

/ Chem. Engng. News *47*, No. 42, p. 30 (1969) / —Ma.
[Rd 121 IE]

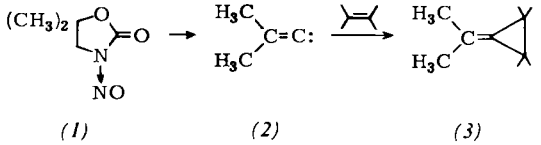
The $TiCl_4$-catalyzed addition of aziridine to cyclic ketones has been investigated by *Su C. Kuo* and *W. H. Daly*. Reaction of C_5- to C_8-ketones in the presence of triethylamine leads to compounds of type *(1)*—*(4)*. The product ratio depends on the size of ring in the ketone and on the molar ratio ketone: $TiCl_4$. Cycloheptanone and cyclooctanone yield *ca.* 20% enamines; no enamine is formed in the reactions with cyclopentanone or cyclohexanone. All aziridine compounds decompose to low molecular polyaziridines at room temperature.



(1) *(2)* *(3)* *(4)*

/ 158th ASC Meeting, 1969, Abstracts of Papers, ORGN 106 / —Ma.
[Rd 122 IE]

Reaction of the carbene 2-methylpropylidene with olefins has been investigated by *M. S. Newman* and *T. B. Patrick*. Treatment of 5,5-dimethyl-*N*-nitrosooxazolidone *(1)* with lithium ethoxide in the presence of olefins leads to the formation of isopropylidenes *(3)* in 30—55% yield. The reactions probably proceed *via* the unsaturated carbene *(2)*, which is formed as intermediate and adds to the olefin. Competing reactions with several olefins showed that *(2)* is electrophilic and reacts more readily with cyclohexene than with tetramethylethylene.



(1) *(2)* *(3)*

/ 158th ACS Meeting, 1969, Abstracts of Papers, ORGN 96 / —Ma.
[Rd 123 IE]

The structures of IF_6^+ and IF_6^- have been investigated by *S. Bukshpan*, *J. Soriano*, and *J. Shamir* by means of the Mössbauer effect of ^{129}I. $IF_6^+AsF_6^-$ was prepared from AsF_5 and IF_7, and $Cs^+IF_6^-$ from CsF and IF_5; IF_5 and IF_7 were 85% enriched with ^{129}I. IF_6AsF_6 shows a single line in the Mössbauer spectrum which indicates an octahedral arrangement of the F atoms about the iodine. The complex spectrum of $CsIF_6$ can best be interpreted as being indicative of a structure in which six fluorine atoms and one lone pair are arranged about iodine in the form of a pentagonal bipyramid, the lone pair occupying an equatorial position. From the chemical shifts it can be concluded that iodine donates an average of 0.93 electrons to each atom of fluorine in the formation of IF_6^+ and 0.88 electrons in the formation of IF_6^-; these values hardly differ from those found in IF_7 and IF_5. / Chem. Physics Letters *4*, 241 (1969) / —Hz. [Rd 136 IE]

The dipole moment of tris(2,4-pentanedionato)aluminum has been determined by *R. D. Nelson jr.* and *C. E. White*. The molar refraction of benzene solutions of this compound has been measured both in the far infrared with the aid of an HCN laser (wavelength 337 μm) and in the microwave region. The component due to reorientation of dipoles is given by the difference between these two polarization values. The dipole moment is 1.1 D; this arises from the fact established earlier by X-ray diffraction that the O-metal-O plane in many pentanedionates is inclined by about 20° to the plane through the CO skeleton of the ligand. Unusually short dielectric relaxation times can be interpreted as being due to a flipping of the ligand plane about the O—O axis. / J. physic. Chem. *73*, 3439 (1969) / —Hz. [Rd 137 IE]

The evaporation of graphite has been investigated by *J. T. Clarke* and *B. R. Fox*. Graphite fibers (cross-section 0.4 × 1 mm) were heated to a temperature of 2500 to 3400 °K in a vacuum or in helium by strong current pulses. At 3400 °K the rate of evaporation was sufficiently great (*ca.* 6 mg cm^{-2} s^{-1}) for a direct determination of the heat of evaporation to be carried out; at 3400 °K this is 102 kcal $mole^{-1}$. It can be concluded from the experimental results, in combination with thermodynamic data about graphite and its evaporation products measured at lower temperatures, that graphite evaporates as C_2 at temperatures above 3000 °K. / J. chem. Physics *51*, 3231 (1969) / —Hz. [Rd 138 IE]

The fractionation of hydrogen isotopes during dehydration of $CuSO_4 \cdot 5H_2O$ has been investigated by *K. Heinzinger*. In this hydrate four hydrogen molecules are known to be coordinated to copper and the fifth to be fixed in the crystal *via* hydrogen bonds. The D/H ratios in these two types of water molecules differ by about 5.7%; the copper-coordinated water is richer in H. Within the period of several days required for the dehydration of the hydrate at room temperature no isotope exchange takes place in the solid. At temperatures below 50 °C the copper-coordinated water is liberated first. / Z. Naturforsch. *24a*, 1502 (1969) / —Hz. [Rd 139 IE]

The equilibrium of the system nitrosyl bromide/bromine/nitrogen monoxide has been investigated by *H. Feilchenfeld*, *J. Kenat*, and *S. Manor* by spectrometric analysis of the vapor phase. In the presence of an excess of Br_2, $NOBr_3$ preponderates in the liquid phase at temperatures below 25 °C and NOBr at temperatures above 40 °C. The boiling point of NOBr is found to be 14—15 °C when an excess of NO is present (2.8 atm); the vapor pressure equation

$$\log p\,(\text{torr}) = 8.368 - 1577.64T\ (°K)$$

derived from measured values yields a figure of 14.5 °C. Previous values given for this boiling point lie between —2

and +30 °C. The heat of evaporation of NOBr at the boiling point and under atmospheric pressure is 7.2 kcal/mole. / Trans. Faraday Soc. *65*, 2350 (1969) / —Hz. [Rd 141 IE]

The reaction of N_2O with copper surfaces has been studied by *J. J. F. Scholten* and *J. A. Konvalinka*; a surface oxide is formed and nitrogen is desorbed. The activation energy of this reaction increases with the degree of covering of the surface. The transition from surface oxidation to internal oxidation involves an incubation time at not too high a temperature. At 90 °C and 200 torr N_2O a coverage degree of 1 (one atom of O per two atoms of Cu) is found. Since further uptake of oxygen is strongly hindered (activation energy *ca.* 20 kcal/mole) this reaction is suitable for the reproducible determination of the areas of free copper surfaces in catalysts./ Trans. Faraday Soc. *65*, 2465 (1969) / —Hz. [Rd 142 IE]

BOOK REVIEWS

Handbook of Chemistry and Physics. Edited by *R. C. Weast.* 49th Edit., The Chemical Rubber Co., Cleveland, Ohio, 1968. 2096 pp., bound, DM 89.80.

It is no simple matter to revise a handbook that has appeared in 48 editions[*] since 1913. Apart from minor corrections, most of the data and numerical tables retain their validity for years on end. At the same time increasing space has to be found for new material as science progesses and new methods are developed. The crucial problem therefore becomes the size of such a work, notwithstanding the use of lightweight paper. The present 49th edition of the "Rubber Handbook", with its total of nearly 2100 pages, is certainly as large as it could be without becoming unwieldy, and it is gratifying to learn from the Foreword that the publishers are thinking in terms of an appreciable reduction in size. Among the measures taken with this in mind is a table, published for the first time, giving the names of all publishers, institutions, laboratories, *etc.* having compilations of physical, physicochemical, or chemical data that are not of sufficiently general interest to be included in the handbook itself. The present edition does in fact again contain some 200 pages of new tables, in particular in the following fields: X-ray data for minerals, wavelengths of characteristic X-rays of elements, properties of semiconductors, heat capacity of organic compounds, physical properties of pigments and commercial plastics, density of heavy water, and viscosity of water between 0 and 100 °C. A number of tables have been brought up to date by the inclusion of new data.

The usefulness and reliability of the work have been established beyond doubt over numerous editions. At the same time one continues to hope for a complete revision of the largest table in the book (500 pages), *i.e.* the table giving the physical properties of organic compounds. In its present form this is below the standard of the rest of the book with regard to the presentation of the formulas and the utterly impractical arrangement of the compounds (even after 20 pages of instructions it is difficult to find a substance, or even to establish whether it is in fact listed somewhere in the table). Perhaps the imminent 50th edition may be seen by the publishers as a suitable occasion for rearranging the whole table, a step which is in any case desirable from the point of view of saving space. In all other aspects the handbook is, as always, highly commendable. *H. Grünewald* [NB 841 IE]

Handbuch der analytischen Chemie (Handbook of Analytical Chemistry). Edited by *W. Fresenius* and *G. Jander*. Part III: Quantitative Bestimmungs- und Trennungsmethoden. (Quantitative Methods of Determination and Separation). Vol. IV aα: Elemente der vierten Hauptgruppe I: Kohlenstoff, Silicium (Elements of the Fourth Main Group I: Carbon, Silicon). Compiled by *H. Grassmann* and *W. Prodinger*. Springer-Verlag, Berlin-Heidelberg-New York 1967. 1st ed., viii + 563 pp., 110 figs., paperback, DM 153.—; bound DM 158.—.

In the section on carbon the author had to face the difficulty of deciding where to draw the line, for the book would have been extended indefinitely if it had covered all methods of organic elemental analysis for all organic compounds. The choice made was to treat combustion methods relatively shortly and methods of determining CO_2 in greater detail. In addition, special methods (spectral analysis, activation analysis, X-ray scattering, β-back-scattering) and determination of carbon in many materials (metals, carbides, ores, soils, *etc.*) are also discussed. Finally there follow chapters on the analysis of some simple compounds (hydrocarbons, ethylene oxide, CO, COS, $COCl_2$, HCN, HCNO, HCNS, HCOOH, CH_3COOH, and oxalic acid).

The material on CO and CO_2 and the chapters on combustion methods and on the determination of HCN, HCNO, HCNS, COS, and $COCl_2$ can be seen as particularly valuable reviews and one is very grateful to have these facts collected from the scattered literature of these compounds. However, it could be maintained that the "purely organic" compounds should have been omitted; at the least their selection is arbitrary and their discussion in this book is unexpected.

The section on silicon deals in detail with the determination of SiO_2 in silicates and fluorspars and of silicon in metals, SiC, and organosilicon compounds; gravimetric, titrimetric, and photometric methods are discussed. It is welcome that the numerous variants of these procedures have been put together clearly. It should also be emphasized that many experimental details are given, which greatly increases the value of this section to the practising chemist.

However, several important methods are missing. That determination of silicon by atomic absorption or gas chromatography is not mentioned may be because these methods were perfected after the manuscript was complete; but that cannot explain the absence of determination by spectrography, X-ray spectral analysis, and activation analysis — processes that are not wholly unimportant.

R. Bock [NB 853 IE]

Kristallisation. Grundlagen und Technik. (Fundamentals and Techniques of Crystallization). By *G. Matz.* Springer-Verlag, Berlin-Heidelberg-New York 1969. 2nd Edit., vii + 418 pp., 174 figs., 55 tables, bound DM 72.—.

The theory and the techniques of crystallization have received much attention in the past twenty years. As a result, a wide variety of better single crystals can now be grown, and many crystalline substances with the required particle size and particle-size distribution can be obtained on a large scale by mass crystallization.

While several good books exist on the art of growing single crystals, this is the first comprehensive and up-to-date book on mass crystallization. In fact, the book deals mainly with the designing and the operation of mass crystallizers, and gives only a sketchy account of the theory and techniques of growing single crystals.

[*] Cf. Angew. Chem. *81*, 90 (1969); Angew. Chem. internat. Edit. *8*, 86 (1969).

Though this is the second edition, the book is completely new in scope and subject matter. It is a successful book, which gives the first comprehensive account of industrial mass crystallization and its theory, and which thus fills a gap in German and other literature.

The first chapter, giving the basic definitions, covers only five pages and is not very satisfactory. This is followed by another short chapter (4 pages) on the methods of crystallization. The bulk is made up of Chapter III on the fundamentals of crystallization (170 pages) and Chapter IV on the techniques of crystallization (200 pages), both of which are successful.

The third chapter deals first with nucleation, growth, and crop-formation, involved in any crystallization whether the product is a crystalline mass or a single crystal. The author surveys all the important theories, namely the Volmer-Becker-Stranski equations for nucleation, the Gibbs-Wulff minimum requirement for crop-formation, Frank's theory of spiral growth, the Kossel-Stranski molecular theory, with its far-reaching deductions for nucleation and growth, and the Nernst-Berthoud diffusion theory (*Berthoud*'s name should be retained here, and Berthoud's diffusion layer should be more clearly distinguished from the two-dimensional Volmer diffusion). This chapter also covers the basic forms of crystallization, *i.e.* crystallization from solution (thermal precipitation, salting-out, freezing-out, and fractional precipitation), from melts (*e.g.* by cooling and zone crystallization), by sublimation (under vacuum, with a carrier, in a fluid bed, and fractional sublimation), and crystallization of adducts.

All the forms of crystallization are illustrated by examples and clear diagrams. Their theories are developed mathematically, with special reference to mass crystallization. As a result, the latter is given a broad and firm theoretical basis.

Besides some general technological problems concerning *e.g.* heat transfer, particle size, particle-size distribution, and crust-formation, Chapter IV is mainly concerned with the industrial apparatus and methods of mass crystallization. The author describes in 160 pages 74 typical examples of industrial crystallizers for *e.g.* solution, fusion, and sublimation crystallization, and gives clear diagrams for various modes of operation, unit processes, and overall schemes. — In fact, this chapter determines the character of the whole book.

This is a good book, despite minor flaws in composition, uniformity, and information, which can always be found in the first comprehensive book on any wide field. It has been written for experienced industrial chemists and technologists dealing mainly with mass crystallization, and is likely to provide a good guide in this field for a long time. It is thoroughly recommended to all who are involved or interested in industrial crystallization processes.

A. Neuhaus [NB 848 IE]

Comprehensive Biochemistry. Edited by *M. Florkin* and *E. H. Stotz*. Vol. 17: Carbohydrate Metabolism. Elsevier Publishing Corp., Amsterdam 1969. 1st Edit., xiii + 292 pp., 59 figs., 30 tables. bound Dfl. 47.50; subscr. price Dfl. 38.—.

Cleavage and oxidation of sugars have been regarded as contrasting metabolic reactions — especially since *Pasteur* established the antagonism between aerobiosis and fermentation. It remained for modern biochemistry to show that there is here no fundamental difference but that we have a regulation phenomenon. Oxidative degradations are repressed in the absence of oxygen, and the electrons are removed by internal oxido-reduction.

As is well known, the fundamental reactions have been laid bare largely among microorganisms. The metabolism of carbohydrates has been treated in very great detail in several recent collective works, but in almost all these cases the main emphasis has been on synthesis and degradation of carbohydrates in mammals. The same limitation applies to this volume of "Comprehensive Biochemistry"[1]. It begins with a short chapter on absorption, digestion, resorption, and transport of mono- and di-saccharides and the control of these processes; here *R. K. Crane* describes in a few pages the most important facts that prove a carrier mechanism.

Then *E. Helmreich* gives an excellent and critical review of the control of synthesis and degradation of the polysaccharides glycogen, starch, and cellulose. A large but deserved space is naturally devoted to phosphorylase and its regulation by the reactants; the literature is covered up to 1968 in this section. — In a further 70 pages *I. A.* and *Z. B. Rose* describe the different steps of glycolysis; the enzymes are characterized by their kinetic data, which are important for the overall reaction. — The oxidation of glucose 6-phosphate and the relevant pentose cycle are reported by *S. Pontremoli* and *E. Grazi*; in this short section particular attention is paid to differentiating the forms of glucose 6-phosphate dehydrogenase that have genetic importance. The "shunt" proper is only briefly mentioned.

The central nervous system obtains almost all its energy from a rapid degradation of glucose. The distinguishing feature of metabolism in the brain is control of these processes; they are clearly explained by *H. S. Bachelard* and *H. McIlwain*. — Conversion into aldonic and uronic acids is a further special area of carbohydrate metabolism; this has been given an exhaustive chapter in which *O. Touster* shows how the sugar acids are formed from metabolic carbohydrates and which special reactions are effective for the purpose. — Amino sugars are present as glucosaminoglycanes in the cell membranes of lower and higher organisms. *A. S. Stoolmiller* and *A. Dorfman* present a good review of this complex area.

In comparison with other reports of carbohydrate metabolism, greater stress is laid in this book on additions to and subtractions from the system, as well as its ramifications, so that the value of the volume is increased — it can also be regarded as an extension of other presentations. The various sections are well chosen and are written by experts in the particular fields. The literature is covered mostly up to the end of 1967. A missing chapter on oxidative degradation of carbohydrates has had to be postponed to the next volume, which, it is hoped, will appear as supplement with the minimum of further delay. *L. Jaenicke* [NB 851 IE]

[1] Cf. Angew. Chem. *81*, 952 (1969); Angew. Chem. internat. Edit. *8*, 995 (1969).

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Distortions of the π-Electron System in Substituted Benzenes

By A. R. Katritzky and R. D. Topsom[*]

The factors leading to substituent effects on the electron distribution in aromatic molecules are discussed, particular attention being paid to the π-electron system. IR spectroscopy has proved an extremely useful probe in this field of study. Substituent d-orbital participation and the relevance of the π-inductive effects are also considered.

1. Introduction

The determination of electronic interactions in aromatic molecules has long been the aim of many chemists. Sure knowledge of the mechanisms and magnitudes of such interactions would allow the prediction of many physical properties, reaction rates, and equilibrium constants, and also assist in the correlation of the mass of existing data. This review is particularly concerned with effects of substituents on the π-electron system in aromatic compounds and makes only passing reference to field and σ-bond inductive effects. No attempt has been made to ensure an exhaustive coverage of the literature, while particular emphasis is placed on the use of the infrared methods that we have recently developed [1–3].

We start below by discussing the overall effect of placing a substituent on a benzene ring. [We generally consider a substituent group as a whole but it must be appreciated that, where this contains more than one atom, much of the charge disturbance may be located in bonds other than that connecting it to the ring.]

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Bundoora, Victoria (Australia)

[1] *R. T. C. Brownlee, A. R. Katritzky*, and *R. D. Topsom*, J. Amer. chem. Soc. *87*, 3260 (1965); *88*, 1413 (1966).

[2] *R. T. C. Brownlee, R. E. J. Hutchinson, A. R. Katritzky, T. T. Tidwell*, and *R. D. Topsom*, J. Amer. chem. Soc. *89*, 1757 (1968).

[3] *P. J. Q. English, A. R. Katritzky, T. T. Tidwell*, and *R. D. Topsom*, J. Amer. chem. Soc. *89*, 1767 (1968).

2. Effect of Substituents on the Benzene Ring

Aromatic and, in particular, benzene derivatives have provided the majority of the series of compounds used by physical organic chemists to examine correlations between structure and reactivity. The benzene nucleus contains both of the usually distinguished types of bond; the σ bond has cylindrical electronic symmetry about the bond direction while the π bond has a node in the bond axis. The π electrons in benzene can also be regarded as delocalized and we thus have a relatively simple and symmetrical system of fixed geometry allowing investigations of features of the major bonding concepts. [Additional advantages of benzene derivatives for such studies are the relative ease of preparation of series of variously substituted derivatives and the availability of several positions at which tests can be made for changes in electric character.]

Many physical organic chemists and theoreticians have recently treated σ and π systems discretely and the accord obtained between predictions and experimental results suggests that the approach is both useful and, at least to some extent, meaningful. The assumption that we can, to a large extent, discuss effects in the π system of benzene independently of its σ framework is thus gradually becoming accepted and we present additional confirmatory evidence in the later part of this review. [At the same time, recent calculations [4–6] including both σ and π electrons

[4] *J. A. Pople* and *M. Gordon*, J. Amer. chem. Soc. *89*, 4253 (1967), and references given therein.

[5] *N. C. Baird* and *M. J. S. Dewar*, Theoret. chim. Acta *9*, 1 (1967).

[6] *J. E. Bloor* and *D. L. Breen*, J. physic. Chem. *72*, 716 (1968); J. Amer. chem. Soc. *89*, 6835 (1967).

have provided measures of the total electrical effect of substituents on aromatic rings.]

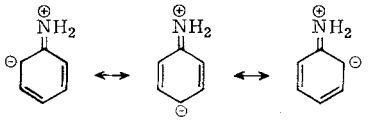
The separate treatment of changes in σ and π electron densities and discussions of the effect of one on the other assumes that we know something of their individual effects. It is relatively easy to observe the former in isolation by considering systems containing saturated linkages. Thus the effect of adding a substituent to an alkyl group has been well explored. The two most likely forms of charge transmission have become known as the σ inductive effect (I_σ) and the field effect (F). The former describes the transmission of charge by the successive and diminishing polarization of a series of adjacent σ bonds:

$$\delta^{\ominus}\ \delta^{\oplus}\quad \delta\delta^{\ominus}\quad \delta\delta\delta^{\ominus}$$
$$Y{-}CH_2{-}CH_2{-}CH_2{-}$$

Earlier workers assumed that this effect would still be appreciable at the second carbon atom and factors such as $^1/_3$ have been suggested [7,120] for the proportion of charge disturbance relayed from one carbon atom to the next. It is now considered by many workers [8–12,121,122], however, that the σ inductive effect is of minor magnitude compared to the direct, through space, electrostatic effect of the polarity of the substituent bonds on the system although this is still subject to argument [123]. Thus the fact that monofluoroacetic acid is stronger than acetic acid is considered to be mainly a result of the increased stabilization of the carboxylate anion brought about by interaction with the C–F dipole. [Recent calculations [13,14] have also suggested that any small I_σ effect might show alternation along a chain of carbon atoms in an aliphatic system but this apparently does not occur [124] in the σ framework of a benzene ring.]

A substituent attached to a benzene ring can still give rise to field and I_σ effects. Recent work on aromatic systems [9,15–17] supports the view that field effects predominate over σ inductive ones. It is not always necessary to distinguish these effects and they are frequently referred to by physical organic chemists under the general term "inductive effects", a practice that can lead to confusion.

Additional effects exist in substituted aromatic systems. Physical organic chemists until recently considered "mesomeric effects" as being the only important contribution to charge disturbance apart from inductive effects. Thus in aniline it was considered that the lone pair of electrons on the nitrogen could interact with the π-electron system of the ring leading to their delocalization and a somewhat enhanced electron density in the ring. In valence-bond language, it was considered that canonical forms of type *(1)* made some contribution to the ground state.



(1)

The amino substituent thus transfers charge to the ring in opposition to its inductive effect. The dipole moment of aniline can be shown to be directed towards the ring and this can be explained if the mesomeric effect is stronger than any inductive effect. In a similar manner, it was suggested that some delocalization of the π electrons of the benzene ring could occur into a substituent such as a nitro or carbonyl group where free orbitals were available.

More recently, the question has arisen as to whether the inductive effect of a substituent could in turn influence the π-electron system. This has been called [9] the inductoelectromeric [18] or π-inductive effect (I_π) [19]. This type of effect had already, however, been considered by spectroscopists and theoretical chemists.

Quantum mechanical calculations need more exact mathematical definitions of the inductive and mesomeric effects than those used by organic chemists. Since the absorption spectra and theory of aromatic systems make no predictions concerning the σ electrons, the inductive effect of a substituent was taken as the effect of the potential field of the substituent *on the π electrons* of the unsubstituted molecule. Thus the inductive effect of a substituent as used by most theoretical chemists does not include the I_σ or F effects above, but consists rather of the I_π effect together with any disturbance of the π system caused by electron repulsion between it and electrons on the substituent group. Some workers [20] include this last effect under the general heading of an I_π effect. [In fact, *Jaffe* [19] originally proposed the term I_π to cover only this perturbation to the π system of the benzene ring effected by the assignment of realistic Coulomb integrals to attached substituent atoms.]

Some doubt has been expressed recently as to whether a single electron-withdrawing substituent attached to a benzene ring does show a mesomeric effect. It has been suggested [21] that the effect of a nitro group and

[7] *S. Ehrenson*, Progr. physic. org. Chem. *2*, 195 (1964).

[8] *J. N. Murrell, S. F. A. Kettle*, and *J. M. Tedder*: Valence Theory. Wiley, London 1965, chapter 16.

[9] *M. J. S. Dewar* and *P. J. Grisdale*, J. Amer. chem. Soc. *84*, 3539, 3548 (1962), and references given therein.

[10] *F. W. Baker, R. C. Parish*, and *L. M. Stock*, J. Amer. chem. Soc. *89*, 5677 (1967).

[11] *C. F. Wilcox* and *C. Leung*, J. Amer. chem. Soc. *90*, 336 (1967).

[12] *P. E. Petersen, R. J. Bopp, D. M. Chevli, E. L. Curran, D. E. Dillard*, and *R. J. Kamat*, J. Amer. chem. Soc. *89*, 5902 (1967).

[13] *J. A. Pople* and *M. Gordon*, J. Amer. chem. Soc. *89*, 4253 (1967).

[14] *R. W. Taft jr.*, personal communication.

[15] *W. Adcock* and *M. J. S. Dewar*, J. Amer. chem. Soc. *89*, 379 (1967).

[16] *W. A. Sheppard* and *R. M. Henderson*, J. Amer. chem. Soc. *89*, 4446 (1967).

[17] *M. J. S. Dewar* and *T. G. Squires*, J. Amer. chem. Soc. *90*, 210 (1967).

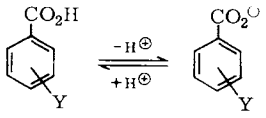
[18] *D. A. Brown* and *M. J. S. Dewar*, J. chem. Soc. (London) *1953*, 2406.

[19] *H. H. Jaffe*, J. Amer. chem. Soc. *77*, 274 (1955).

[20] *D. T. Clark*, Chem. Commun. *1966*, 390.

[21] *O. Exner*, Collect. czechoslov. chem. Commun. *31*, 65 (1966).

other similar electron-withdrawing substituents on the π-electron system of the benzene ring is solely due to the π-inductive effect in the ground state. This result is based on the acidity of *p*-substituted benzoic acids.



Since both the carboxy and the carboxylate groups are electron-withdrawing in their own right, it is quite possible that the nitro group shows no particular change in mesomeric effect in this ionization. This result is therefore not necessarily relevant to the ground state of nitrobenzene itself. Further, these mesomeric effects are small and in the same direction as inductive effects, which makes them difficult to investigate by the method used. Evidence has been offered [22] for an appreciable amount of mesomeric interaction in the ground state of nitrobenzene, which will be discussed further below.

It has also recently been suggested [20] that the major part of π-electron disturbances caused by substituents having free electrons on the atom attached to the ring is caused by non-bonded repulsions rather than mesomeric interaction. There are some measurable differences to be expected depending as to whether the π disturbance in a molecule such as aniline arises from a mesomeric effect or from electron repulsion. In the former case the amino group should be approximately coplanar with the benzene ring to allow for maximum mesomeric interaction, which should result in the most stable molecule. The ring-nitrogen bond should be slightly shorter as a consequence. On the other hand, π-electron repulsion is greatest when the amino group is coplanar with the benzene ring. Electron diffraction work [23] does suggest substantial bending of the amino group in aniline with respect to the ring and this has been interpreted [20] as evidence for the dominance of repulsion terms. There is some X-ray and neutron diffraction evidence for $C_{Ar}-N$ bond shortening in some *p*-substituted aniline derivatives, but this may be related to the possibility of "through conjugation" between the two substituents (see Section 4).

It seems clear from an analysis [24] of the second order inductive shifts of the benzene 2600 Å band in substituted benzenes and the first order inductive shift of the azulene visible band that some mesomeric contribution certainly exists in the excited state and we consider that present evidence suggests that this also occurs in the ground state.

The effect of the potential of the substituent atoms on the π-system of the ring has recently been discussed in several semi-theoretical papers. The lack of marked change in the ultraviolet spectrum of the anilinium ion compared to benzene posed a problem [25] since a considerable disturbance of the π electrons would be anticipated if the I_π effect were of any significance.

It has been suggested [26,27] that inductive effects on the π system can be subdivided into two classes. *Craig* and *Doggett* [26] have proposed that inductive effects of the I_π type be differentiated from repulsive orbital terms arising from electron exchange between overlapping π orbitals. They suggest that the latter be known as "orbital penetration effects". Our own work [3] provides evidence for the importance of such effects; for example the $[N(CH_3)_3]^+$ substituent is a slightly stronger resonance donor than a tertiary butyl group. These orbital penetration effects are claimed, however, to be considerably smaller in magnitude than mesomeric effects in compounds like aniline and phenol although they act in the same direction.

Murrell and *Williams* [27] and *Godfrey* [28] subdivide the inductive effect of a substituent on the π system into short- and long-range forces. They show that exchange terms can be treated empirically as though they arose from short-range effects. Coulomb terms must be considered both as short- and long-range effects. The I_π effect is considered to arise mainly from the short-range contributions. The fact that the overall effect of the chlorine atom in chlorobenzene is to distort the π system of the nucleus away from the substituent is therefore interpreted as showing the predominance of the exchange terms over the coulombic ones, since the mesomeric contribution is considered to be low in this case.

This explanation has come in for some criticism as a result of work [29] on vertical ionization potentials which suggests a slight overall π-electron withdrawal by chlorine. The suggestion that this would indicate a similar effect in the ground state conflicts with results [3,30,31] showing that the chloro substituent repels the π-electron system. *Murrell* and *Williams* suggest that for a methyl group the inductive perturbation is almost entirely of the short-range type and is probably dominated by the exchange terms. They also advocate including both field and exchange terms within the "inductive effect" since it is hard to differentiate them.

Thus, from a semi-theoretical point of view, π-electron disturbances in the ground state of substituted benzenes can be caused by:

1. Mesomeric effects
2. Coulombic effects
3. Exchange or orbital repulsion effects.

[22] *W. F. Baitinger, P. v. R. Schleyer, T. S. S. R. Murty,* and *L. Robinson,* Tetrahedron *20,* 1635 (1964).

[23] *J. C. D. Brand, D. R. Williams,* and *T. J. Cook,* J. molecular Spectroscopy *20,* 359 (1966).

[24] *M. Godfrey* and *J. N. Murrell,* Proc. Roy. Soc. (London) Ser. A *278,* 64 (1964).

[25] *D. M. Bishop* and *D. P. Craig,* Molecular Physics *6,* 139 (1963).

[26] *D. P. Craig* and *G. Doggett,* Molecular Physics *8,* 485 (1964).

[27] *J. N. Murrell* and *D. R. Williams,* Proc. Roy. Soc. (London) Ser. A *291,* 224 (1966).

[28] *M. Godfrey,* J. chem. Soc. (London) *B 1967,* 799; *1968,* 751.

[29] *D. P. May* and *D. W. Turner,* Chem. Commun. *1966,* 199.

[30] *R. W. Taft jr.* and *I. C. Lewis,* J. Amer. chem. Soc. *81,* 5343 (1959).

[31] *G. E. Maciel* and *J. J. Natterstad,* J. chem. Physics *42,* 2427 (1965), and references given therein.

3. Hammett Relationships

We now wish to go back and consider the development of various physical organic concepts in the light of the discussion above. It is very important to understand that some properties discussed are ground state ones (dipole moments, NMR, IR), some are transition state ones (reactions), while others represent differences between various ground state energies (equilibria) or between ground and excited states (UV). There are numerous examples in the literature where authors have, either knowingly or otherwise, correlated properties of two different classes.

Early studies of electron disturbances in benzene derivatives were mainly limited to the interpretation of dipole moment measurements and ultraviolet spectra. The former is a ground state property which depends on the charge separation in the molecule with respect to both the amount of charge and the effective distance apart. So-called "mesomeric moments" for benzene derivatives have been obtained [32] by subtracting the dipole moment found for alkyl derivatives from that for the corresponding benzene derivative. These have been further modified by some workers [33] to allow for a distance term. Mesomeric moments do show a general relationship with some indices of charge disturbance in the benzene ring but fail to correlate well with the disturbance of the π system. They are therefore best used, until better understood, as providing a general guide to the direction and order of magnitude of the effect of a substituent on the π-electron density in substituted benzenes.

Changes in frequency and intensity of ultraviolet absorptions caused by the $\pi \rightarrow \pi^*$ exaltation in substituted benzenes also provide some information about electronic movements. The absorptions, however, depend on the difference in π-electron distribution between the ground and excited state and thus do not necessarily mirror the effect in the ground state itself. The results of UV studies can prove useful [125,126] in an analysis of the factors leading to the π-electron disturbances as indicated above. Optical exaltations have also been used [34] as a measure of π-electron movement.

Most of the work in this field from 1940 to 1960 was concentrated on the linear free energy relationships pioneered by *Hammett* [35]. In this work the effect of a substituent on a standard equilibrium, rate of reaction, or physical property was observed. The Hammett equation

$$\log k/k_0 = \rho\sigma$$

was used to correlate the results. The value of ρ varies according to the electronic demands of the reaction or property measured but is a constant for a fixed set of conditions. The σ constant for a substituent Y in the *meta* or *para* position (*ortho* positions are complicated by steric interactions which are beyond the scope of this review) gives a measure of its electronic effect on the reaction or measurement center X.



(2) *(3)*

The σ constant is thus rather a measure of the transmission of the substituent's electronic effect to the reaction site than a measure of its effect on the benzene ring in isolation. The acidity of *m*- and *p*-substituted benzoic acids was originally taken as a standard reaction and ρ arbitrarily taken as unity. The σ values derived were found to be broadly applicable to some other equilibria and physical properties. However, *Hammett* [35] had pointed out that σ constants might vary for certain substituents depending on the electronic requirements of X in cases where X and Y could interact. Thus in the aniline-anilinium ion equilibrium, it is possible for an electron-withdrawing substituent such as a nitro group to interact more in the neutral molecule than in the charged one when situated in the *para* position.

This "through conjugation" *(3)* leads to a different σ value here compared to the value obtained from the benzoic acid-benzoate anion equilibrium. The value obtained for the *m*-nitro substituent is similar in both cases since no low energy conjugated forms are possible. Obviously substituents having a free electron pair on the α atom can show enhanced electron donation if the reaction center places a demand on it. New substituent constants, σ^+ and σ^-, were obtained [36] for cases where the property measured placed a demand on electrons or had a surplus of them, respectively. The σ values thus depend on the reaction studied and some authors [36,37] have pointed out that a whole range of values, between σ^+ and σ^- as extremes, may be required. Attempts have been made, notably by *Yukawa* and *Tsuno* [38], to relate the σ value for a substituent to a second constant typical of the particular reaction being studied (cf. [7,36,39–41]). Other workers [42] have tried to define new sets of constants allowing for exalted substituent values and variable

[32] *K. B. Everard* and *L. E. Sutton*, J. chem. Soc. (London), *1951*, 2818.

[33] *O. Exner*, Collect. czechoslov. chem. Commun. *25*, 642 (1960).

[34] *B. A. Zaitsev*, Org. Reactivity (Tartu State Univ.) *4*, 726, 740 (1967).

[35] *L. P. Hammett*: Physical Organic Chemistry. McGraw-Hill, New York 1940.

[36] *C. D. Ritchie* and *W. F. Sager*, Progr. physic. org. Chem. *2*, 323 (1964), and references given therein.

[37] *H. Van Bekkum*, *P. E. Verkade*, and *B. M. Wepster*, Recueil Trav. chim. Pays-Bas *78*, 815 (1959).

[38] *Y. Yukawa*, *Y. Tsuno*, and *M. Sawada*, Bull. chem. Soc. Japan *39*, 2274 (1966).

[39] *G. Schott*, Z. Chem. *6*, 321 (1966).

[40] *P. R. Wells*, Chem. Reviews *63*, 171 (1963).

[41] *C. G. Swain* and *E. C. Lupton jr.*, J. Amer. chem. Soc. *90*, 4328 (1968).

[42] *G. Thirot*, Bull. Soc. chim. France *1967*, 739.

reaction conditions, but this appears to offer no advantage over extra-parameter equations using σ values.

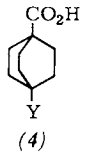
Physical properties such as IR and NMR spectra have also been correlated with σ constants. For example, the frequency of the carbonyl stretching vibration in *m*- and *p*-substituted acetophenones correlates reasonably with normal σ constants [43,44]. The frequency of an infrared absorption depends on the environment of the vibrating atoms in the molecule, but includes mass effects and usually has contributions from vibrations of neighboring bonds. The intensity is related to the way the dipole moment alters with the normal coordinate during the vibration being considered. The intensity should thus be extremely useful for correlation purposes, but difficulties in obtaining reliable values have until recently limited such work. The intensities of the C≡N stretching vibrations in substituted benzonitriles have recently been shown [45] to correlate with σ^+ values. However, infrared properties may also fail to correlate [46] well with any particular set of σ constants.

The realization that a large part of the variation in σ values could be ascribed to direct conjugation between the substituent and the reaction site led to an attempt to estimate σ^0 values for systems where such interactions were precluded or minimized. The σ^0 values should thus be a measure only of the interaction of the substituent with the benzene ring as felt at the reaction site. The usual approach has been to measure properties such as the acidity of substituted phenylacetic acids where the reaction site is one atom removed from the ring.

Fair agreement is found for σ^0 values from various sources; as with normal σ values, different values are required for *meta* and *para* substitution. [Both σ and σ^0 values can be affected [47] by the solvent where specific interactions such as hydrogen bonding exist.]

A rather more detailed knowledge of the way in which a single substituent interacts with a benzene ring would be very valuable as a foundation to the understanding of the types of reactions and equilibria mentioned above which effectively involve the transmission of electronic effects in disubstituted benzenes. *Taft* and his co-workers [48] pioneered attempts to split σ values into inductive and "resonance" contributions. The inductive part was considered as the electrical disturbance in the σ bonds and through space arising from the charge distribution in the substituent, while the resonance part consisted of all disturbances observed in the π system of the ring. It is important to note the difference between this division and terminology and those used by the theoretical chemists (Section 2).

A measure of the inductive effects of substituents was obtained from 1) a comparison [49] of the rates of acid and alkaline hydrolysis of aliphatic ester (σ^*), 2) the acidities of a series of 4-substituted bicyclo[2.2.2]-octane-1-carboxylic acids [50] *(4)* which show a geometrical similarity to *p*-substituted benzoic acids, and



(4)

3) a comparison [48] of σ_m and σ_p values assuming an identical inductive component for each and that a constant proportion of the resonance effect of a substituent was relayed from the *ortho* or *para* positions to the *meta* one.

$$\sigma_m = \sigma_I + \alpha\sigma_{R(p)}$$

$$\sigma_p = \sigma_I + \sigma_{R(p)}$$

Values of 0.33 or 0.5 have been suggested [48] for α.

After scaling to a common basis these σ_I values were remarkably constant [36,39] and suggested that they have a real meaning. Further confirmation was found in the accurate correlation of ^{19}F–NMR shifts of *m*-substituted fluorobenzenes with σ_I values, although the reason why these shifts fail to correlate with σ_M has presented a difficulty [15,51]. Nevertheless, it is unlikely that σ_I values should be the same for *meta* and *para* positions whether they are mainly caused by field or I_σ effects. *Schmid* [52] has recently shown however, that the intensity of C–H stretching modes in the *ortho*, *meta*, and *para* positions of monosubstituted benzenes are functions of σ_I. It may thus be that $\sigma_{I(m)}$ is linearly related to $\sigma_{I(p)}$ as recently suggested in empirical equations [41,53].

If σ_I can be obtained, then the resonance contribution can be found:

$$\sigma_R = \sigma - \sigma_I$$

$$\sigma_R^0 = \sigma^0 - \sigma_I$$

The second value, σ_R^0, represents the disturbance of the π system in a monosubstituted benzene. It is thus a constant value, unlike σ_R which varies with the method of measurement since the possibility of conjugation with the reaction site is present. The value of σ_R^0 may vary with temperature and solvent, but provided these are fixed, affords a quantity of physical

[43] *R. N. Jones, W. F. Forbes*, and *W. A. Mueller*, Canad. J. Chem. *35*, 504 (1957).

[44] *C. N. R. Rao*: Chemical Applications of Infrared Spectroscopy. Academic Press, New York 1963, pp. 568–577.

[45] *O. Exner* and *K. Bocek*, Tetrahedron Letters *1967*, 1433.

[46] *A. Courville* and *D. Peltier*, Bull. Soc. chim. France *1967*, 2164.

[47] *P. E. Peterson, D. M. Chevli*, and *K. A. Sipp*, J. org. Chemistry *33*, 972 (1968), and references given therein.

[48] *R. W. Taft jr.*, J. physic. Chem. *64*, 1805 (1960).

[49] *R. W. Taft jr.*, J. Amer. chem. Soc. *74*, 2729, 3120 (1952); *75*, 4231 (1953).

[50] *J. D. Roberts* and *W. T. Moreland jr.*, J. Amer. chem. Soc. *75*, 2167 (1953).

[51] *Y. Takeuchi*, Sci. Papers Coll. gen. Educat. Univ. Tokyo *16*, 231 (1967).

[52] *E. D. Schmid et al.*, Spectrochim. Acta *22*, 1615, 1621, 1633, 1645, 1659 (1966); *V. Hoffmann* and *E. D. Schmid*, Z. Naturforsch. *22a*, 2044 (1967).

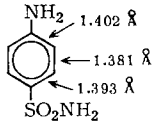
[53] *Y. Yukawa*, personal communication.

meaning and a basis for calculations [7]. Thus the calculated total charge transfer between a substituent and the ring in a series of monosubstituted benzenes has been shown [54] to be proportional to σ_R^0.

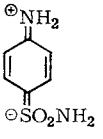
4. π-Electron Disturbances

The value of σ_R^0 determined in the *para* position of a substituted benzene should provide a measure of the π-electron disturbance along the major axis of the corresponding monosubstituted benzene. Various techniques have been used which provide qualitative or quantitative measures of such disturbances. The solvent and temperature conditions are not always the same.

X-Ray results: π-Electron disturbances should affect the bond lengths in the benzene nucleus. In practice such changes are very small and only accurate neutron diffraction work allows even a qualitative result in favorable cases. Thus the bond lengths in β-sulfanilimide *(5)* [55] indicate the contribution of structure *(6)*.



(5)



(6)

Dipole moment results: Mesomeric moments do not show a reasonable correlation with σ_R^0 values as indicated in the previous section. Some correlation is found between the corrected values of *Exner* and σ^+ or σ^- values but it is difficult to see why enhanced σ values are required.

NMR results, chemical shifts: The chemical shifts of the hydrogen or substituent atoms attached to a benzene ring or of the carbon atoms themselves (^{13}C) should in principle give a measure of the electron density at the position in question, provided anisotropic and ring current effects are not important. It has been recently suggested [56] that after allowing for ring current variation, *p*-hydrogen chemical shifts in a series of monosubstituted benzene derivatives depend linearly on the π-electron density variations on the adjacent carbon atom as calculated by a non-empirical Hückel LCAO method. It has been shown that *p*-hydrogen shifts are linear with *p*-^{13}C shifts [57] and ^{19}F shifts [127] in the corresponding compounds suggesting that the shifts are mainly caused [58] by changes in the π-electron density. Other calculations (HMO) for both *o*-H and *p*-H chemical shifts have indicated [128] dependence on π-electron densities on the corresponding carbon atom and it was further suggested that *m*-H shifts [59] are affected by the π-charge on the carbon atoms next to the *m*-C atom.

Thus the evidence for the small effect of inductive or field effects on proton shifts in benzene derivatives has been adduced [129] but this conflicts with an analysis [130] of the results.

m-^{13}C shifts [60] in monosubstituted benzenes are small, rather random, and do not correlate with *m*-H values. A very good correlation with σ_R^0 is obtained [30], nevertheless, when the *p*-^{13}C shift is corrected by the corresponding *meta* value. Some theoretical justification has also been produced [61] for a correlation of ^{13}C shifts with π-electron density. However, *Bloor* [6] has suggested that ^{13}C shifts in *all* ring positions of monosubstituted benzenes are well correlated by the total electron density as calculated by a CNDO method. He suggests that there may be a fortuitous and close relationship between the π-electron and total electron density in the case of *p*-carbons.

Taft and his co-workers [62] have made quite an extensive study of ^{19}F chemical shifts of *m*- and *p*-substituted fluorobenzenes. The *meta* shifts relative to fluorobenzene are shown [67] to accurately follow a linear correlation with σ_I values while the *para* shifts, when corrected by the corresponding *meta* values, correlate well [63] with σ_R^0.

$$\sigma_R^0 = -0.339\left(\int_H^{p-X} - \int_H^{m-X}\right)$$

where $\int_H^{p-X}$ is the ^{19}F chemical shift difference between *p*-X-fluorobenzene and fluorobenzene, and $\int_H^{m-X}$ is the analogous quantity for the *meta* derivative. These σ_R^0 values are almost solvent independent except where specific solute-solvent interaction occurs. They could, however, be somewhat in error for cases where the fluorine atom can conjugate with an electron-withdrawing *para* substituent, for example in *p*-nitrofluorobenzene or donate into d-orbitals, for example in *p*-iodofluorobenzene (see Section 9).

The corrected shifts here thus correlate well with the corresponding corrected C-13 shifts as well as with σ_R^0 values obtained from chemical experiments involving the determination of σ^0 and σ_I. *p*-F shifts have been shown [131,132] to follow the calculated π den-

[54] *R. T. C. Brownlee* and *R. W. Taft jr.*, J. Amer. chem. Soc. *90*, 6537 (1968).

[55] *A. M. O'Connell* and *E. N. Maslen*, Acta crystallogr. *22*, 134 (1967).

[56] *H. P. Figeys* and *R. Flammang*, Molecular Physics *12*, 581 (1967).

[57] *Y. Sasaki* and *M. Suzuki*, Chem. pharmac. Bull. (Japan) *15*, 1429 (1967); *16*, 1187 (1968).

[58] *H. Spiesecke* and *W. G. Schneider*, J. chem. Physics *35*, 731 (1961).

[59] *S. Castellano*, *C. Sun*, and *R. Kostelnik*, Tetrahedron Letters *1967*, 5205.

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[61] *T. K. Wu* and *B. P. Dailey*, J. chem. Physics *41*, 2796 (1964); see also *H. L. Retcofsky*, *J. M. Hoffman jr.*, and *R. A. Friedel*, *ibid. 46*, 4545 (1967).

[62] *R. W. Taft jr.*, *E. Price*, *I. R. Fox*, *I. C. Lewis*, *K. K. Andersen*, and *G. T. Davis*, J. Amer. chem. Soc. *85*, 709 (1963).

[63] *R. W. Taft jr.*, *E. Price*, *I. R. Fox*, *I. C. Lewis*, *K. K. Andersen*, and *G. T. Davis*, J. Amer. chem. Soc. *85*, 3146 (1963).

sity at the fluorine or attached carbon atom and to be insensitive to σ electron effects. Allowance must be made [132] for the effect of *ortho* substituents in such correlations.

Some work on nitrogen shifts of substituted nitrobenzenes and pyridines has also been reported [64–67] some of which show broad correlations with electron densities.

NMR results, coupling constants: Proton-proton coupling constants have been used frequently [60,68] to gain information about the electronic structure of olefinic and aromatic compounds. The values are relatively insensitive and this makes it hard to interpret the reasons for the variations noticed. Some limited correlations of J_{H-H} values with electronegativity values [60,69] or proton chemical shifts [70,71] have been reported, but there is disagreement [59,72–74, 133] as to whether inductive effects or changes in π-electron density are the more important. Both could well contribute in approximately equal amounts [134]. Two recent papers [75,76] report that the geminal coupling constants between the nonequivalent protons of a benzylic methylene group in 2-benzyloxytetrahydropyrans vary as the Hammett value of a substituent in the *meta* or *para* position.

$^{13}C-H$ coupling constants may show similar effects but only limited results are available [60,77,135] and the changes are rather small. Some work has also been reported on fluorine-fluorine [78], fluorine-hydrogen [72,79,136], and nitrogen-hydrogen coupling constants [137].

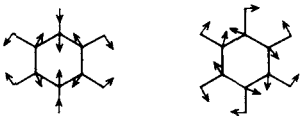
Nuclear quadrupole and electron spin resonance: NQR frequencies of some monosubstituted [^{35}Cl]-chlorobenzenes vary [80] almost linearly with inductive effects presumably because the measurements are not very sensitive to changes in the double bond character of the C–Cl bond. Nevertheless, they may be somewhat sensitive to π-electron densities [81]. Some related ESR results reported include a correlation [82] with σ values for *m*- and *p*-substituted diaryl nitroxides.

IR spectra: We have recently shown [1,2] that the intensities of the ν_{16} ring-stretching bands of monosubstituted benzenes give a quantitative measure of the distortion of the π system of the ring along the main axis. This integrated area A of the bands near 1600 and 1585 cm^{-1} is related to σ_R^0 for the substituent.

$$A = 17600\,(\sigma_R^0)^2 + 100 \qquad (1)$$

The small constant term in the equation is required since an overtone band also occurs in this frequency range. This was the first correlation between aromatic ring vibrations and substituent constants for substituted benzenes, although it had earlier been recognized [83] that the intensities of certain ring vibrations were qualitatively related to the electron donating or withdrawing power. Some Raman absorptions [84] and optical exaltations [34] have been shown to follow a similar pattern.

The 1600 cm^{-1} (ν_{16a}) and 1585 cm^{-1} (ν_{16b}) bands in monosubstituted benzenes arise from the IR forbidden, in-plane ν_{16} benzene vibration at 1585 cm^{-1}. The direction of the atomic displacements in the degenerate pair in benzene itself is shown below.



Such diagrams of the forms of the normal modes are the result of force-field calculations on benzene, and a comparison of the calculated and observed frequencies in its halogenation and deuterated analogs [85,138].

The degeneracy is lifted when the symmetry is reduced from D_{6h} to C_{2v} by attaching one symmetrical substituent to the ring and two infrared active vibrations are obtained. Calculations [85] show that the forms of the normal coordinates are very similar to benzene itself.

A considerable amount of the potential energy of the vibration of these modes is involved in C–H bending. *Scherer* [86] has calculated the actual potential energy distribution and showed that the contribution from C–H bending is about 30 %. Most of the intensity

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[68] *H. Gunther,* Tetrahedron Letters *1967,* 2967.

[69] *S. Castellano* and *C. Sun,* J. Amer. chem. Soc. *88,* 4741 (1966).

[70] *J. M. Read* and *J. H. Goldstein,* J. molecular Spectroscopy *23,* 179 (1967).

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[77] *S. Mohanty* and *P. Venkateswarlu,* Molecular Physics *12,* 277 (1967).

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[83] *A. R. Katritzky* J. chem. Soc. (London) *1958,* 4162.

[84] *Y. S. Bobovich* and *N. M. Belyaevskaya,* Optics and Spectroscopy *19,* 111 (1965); *Y. S. Bobovich, ibid. 20,* 136 (1966).

[85] *J. R. Scherer*: Planar Vibrations of Chlorinated Benzenes. The Dow Chemical Co., Midland, Michigan 1963.

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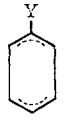
arises from the ν_{16a} vibration, however, and it can be seen that the C–H bending modes are symmetrical and any contributions they may make to the dipole moment will cancel out. The intensity thus derives from C–C stretching modes. The contribution to the potential energy from the C–H and C–X stretching modes has been shown [86] to be negligible.

If the substituent is not symmetrical the ν_{16a} and ν_{16b} vibrations have A symmetry and thus intensity can be shared. Because of this mixing and the closeness of the two absorption frequencies, the combined intensities are always used for correlations.

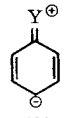
Some insight into the nature of the substituent-ring interaction may be obtained by a valence bond treatment. In a monosubstituted benzene, during the vibration ν_{16a} there is a distortion of the molecule in the sense of *(7)* ⇌ *(8)* (where the effect is much exaggerated).



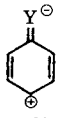
(7)



(8)



(9)



(10)

The shorter bonds will have greater double-bond character and the longer bonds greater single-bond character. If the substituent Y is capable of resonance interaction with the ring, then canonical forms of types *(9)* or *(10)* (whether *(9)* or *(10)* will depend on whether Y is an electron donor or acceptor) will be of greater importance for *(7)* than for *(8)*. This will lead to an oscillating dipole during the vibration and hence to an increased intensity in the infrared spectrum. The π-dipole moment change with respect to the normal coordinate of the vibration is evidently directly proportional to σ_R^0, for together with equation (2) this leads to the relationship observed in equation (1).

$$A = \frac{N\pi}{3c^2}\left(\frac{\partial\mu}{\partial Q}\right)^2 \qquad (2)$$

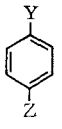
We have calculated [139] $\partial\mu/\partial Q$ for these vibrations from a knowledge of normal coordinates. Values based on π-electron densities (HMO) show very reasonable agreement with those observed experimentally while more elaborate calculations [140] (CNDO) allow discussion of the effects of π- and σ-electron densities. A molecular orbital model involving vibronic formalism has also been used [141] to explain the relationship between these intensities and σ_R^0.

A similar relationship between A and σ_R^0 has been found [87] for the ν_{13} vibrations of monosubstituted benzenes but the analysis is somewhat more complex here since C–H bending modes contribute to the overall intensity.

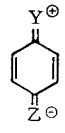
[87] *R. T. C. Brownlee, P. J. Q. English, A. R. Katritzky,* and *R. D. Topsom,* J. physik. Chem. *73,* 557 (1969).

5. Disubstituted Benzenes

In a disubstituted benzene *(11)*, clearly both Y and Z can exert their normal mesomeric, π-inductive, and orbital-repulsion effects. There is the additional possibility of through conjugation *(12)*, which would lead



(11)



(12)

to further π distortions. Some direct evidence for this comes from X-ray or neutron diffraction work with *p*-sulfanilimide [55] (Section 4) and *o*- [88] and *p*-aminobenzoic acids [88, 142]. In addition it is possible that the effects of one substituent can alter those of the other [89]. Thus it is feasible that a substituent Z with a strong inductive effect might alter the mesomeric contribution of a second substituent Y. Some substituents may also accept electrons into d-orbitals if opposed by a second, strongly electron-donating substituent (Section 9) and this may account for the X-ray observed [90] C_{Ar}–N bond shortening in *p*-chloroaniline. Careful investigation of π-electron disturbances should provide evidence about these additional interactions and this is obviously best carried out on the ground state.

Dipole moment measurements can provide some evidence of π-electron disturbances but their limitations have already been discussed. Proton, carbon-13, or fluorine chemical shifts are of limited value, since the positions involved in disubstituted benzenes are nearly all in close proximity to the substituent and thus likely to be subject to anisotropic effects. Some evidence can be adduced, however, from the observation that proton shifts are frequently approximately additive based on the corresponding monosubstituted benzenes. Deviations from additivity are found [91] where the two substituents can conjugate with each other through the aromatic ring. Proton-proton coupling constants can similarly suggest [92] quinonoid contributions, although they are usually approximately additive [93, 135] as are C–H [135] and H–F coupling constants [136]. However, the most general method at

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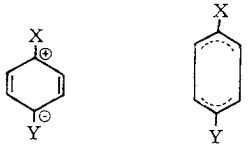
[91] *J. S. Martin* and *D. P. Dailey,* J. chem. Physics *39,* 1722 (1963).

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present is the infrared one, since this provides a measurement of the disturbance in the benzene nucleus itself.

A quantitative correlation might be expected between the summed band intensity ($A\nu_{16a} + A\nu_{16b}$) of *p*-disubstituted benzenes and the intensities of the corresponding monosubstituted benzenes, provided no interaction occurs between the substituents. Thus, calculations on *p*-dichlorobenzene[85,86] suggest that ν_{16} for *p*-disubstituted benzenes has normal coordinates similar to those for the monosubstituted analogs. If the two substituents in a *p*-disubstituted benzene act independently then by using the valence bond approach it follows that the stabilization of the dipolar character of the form *(13)* of the vibrational transition *(13)* ⇌ *(14)* will be the difference (both substituents donors or acceptors) or sum (one donor, one acceptor) of the charge stabilization for the



(13)

(14)

corresponding monosubstituted benzenes. If the dipole contributions by the two substituents are added vectorially, then this relation becomes equation 3 for all combinations of substituent types.

$$\partial\mu/\partial Q_p = (\partial\mu/\partial Q_1) - (\partial\mu/\partial Q_2) \quad (3)$$

$$A_p = b\,(\sigma_R{}^01 \cdot \sigma_R{}^02)^2 + c \quad (4)$$

The intensity of the ν_{16} band for *p*-disubstituted benzenes should therefore be given by (4) where *c* represents the contribution from overtone and combination bands and *b* is a constant. The constant *b* would be expected to be near that of 17600 found for monosubstituted benzenes; however, the exact form of the normal vibration is likely to vary somewhat.

Non-interacting substituents were indeed found to follow this relationship as described later. More complex formulas were necessary[3] for substituents of low symmetry. Similar relationships were found to describe the intensity of the ν_{13a} vibration of *p*-disubstituted benzenes[87] and the ν_{16} vibrations of *o*- and *m*-disubstituted benzenes[94], substituted pyridines[95], and substituted durenes[2]. These relationships allow one to study the steric and electronic effects on the π-electron distribution in the aromatic ring brought about by a second or further substituent.

6. Monosubstituted Benzenes

Table 1 lists the $\sigma_R{}^0$ values for some 140 monosubstituted benzenes calculated from the intensities of their ν_{16} vibrations using eq. (1). The intensities of the vibrations are almost independent of solvent[1,2] unless specific interaction such as hydrogen bonding occurs. Thus, while the intensity of the ν_{16} bands of anisole is almost identical in carbon tetrachloride and isopropanol, the value for phenol increases quite markedly in the latter solvent. We are currently using this technique to investigate[96] various aspects of hydrogen bonding and complex formation.

In equation (1) the constant term (100 units, l/mole^{-1} cm^{-1}) allows for the f plus g combination[97] of the C–H in-phase wagging modes which occur in the vicinity of 1600 cm^{-1}. This is probably of variable intensity and we estimate a resulting error of ±50 units. Values of $\sigma_R{}^0$ below 0.1 units are therefore better determined from the intensities of polysubstituted benzenes and, in particular, from those found for *m*-disubstituted benzenes where the two substituents are not likely to interact, or from the intensities of olefins.

The measurement of the ν_{16} intensities gives a measure of the π-electron disturbance but does not determine whether this is towards or away from the substituent. This is obvious for many substituents from other work such as NMR spectroscopy but the ν_{13} inten-

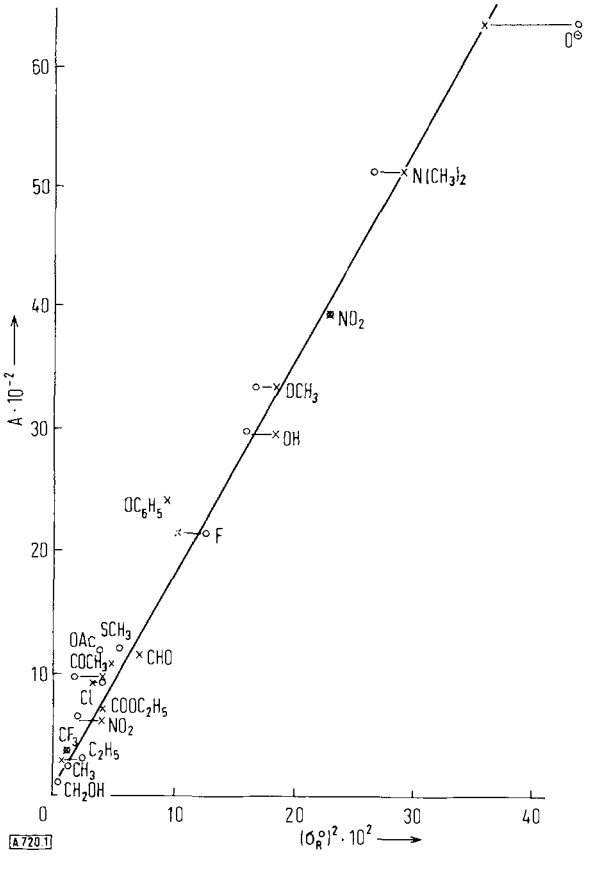


Fig. 1. Correlation of *A* (1 mole^{-1} cm^{-2}) with $(\sigma_R{}^0)^2$ according to eq.(1). o: values from reactivity measurements; ×: values from ^{19}F-NMR spectra.

[94] *A. R. Katritzky, M. V. Sinnot, T. T. Tidwell,* and *R. D. Topsom,* J. Amer. chem. Soc. *91,* 628 (1969).

[95] *A. R. Katritzky, C. R. Palmer, C. R. Swinbourne, T. T. Tidwell,* and *R. D. Topsom,* J. Amer. chem. Soc. *91,* 636 (1969).

[96] *A. R. Katritzky, S. Ohlenrott, B. Ternai,* and *R. D. Topsom,* unpublished results.

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Table 1. Calculated σ_R^0 values.

Compound	Infrared Solvent	$\pm \sigma_R^0$, calcd.	Compound	Infrared Solvent	$\pm \sigma_R^0$, calcd.	Compound	Infrared Solvent	$\pm \sigma_R^0$, calcd.
PhH	CCl_4	0.00	Ph_3N	CCl_4	−0.44	$PhCH_2OH$	CCl_4	0.00
PhD	CCl_4	0.00	$PhN(CF_3)_2$	CCl_4	0.13	$PhCH_2OMe$	CCl_4	0.05
PhF	CCl_4	−0.34	$PhNHNH_2$	C_6H_{12}	−0.49	$PhCHBr_2$	CCl_4	0.00
PhCl	CCl_4	−0.22	$Ph_2(NH)_2$	CCl_4	−0.44	$PhCH_2Cl$	CCl_4	0.00
PhBr	CCl_4	−0.23	PhNHOH	$CHCl_3$	−0.22	Ph_3CH	CCl_4	−0.11
PhI	CCl_4	−0.22	PhNMeCOMe	$CHCl_3$	−0.41	$PhCH(OCH_3)_2$	CCl_4	0.00
$PhICl_2$	$CHCl_3$	0.12	PhNHCOMe	$CHCl_3$	−0.41	$PhCH_2Br$	CCl_4	0.00
Ph_2I^+	DMSO	+0.28	PhNO	CCl_4	0.07	$PhCHCl_2$	CCl_4	0.00
PhOH	CCl_4	−0.40	Ph_2N_2	CCl_4	0.06	Ph_4C	C_6H_6	−0.13
PhOMe	CCl_4	−0.43	PhNCO	CCl_4	−0.40	$PhCH_2ND_3^+Cl^-$	D_2O	0.00
PhOEt	CCl_4	−0.44	PhNCS	CCl_4	−0.35	$PhCCl_3$	CCl_4	0.00
PhOPr^n	CCl_4	−0.43	PhNSO	CCl_4	0.09	$PhCBr_3$	CCl_4	0.00
Ph_2O	CCl_4	−0.36	PhNCNPh	CCl_4	−0.46	$PhCF_3$	CCl_4	+0.11
PhOCOMe	CCl_4	−0.24	$PhNO_2$	CCl_4	+0.17	PhC_2F_5	CCl_4	+0.08
$PhOCOCF_3$	CCl_4	−0.23	$PhN_2^+BF_4$	D_2O	+0.30	Ph_2	CCl_4	−0.10
$PhOSO_2Me$	CCl_4	−0.26	$PhND_3^+Cl^-$	D_2O	−0.18	$PhCHCH_2$	CCl_4	0.05
$PhOCF_3$	CCl_4	−0.25	$PhND_2Me^+Cl^-$	D_2O	−0.15	PhCHCHCOOEt	CCl_4	0.10
PhOH	D_2O	−0.42	$PhNDMe_2^+Cl^-$	D_2O	−0.14	$PhCHCHNO_2$	CCl_4	0.13
PhO^-Na^+	D_2O	−0.59	$PhNMe_3^+Cl^-$	D_2O	−0.15	$PhCHCHN(CH_2)_5$	C_6H_{12}	−0.31
PhSH	CCl_4	−0.20	$PhNDCMeNDPh^+Cl^-$	D_2O	−0.59	PhCHO	CCl_4	+0.24
PhSMe	CCl_4	−0.25	$PhPCl_2$	$CHCl_3$	0.06	PhCOMe	CCl_4	+0.22
PhSEt	CCl_4	−0.19	$PhPMe_2$	C_6H_{12}	0.08	Ph_2CO	CCl_4	+0.19
Ph_2S	CCl_4	−0.19	Ph_3P	CCl_4	0.06	PhCOOH	CCl_4	+0.29
PhSCOMe	CCl_4	0.08	$PhPMe_3^+Cl^-$	D_2O	0.08	PhCOOMe	CCl_4	+0.16
$PhSCF_3$	CCl_4	0.00	$Ph_4P^+Br^-$	$CHCl_3$	0.08	PhCOOEt	CCl_4	+0.18
PhS^-Na^+	D_2O	−0.33	$PhP(O)(OH)SiMe_3$	$CHCl_3$	0.09	PhCOCl	CCl_4	+0.21
$PhSO_3^-Na^+$	D_2O	0.00	$PhPO(OH)_2$	D_2O	0.08	Ph_2C_2	CCl_4	0.15
Ph_2SO_2	$CHCl_3$	0.06	$PhP(O)(OH)GeMe_3$	$CHCl_3$	0.08	PhCCH	CCl_4	0.07
$PhSO_2Me$	$CHCl_3$	+0.07	Ph_5P	$CHCl_3$	0.03	PhCN	CCl_4	+0.09
$PhSO_3Me$	CCl_4	+0.09	Ph_3As	$CHCl_3$	0.07	$PhCF(CF_3)_2$	CCl_4	0.02
$PhSO_2Cl$	CCl_4	+0.11	Ph_5As	$CHCl_3$	0.04	$PhC(OH)(CF_3)_2$	CCl_4	0.11
$PhSO_2^-Na^+$	D_2O	0.00	Ph_3Sb	$CHCl_3$	0.07	$PhC(OMe)_3$	CCl_4	0.00
Ph_2SO	CCl_4	0.07	Ph_5Sb	$CHCl_3$	0.06	$PhSiMe_3$	CCl_4	0.00
$PhSF_5$	CCl_4	0.00	Ph_3Bi	$CHCl_3$	0.10	Ph_4Si	$CHCl_3$	0.00
Ph_2Se	$CHCl_3$	−0.19	PhMe	CCl_4	−0.10	$PhGeMe_3$	CCl_4	−0.10
$PhND_2$	CCl_4	−0.47	PhEt	CCl_4	−0.10	Ph_4Ge	$CHCl_3$	0.00
PhNHMe	CCl_4	−0.52	PhPr^n	CCl_4	−0.11	Ph_4Sn	$CHCl_3$	0.00
PhNDMe	CCl_4	−0.52	PhPr^i	CCl_4	−0.12	Ph_4Pb	$CHCl_3$	0.00
$PhNMe_2$	CCl_4	−0.53	PhBu^s	CCl_4	−0.12	$PhBCl_2$	CCl_4	+0.30
PhNHEt	CCl_4	−0.52	PhBu^t	CCl_4	−0.13	$PhB(OH)_2$	DMSO	+0.23
PhNHBu^n	CCl_4	−0.54	$PhCH(CH_2)_2$	CCl_4	−0.18	$Ph_3B^-Na^+$	DMSO	−0.13
PhNHPr^i	CCl_4	−0.53	$PhCH(CH_2)_3$	CCl_4	−0.12	Ph_3B	ether	+0.22
$PhNEt_2$	CCl_4	−0.57	$PhCH(CH_2)_4$	CCl_4	−0.14	Ph_3Al	ether	0.11
$PhN(CH_2)_2$	CCl_4	−0.38	$PhCH(CH_2)_5$	CCl_4	−0.13	Ph_2Zn	ether	0.11
$PhN(CH_2)_3$	CCl_4	−0.55	$PhCH_2CHO$	CCl_4	0.11	Ph_2Cd	ether	0.10
$PhN(CH_2)_4$	CCl_4	−0.63	$PhCH_2CN$	CCl_4	0.09	Ph_2Hg	$CHCl_3$	0.03
$PhN(CH_2)_5$	CCl_4	−0.47	Ph_2CH_2	CCl_4	0.12	PhLi	ether	0.14
Ph_2NH	CCl_4	−0.50						

sities are also useful in this respect. This band is allowed in benzene itself and the intensity is found [87] to be increased by electron-donating substituents and reduced by electron-withdrawing ones. There may be some confusion with substituents showing only weak effects but results from polysubstituted compounds usually allow a definite decision to be made. The direction of the π-electron disturbance is shown in the Table where this is well established; electron donating substituents have negative σ_R^0 values. Signs for substituents having little effect, for example derivatives of Group IV and V elements [98], were generally assigned using *meta* derivatives.

The results obtained generally show very good agreement with σ_R^0 values obtained by NMR or reactivity methods where these values are available (Fig. 1). The results for individual substituents have been fully discussed elsewhere [2] and we limit ourselves in this review to just a few examples.

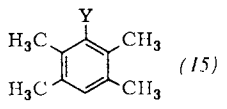
We earlier concluded [2] that σ_R^0 values derived from infrared intensities are indeed a measure of mesomeric interaction and recent theoretical calculations [54,99] support this view.

7. Steric Effects. Results of Studies on Durenes

The concept of the reduction of mesomeric interaction between ring and substituent by twisting is fundamental to present theories on conjugation. For example, from the ^{19}F-NMR spectrum of 4-fluoro-*N*,*N*,2-trimethylaniline, *Taft et al.* [63] found the value $\sigma_R^0 = -0.24$ for the twisted $N(CH_3)_2$ group, a reduction of 56 % by the steric effects of one *o*-methyl group. We utilized substituted durenes *(15)* to test the effect of steric hindrance on infrared intensities. The IR spectrum of durene [*(15)*, Y = H] shows no band near 1600 cm^{-1}; the ν_{16} mode is forbidden because of the

[98] *J. M. Angelleli, R. T. C. Brownlee, A. R. Katritzky, R. D. Topsom*, and *L. Yakhontov*, J. Amer. chem. Soc. *91*, 4500 (1969).

[99] *A. K. Chandra*, Molecular Physics *14*, 577 (1968).



(15)

D_{2h} symmetry of the molecule. Although a normal coordinate analysis has apparently not been carried out for durene, the form of the modes for 1,2,4,5-tetrachlorobenzene[85] suggests that the ν_{16a} mode will not be very different from that in benzene. Steric hindrance in durenes has been the subject of considerable work, and a decrease in conjugation of substituents compared with that in phenyl derivatives has been demonstrated by UV spectra[100], dipole moments[101], NMR shielding[102], and chemical reactivity[103].

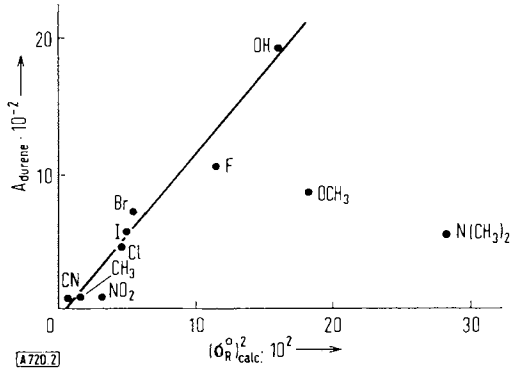


Fig. 2. Correlation of A_{durene} (1 mole^{-1} cm^{-2}) with $(\sigma_R^0)^2$ according to eq. (5).

In Figure 2 the A values for the durenes are plotted against $(\sigma_R^0)^2$ for the corresponding substituent. Substituents with cylindrical symmetry (CN, CH_3, halogens, and possibly OH) show a linear relation found by the least-squares procedure to be as in eq. (5); the small non-zero intercept is probably not significant. The lower overall values for the durenes for the symmetrical substituents may be a result of a decreased contribution of CH wagging mode to the ν_{16} for durene as compared with benzene[86].

$$A_{durene} = 11300\ (\sigma_R^0)^2 - 30 \qquad (5)$$

Equation (5) indicates that in the durene system, the substituents of low symmetry, $N(CH_3)_2$, OCH_3, NO_2, exhibit effective σ_R^0 values of 0.23, 0.28, and 0.10 respectively. This suggests steric inhibition of respectively 58, 35, and 41 % of the resonance interaction. If the angle of twist is related to the resonance interaction by an equation of the type

$$\sigma_R t = \sigma_R^0 \cos \Phi$$

where σ_R^t indicates the value for the twisted substituent, then this corresponds to angles of twisting as follows: $N(CH_3)_2$, 65 °; OCH_3, 49 °; NO_2, 54 °. (Such treatment assumes implicitly that π-inductive effects are completely absent; see below.) These results agree[2] fairly well with those reported in the literature. Other work[38,104] also suggests that the OH group in hydroxydurene is still substantially coplanar with the ring.

[100] *B. M. Wepster*, Recueil Trav. chim. Pays-Bas *76*, 355 (1957).

[101] *H. Kofod, L. E. Sutton, P. E. Verkade*, and *B. M. Wepster*, Recueil Trav. chim. Pays-Bas *78*, 790 (1959); *R. H. Birtles* and *G. C. Hampson*, J. chem. Soc. (London) *1937*, 10.

[102] *P. Diehl* and *G. Svegliado*, Helv. chim. Acta *46*, 461 (1963).

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8. *p*-Disubstituted Benzenes

Equation (4) gives the expected intensity of IR bands in *p*-disubstituted benzenes with non-interacting substituents, where c is the contribution from overtone and combination bands. *p*-Disubstituted benzenes show overtone bands near 1900 cm^{-1} and near 1630 cm^{-1}. The species of these bands[97] are A_1 for compounds of C_{2v} symmetry and B_{3u} for symmetrically substituted (V_h) compounds. Hence for compounds of C_{2v} symmetry, mixing is to be expected between the 1630 cm^{-1} band and the bands under discussion.

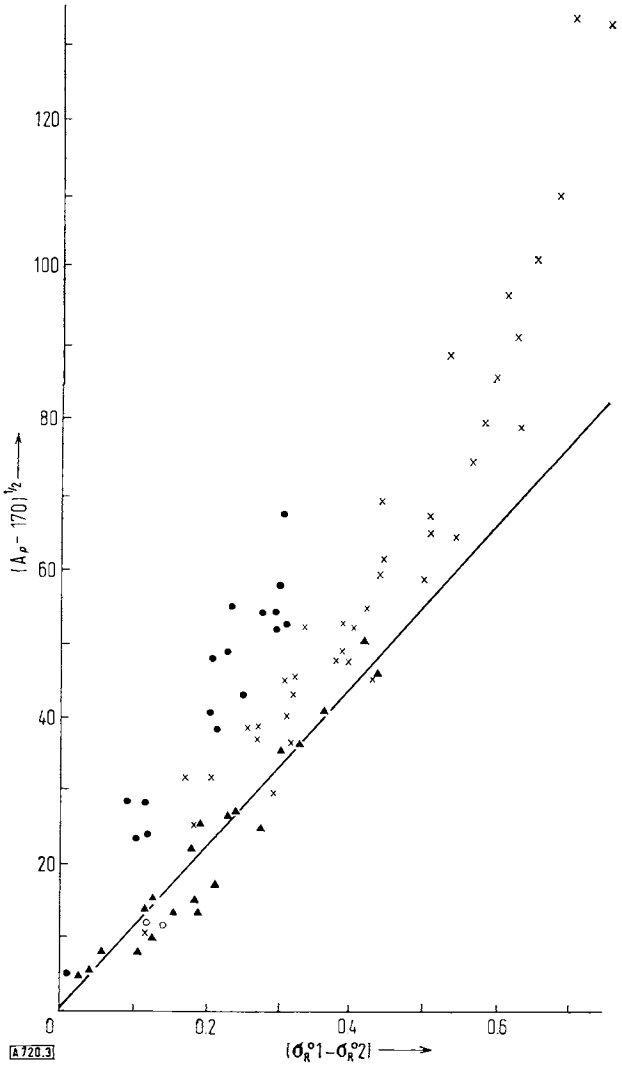


Fig. 3. Plot of equation (6) with correction for asymmetry effect; ●, strong donor paired with d-orbital acceptor; ▲, other donor-donor compounds; ×, donor-acceptor compounds. The line shown is that found by a least-squares plot of the points of type ▲.

[104] *C. E. Ingham* and *G. C. Hampson*, J. chem. Soc. (London) *1939*, 981; *N. A. Puttnam*, *ibid. 1960*, 5100.

Measurement of the 1630 cm^{-1} band intensity is possible [3] for symmetrically *p*-disubstituted compounds, since the ν_{16} vibration is forbidden here, and also approximately for some of the less symmetrical compounds. The average value found is 170 units and this value was therefore taken for *c*. A plot of $(A_p - 170)^{1/2}$ against $\sigma_R{}^01 - \sigma_R{}^02$ is shown in Figure 3. This plot omits nitrobenzenes substituted with another electron-withdrawing group in the *p*-position since these compounds give [3] very anomalous results. This may be caused by the relatively low ionization potential of the nitro group leading to a reversal of its normal π-electron-withdrawing properties and a series of benzenes with *p*-nitroso- and *p*-azo substituents is currently being investigated [105] since these substituents have even lower ionization potentials.

Figure 3 shows that most compounds with donor-donor and acceptor-acceptor substituents follow our expectation and the line is drawn to fit these by a least-square plot leading to the equation

$$A_p = 11\,800\,(\sigma_R{}^01 - \sigma_R{}^02) + 170 \qquad (6)$$

It was necessary to use a somewhat more complex formula [3] where the compounds contained asymmetric substituents since $\sigma_R{}^0$ is a vector quantity. The points in Figure 3 are corrected for this.

The two classes of compounds that do not fit this line are those with donor-acceptor substituents and those where a strong donor, $\sigma_R{}^0 < -0.3$ (*e.g.* $N(CH_3)_2$, OCH_3, F), is paired with a substituent possessing a vacant d-orbital next to the ring (*e.g.* Cl, Br, I, SMe).

The positive discrepancies observed for the compounds containing donor-acceptor substituents can be ascribed [3] to resonance interaction between the substituents leading to some contribution of the *p*-quinonoid form *(12)*. All these points can be fitted to the line if a correction term is introduced in eq. (6) leading to eq. (7).

$$A_{p-A/D} = 11\,800\,[\sigma_R{}^0D - \sigma_R{}^0A + K_A\,(\sigma^+D - \sigma D)] + 170 \qquad (7)$$

The power of the donor to increase its interaction here is well represented by $(\sigma^+ - \sigma)$ but empirically found factors for the acceptor (K_A) are roughly proportional to $\sigma_R{}^0$ not $(\sigma^- - \sigma)$. The important thing to note, however, is that one value of K_A fits an acceptor substituent for interaction with any donor in the *para* position. The results for *p*-disubstituted benzenes containing donor-acceptor substituents plotted according to eq. (7) are shown in Figure 4. Values of K_A for important substituents are 0.36 (CO_2CH_3 and $CO_2C_2H_5$), 0.57 (CHO), 0.45 ($COCH_3$), 0.55 (NO_2), and 0.29 (CN).

The results above do suggest some additional interaction in fluorobenzenes containing an electron-accepting substituent and thus the ^{19}F–NMR results will not give accurate $\sigma_R{}^0$ values for these substituents.

[105] *A. R. Katritzky, S. Ohlenrott,* and *R. D. Topsom,* unpublished results.

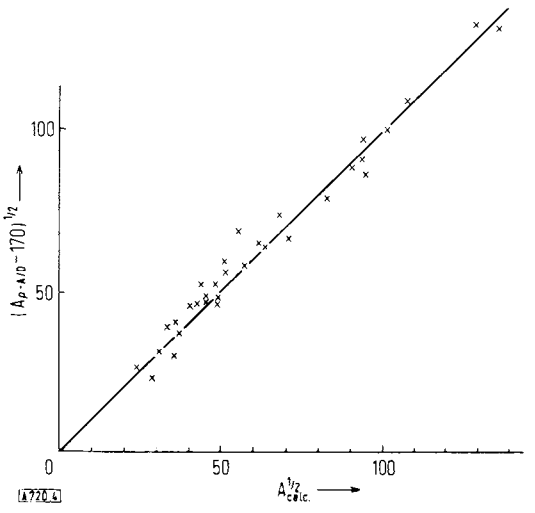


Fig. 4. Comparison of calculated and observed *A* values for donor-acceptor compounds [cf. eq. (7)]. The line shown has unit slope.

However, the $\sigma^+ - \sigma$ value for F is small (– 0.11) and such resonance interaction would not be expected to increase the observed $\sigma_R{}^0$ value by more than 0.03 unit.

9. d-Orbital Interactions

The halogens normally behave as resonance donor groups with negative $\sigma_R{}^0$ values. However, for compounds where Cl, Br, or I (but not F) is placed *para* to a strong donor substituent, the observed intensity is significantly greater than expected from eq. (6). Similar results are found for other substituents which have vacant d-orbitals on the atom next to the ring and we have therefore suggested [3,98] that this arises from direct resonance interaction between the *para* substituents.

The effect is greater in the series I > Br > Cl for the halogens d-orbital acceptors and $N(CH_3)_2 > NHCH_3 > ND_2 > OCH_3 > F$ for the donor group. The discrepancies are fitted [3] by introducing a correction term in eq. (6) leading to eq. (8)

$$A_{p\,X-D} = 11\,800\,(\sigma_R{}^0D - \sigma_R{}^0X + K_X\,\sigma_R{}^0D)^2 + 170 \qquad (8)$$

where X refers to the d-orbital acceptor. Some values [3,98] of K_X are listed in Table 2.

Table 2. Values of K_X for d-orbital acceptors.

Substituent	K_X	Substituent	K_X
Cl	0.32	$SiMe_3$	0.48
Br	0.42	$GeMe_3$	0.50
I	0.55	$SnMe_3$	0.65
SMe	0.44		
SMe_2^+	0.67		

A plot of observed *A* values against those calculated by eq. (8) is shown for some halobenzenes containing *p*-electron-donating substituents in Figure 5. It is evident that the one K_X value per substituent fits all cases. It should be noted that eq. (8) is of different

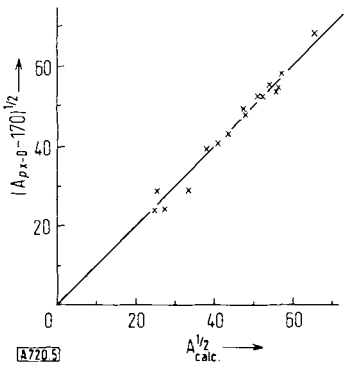


Fig. 5. Comparison of calculated and observed A values for strong donor-d-orbital acceptor compounds [cf. eq. (8)]. The line shown has unit slope.

form from eq. (7) for normal donor-acceptor compounds.

We have discussed elsewhere[3,98] the considerable previous evidence for the participation of d orbitals in π bonding. The IR results, which include the charged $[S(CH_3)_2]^+$ substituent, cannot be reasonably explained on alternative theories such as the polarizability of the bond connecting the d-orbital substituent to the ring. Additional evidence comes from our results[87] on the 1500 cm^{-1} band since the form of this vibration for *p*-substituted benzenes allows one to determine that *both* of the substituents are showing an increased resonance interaction with the ring in these compounds.

Interaction of this type between fluorine (as donor) and d-orbital acceptors would be expected to effect the σ_R^0 values obtained for such substituents by the ^{19}F–NMR methods. The direct exaltation is $K_X \sigma_R^0(F)$ and we can correct σ_R^0 values if we assume that half of the change is due to the fluorine atom behaving as a stronger donor and half is due to the d-orbital interaction. Thus the reported σ_R^0 value for iodine determined by the ^{19}F–NMR method is 0.17 but the addition of 0.08 units $[1/2 K_X \sigma_R^0(F)]$ gives a value of 0.25 in agreement with our work on mono-substituted benzenes (Table 1).

10. The π-Inductive Effects of Charged Substituents

The results for eight *p*-substituted compounds containing the groups $[N(CH_3)_3]^+$ or $[ND_3]^+$ show[3] clearly that these groups are resonance donors with σ_R^0 values of −0.15 and −0.18 respectively. The $[S(CH_3)_2]^+$ substituent[98] is also apparently a weak donor (−0.09) while the $[P(C_6H_5)_3]^+$ substituent[98] has only a small resonance effect of indeterminate sign. These disturbances of the π system away from the charged substituent are in accord with other evidence: pK_a measurements indicate[106] σ_R of −0.11 for $[N(CH_3)_3]^+$; ^{19}F–NMR data[107] from *p*-fluorotrimethylanilinium chloride indicate a σ_R^0 of −0.08 for $[N(CH_3)_3]^+$; pK values of substituted phenols[108] and the equation $\sigma_R = 1.5\,(\sigma_p - \sigma_m)$ give $\sigma_R = -0.12$ for $[N(CH_3)_3]^+$ (but +0.25 for $[S(CH_3)_2]^+$). The effect of $[N(CH_3)_3]^+$ groups on benzenoid chemical shifts has been shown[109] to indicate a somewhat higher electron density at the *para*, rather than the *meta* position to $[N(CH_3)_3]^+$, but this was ascribed to the weakening of the inductive effect with distance. Resonance interactions between the ring and substituents were not considered.

The reactivity of charged substituents has attracted much recent attention[110–112,143] since kinetic and product studies have shown that a considerable amount of *para* substitution occurs with electrophilic reagents. The oxonium group has been reported[113] to be 100 % *para* directing. Some, at least, of these authors[111,143] have recognized that the substituent may increase the electron density at the *para* position by interaction of the filled p orbitals of the substituent with the ring. Our work affords strong evidence for this and may have an effect on theoretical calculations[25,114,144] which have considered effects on the π system of ammonium or trimethylammonium substituents as arising mainly from π-inductive effects acting in the opposite direction.

The idea that a substituent may have any substantial I_π effect, that is disturb the π-electron system of an aromatic ring either as a secondary result of changing the σ charge distribution on the aromatic carbon to which it is attached or by a through-space field effect, is made untenable by these results since it would act in the opposite direction to that observed. Other strong evidence comes from the absence of any significant effect on the π system shown by substituents such as $[CH_2NR_3]^+$[115], $C(CN)_3$[16,116], and CCl_3[2,116], which all presumably have strong primary inductive effects, and the marked reduction in σ_R^0 value of unsymmetrical substituents when these are twisted[2,117] out of the aromatic plane. The CF_3 substituent remains somewhat of an anomaly[2,118,119].

[106] *W. A. Sheppard*, unpublished results quoted in ref. [3].

[107] *R. W. Taft jr.*, unpublished results quoted in ref. [3].

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Our results do not allow detailed conclusions to be drawn about the extent of repulsive interaction between filled orbitals on the substituent and the π system of the ring. The occurrence of this for $[N(CH_3)_3]^+$ suggests that similar effects do exist for CR_3 and presumably also in substituents such as NR_2 which contain lone pairs. However we feel that most of the π disturbance in NR_2 is caused by conjugative electron donation. It was noted earlier that repulsive interactions are included in the "I_π effect" by some authors. Even though we consider I_π effects induced by polarity of substituent bonds to be negligible, this repulsive interaction is in the opposite direction and we strongly suggest that it should be made clear which effect is referred to in each instance. There has been some suggestion[119] that repulsive interactions directly affect positions other than the one to which the substituent is connected in certain cases and further work on model compounds in which various atoms of a substituent are held close to the *ortho* and *meta* positions is highly desirable.

11. Conclusions

To summarize, our own and recent other work leads us to conclude that in non-crowded systems there are only three important effects of a substituent on a benzene ring.

1. Conjugative or mesomeric interactions. This effect is felt mainly at the *ortho* and *para* positions and results in transfer of electron density from ring to substituent or *vice versa*.

2. Repulsion of the π electrons of the ring by p electrons of the substituent. This is felt mainly at the *ortho* and *para* positions but the nett result is a redistribution of the existing π density of the ring.

3. A direct field effect of the substituent potential on a reaction or measurement site elsewhere in the ring. This factor will only be obvious if the method of measurement is susceptible to a field effect. A recent example of this[17,145,146] is found in the observation that unless highly polar solvents are used alicyclic fluorides do not show ^{19}F–NMR shifts caused by field effects from remote substituents while aryl fluorides do. This apparently occurs because in the latter case the unshared p electrons on the fluorine atom can be induced by the field effect to conjugate further with the π system of the aromatic ring; this is not possible with the alicyclic compounds.

In addition there is probably a small σ-inductive effect but this will diminish rapidly, albeit alternatively, with the length of the carbon chain.

In disubstituted benzenes, there is the additional possibility of interaction between the substituents which will mainly be shown in the form of conjugative effects which require them to be placed *ortho* or *para* to one another.

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Organogold Chemistry

By Brunhilde Armer[*] and Hubert Schmidbaur[**]

Organogold compounds having at least one Au–C σ or π bond and gold-carborane complexes have recently received rapidly increasing attention, from the point of view of valence theory and structure as well as on practical grounds. Interesting possibilities are offered particularly in connection with the use of gold and its derivatives as heterogeneous or homogeneous catalysts for organic reactions, and new problems also arise.

1. Introduction

In the chemistry of the noble metals[1], the organo derivatives of these elements have been growing in importance for a number of years. This growth has reached a very advanced stage *e.g.* in the cases of iridium and platinum[2,3]. Increasing interest has recently also been shown in organogold compounds, largely because of their potential applications. Well-known examples are the catalytic activity of metallic gold in many syntheses and the use of thermally unstable organogold compounds for the production of very pure, firmly adhering gold coatings on suitable support materials.

In the 30 or so years that have elapsed since the publication of the classical work by *Krause* and *v. Grosse*[4], which covers the literature on organometallic chemistry up to 1936, no further comprehensive reviews of this field have appeared. Even in more recent monographs it has been either omitted altogether[2] or discussed only briefly[3]. In the present article we present a critical review of articles on organogold compounds published up to 1969. In accordance with a generally accepted definition[2], we shall consider only compounds that contain at least one gold-carbon bond, excluding simple and complex gold cyanides.

2. Organogold Compounds Containing Gold-Carbon σ Bonds

2.1. Trialkylgold(III) Compounds and their Derivatives

Though the first efforts to prepare organogold compounds were made[5,6] more than 100 years ago, *i.e.* in the very early stages of organometallic chemistry, it was only at the beginning of the present century that their existence was conclusively demonstrated[7]. Even then, however, it was not yet possible to isolate the parent compounds. This achievement was reserved for the experiments of *Gilman*[8,9] and *Coates*[10] in the 1940's and 1960's respectively. The first information about the functional compounds of the types R_2AuX and $RAuX_2$, which had been obtainable even earlier, nearly all came from the laboratory of *Gibson*, who practically single-handed laid the foundations for later and more extensive investigations (see Sections 2.2 and 2.3).

2.1.1. Trimethylgold

Trimethylgold[8,9] is formed on reaction of a suspension of gold tribromide or dimethylgold bromide in ether with methyllithium at −65 °C:

$$[AuBr_3]_2 + 6\,LiCH_3 \xrightarrow{(C_2H_5)_2O} 2\,(CH_3)_3Au \cdot O(C_2H_5)_2 + 6\,LiBr$$

$$[(CH_3)_2AuBr]_2 + 2\,LiCH_3 \xrightarrow{(C_2H_5)_2O} 2\,(CH_3)_3Au \cdot O(C_2H_5)_2 + 2\,LiBr$$

The ether solutions, which contain the reaction product as the ether adduct, show signs of decomposition even at −40 to −35 °C, with formation of a gold mirror and a mixture of methane and ethane. $(CH_3)_3Au$ cannot be freed from solvent even at low temperatures, and its physical properties are accordingly still unknown.

An interesting parallel is found in the cases of platinum and iridium, where the pure alkylmetal compounds have similarly defied isolation so far[11]. $(CH_3)_4Pt$ and $(CH_3)_3Ir$ appear to be capable of existing only as components of complexes. The same is true of $(CH_3)_3Au$.

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87 Würzburg, Röntgenring 11 (Germany)

[1] *W. P. Griffith*: The Chemistry of the Rarer Platinum Metals. Interscience, London 1967.

[2] *M. Dub*: Organometallic Compounds. 2nd Edit., Springer, New York 1966, Vol. 1.

[3] a) *M. L. H. Green* in *G. E. Coates, M. L. H. Green*, and *K. Wade*: Organometallic Compounds. Methuen, London 1968, Vol. 2, p. 28, 208, 255–257, 274, 277–280; b) *G. E. Coates* and *F. Glockling* in *H. H. Zeiss*: Organometallic Chemistry. Reinhold, New York 1960, p. 426.

[4] *E. Krause* and *A. v. Grosse*: Die Chemie der metall-organischen Verbindungen. Bornträger, Berlin 1937.

[5] Cf. *R. Jones*, Chem. Reviews *68*, 785 (1968).

[6] *E. Frankland* and *D. F. Duppa*, Liebigs Ann. Chem. *130*, 125 (1864); J. chem. Soc. (London) *17*, 21 (1864).

[7] *W. J. Pope* and *C. S. Gibson*, J. chem. Soc. (London) *91*, 2061 (1907).

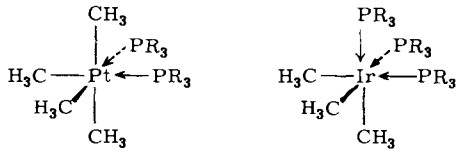
[8] *L. A. Woods* and *H. Gilman*, Proc. Iowa Acad. Sci. *49*, 286 (1943); Chem. Abstr. *37*, 5696 (1943).

[9] *H. Gilman* and *L. A. Woods*, J. Amer. chem. Soc. *70*, 550 (1948).

[10] *G. E. Coates* and *C. Parkin*, J. chem. Soc. (London) *1963*, 421.

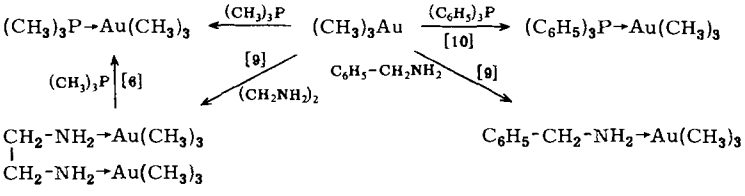
[10a] *B. J. Gregory* and *C. K. Ingold*, J. chem. Soc. (London) *A 1969*, 276.

[11] a) *J. D. Ruddick* and *B. L. Shaw*, Chem. Commun. *1967*, 2025; b) *J. Chatt* and *B. L. Shaw*, J. chem. Soc. (London) *A 1966*, 1836; c) *B. L. Shaw* and *A. C. Smithies*, *ibid. A 1967*, 1047.



2.1.2. Complexes of Trimethylgold with n-Donors

The influence of the coordinately bound ether is evidently not sufficient to stabilize $(CH_3)_3Au$ under normal conditions; trimethylgold can however be stabilized with nitrogen donors and above all with phosphorus donors, and the resulting coordination



compounds can be handled without difficulty at or above room temperature [9,10].

These adducts can all be prepared by reaction of the ether solution of trimethylgold with the bases [9,10]. Trimethylgold-trimethylphosphine can also be obtained from the ethylenediamine adduct by a displacement reaction. Trimethylgold-diethyl ether does not however react with aniline, dimethylaniline, *p*-phenylenediamine, piperidine, ethylamine, dimethylamine, or glycosine. The IR bands of the phosphine complexes of $(CH_3)_3Au$ have been substantially assigned, and the dipole moments of the compounds have also been determined [10]. Characteristic temperatures for trimethylgold adducts are given in Table 1.

Table 1. Trimethylgold addition compounds.

	M.p. (°C)	Dec. (°C)	Ref.
$(CH_3)_3Au \cdot O(C_2H_5)_2$	–	−40 to −35	[8, 9]
$(CH_3)_3Au \cdot NH_2CH_2CH_2NH_2 \cdot Au(CH_3)_3$	–	94–98	[9]
$(CH_3)_3Au \cdot$ 2-Aminopyridine	–	–	[9]
$(CH_3)_3Au \cdot NH_2CH_2{-}C_6H_5$	51.5–53	–	[9]
$(CH_3)_3Au \cdot P(C_6H_5)_3$	120 (dec.)	–	[10]
	119	–	[10a]
$(CH_3)_3Au \cdot P(CH_3)_3$	23 (Subl.-pt. 25/0.004 torr)	–	[10]

These compounds are very probably approximately square-planar complexes of Au^{III} (dsp^2); however, this assumption has not yet been experimentally checked.

The thermal decomposition of trimethyl(triphenylphosphine)gold(III) proceeds in steps [10]:

$$(C_6H_5)_3P{\rightarrow}Au(CH_3)_3 \xrightarrow{\Delta} C_2H_6 + (C_6H_5)_3P{\rightarrow}AuCH_3$$
$$\xrightarrow{\Delta} {}^1/_2\,C_2H_6 + (C_6H_5)_3P + Au$$

This decomposition leads only to ethane (no methane).

2.1.3. Reactions of Trimethylgold with Acids

Reaction of trimethylgold with acids HX leads to cleavage of a gold-carbon bond and formation of methane:

$$(CH_3)_3Au + HX \rightarrow (CH_3)_2AuX + CH_4$$
$$X = Cl, SC_6H_5, SCH_2COOH$$

In the presence of bromide, cleavage with hydrogen chloride yields dimethylgold *bromide* instead of dimethylgold chloride. It has surprisingly been found that trimethylgold is stable to phenol and trichloroacetic acid. The course of the commutation reaction

$$2\,(CH_3)_3Au + AuBr_3 \rightarrow 3\,(CH_3)_2AuBr$$

with the Lewis acid $AuBr_3$ [9] is as expected from the behavior of the alkylmetal compounds of aluminum, gallium, indium, or thallium [3].

Very little information is available at present on higher homologs of trimethylgold. The almost complete lack of information about the possible range of existence of tri*aryl*gold compounds is particularly striking. We seem to have here a completely unexplored, and possibly unfriendly, new territory.

2.2. Dialkylgold(III) Halides and Related Compounds

There are numerous known examples of organogold compounds having the general formula R_2AuX, where X may be either a monodentate (*e.g.* halide or cyanide) or a polydentate ligand (*e.g.* 2,4-pentanedionate, 8-quinolinolate, sulfate); Some of the earliest known organogold compounds belong to this group.

2.2.1. Dialkylgold Halides and Pseudohalides

2.2.1.1. Preparation

Dialkylgold halides (see Table 2) are generally formed in the reaction of gold(III) halides [7,12] with alkylmagnesium halides in ether:

$$AuX_3 + 2\,RMgY \rightarrow R_2AuY + MgX_2 + MgXY$$

Tetrabromoauric acid [13] and the pyridine complexes of gold tribromide and trichloride [14,15] can also be used as the gold halide component. $AuCl_3 \cdot py$ and the Grignard reagent from 1,5-dibromopentane and magnesium [16,17] give mainly decamethylenegold bromide and (in small quantities) pentamethylenegold bromide, which can be isolated as ethylenediamine complexes. The action of hydrobromic acid on the complex of the latter compound yields colorless crystals whose analytical data point to a dimer having a composition $(C_5H_{10}AuBr)_2$:



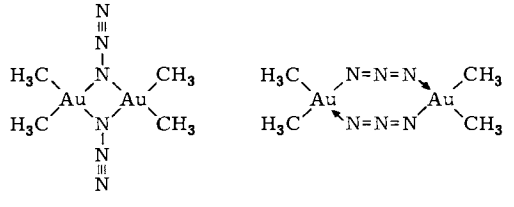
Dialkylgold cyanides can be obtained from the bromides by reaction with silver cyanide [12].

$$R_2AuBr + AgCN \rightarrow R_2AuCN + AgBr$$

Recently the explosive dimethylgold azide has also been prepared and characterized using analytical and spectroscopic methods [12a].

$$[(CH_3)_2Au \cdot en]I + AgN_3 \rightarrow [(CH_3)_2Au \cdot en]N_3 + AgI$$
$$[(CH_3)_2Au \cdot en]N_3 + 2\,HCl \rightarrow {}^1/_2[(CH_3)_2AuN_3]_2 + en \cdot 2\,HCl$$

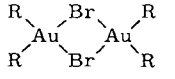
Two possible structures are suggested from the results of molecular weight determinations and from IR- and NMR-spectra (both D_{2h}!):



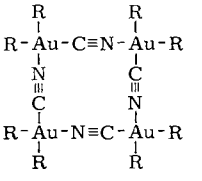
No dialkylgold fluorides have been described as yet. Extensive efforts to prepare dimethylgold fluoride, whose structure is particularly interesting in view of the peculiar situation in gold trifluoride [18], have had little success [19]. This compound has not been isolated in the pure crystalline state, though its existence is beyound doubt, as is adequately demonstrated by IR and NMR spectra. The hope of discovering a molecular structure corresponding on the one hand to that of AuF_3 and on the other to that of the (isosteric) $(CH_3)_2AuOH$ (see Section 2.2.2) has not yet been fulfilled.

2.2.1.2. Properties

The characteristics of the known dialkylgold halides and cyanides are listed in Table 2. All the compounds are sensitive to light. Molecular weight determinations on some of the halides in benzene or $CHBr_3$ [14,15,20] point to a dimeric molecular structure. The small dipole moment of diethylgold bromide (1.37 D) [21,22] and results of its X-ray structural analysis [22] confirm the four-membered ring structure with an approximately square-planar arrangement of the ligands around the gold atoms, as expected for the dialkylgold(III) halides:

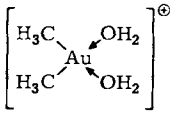


A square-planar arrangement of the ligands has also been found for diethylgold and dipropylgold cyanides. The compounds are tetrameric [23]. Dipropylgold cyanide has a dipole moment of only 1.47 D [22]. X-ray studies [24] have shown that four monomer units combine to form a square having an edge length of 5.18 Å, with twelve atoms on the edges and corners of the square.



Only a few dialkylgold halides have been examined spectroscopically. The ^{1}H-NMR spectra of diethylgold bromide [25] and dimethylgold iodide [25,26] in $CCl_4/CHCl_3$ and of aqueous solutions of dimethylgold nitrate and dimethylgold perchlorate [26] each show only one signal, and so confirm the symmetrical arrangement of the ligands in the oligomers.

The Raman spectra of aqueous solutions of dimethylgold nitrate or dimethylgold perchlorate and of sodium dimethyldihydroxoaurate [26] show that the structural unit $(CH_3)_2Au$ is not linear, but angular. Thus the methyl groups in the solvated dimethylgold ion are in the *cis* position:



[12] *M. S. Kharasch* and *H. S. Isbell*, J. Amer. chem. Soc. *53*, 2701 (1931).

[12a] *W. Beck*, *W. P. Fehlhammer*, *P. Pöllmann*, and *R. S. Tobias*, Inorg. chim. Acta *2*, 467 (1968).

[13] *C. S. Gibson* and *W. M. Colles*, J. chem. Soc. (London) *1931*, 2407.

[14] *A. Buraway* and *C. S. Gibson*, J. chem. Soc. (London) *1934*, 860.

[15] *F. H. Brain* and *C. S. Gibson*, J. chem. Soc. (London) *1939*, 762.

[16] *C. S. Gibson*, Nature *131*, 130 (1933).

[17] *A. Buraway* and *C. S. Gibson*, J. chem. Soc. (London) *1936*, 324.

[18] *F. W. B. Einstein*, *P. R. Rao*, *J. Trotter*, and *N. Bartlett*, J. chem. Soc. (London) *A 1967*, 478.

[19] *M. Bergfeld* and *H. Schmidbaur*, unpublished.

[20] *C. S. Gibson* and *J. L. Simonsen*, J. chem. Soc. (London) *1930*, 2531.

[21] *A. Buraway* and *C. S. Gibson*, J. chem. Soc. (London) *1935*, 219.

[22] *A. Buraway*, *C. S. Gibson*, *G. C. Hampson*, and *H. M. Powell*, J. chem. Soc. (London) *1937*, 1690.

[23] *A. Buraway*, *C. S. Gibson*, and *S. Holt*, J. chem. Soc. (London) *1935*, 1024.

[24] *R. F. Phillips* and *H. M. Powell*, Proc. Roy. Soc. (London), Ser. A *173*, 147 (1939).

[25] *H. Schmidbaur* and *M. Bergfeld*, Inorg. Chem. *5*, 2069 (1966).

[26] *M. G. Miles*, *G. E. Glass*, and *R. S. Tobias*, J. Amer. chem. Soc. *88*, 5738 (1966).

Table 2. Dialkylgold halides and cyanides, R_2AuX.

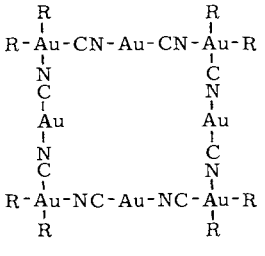
X = / R =	Chloride			Bromide			Iodide			Cyanide		
	M.p.	Dec.	Ref.	M.p.	Dec.	Ref.	M.p.	Dec.	Ref.	M.p.	Dec.	Ref.
	(°C)	(°C)		(°C)	(°C)		(°C)	(°C)		(°C)	(°C)	
Methyl	71–72	–	[9]	68–69	–	[9, 15, 25, 30]	95–96	–	[26–28]	–	–	–
Ethyl	48	48	[12]	58	–	[7, 12, 14, 20–22, 29]	67–68	70–71	[20]	103–105	110–120	[12, 23]
Propyl	liq.	107	[12]	liq.	95	[12, 13, 21, 22]	–	–	–	94–95	105	[12, 23, 24]
Isopropyl	dec.	95	[12]	dec.	100–130	[12]	–	–	–	88–90	121–133	[12]
n-Butyl	–	–	[12]	liq.	65	[12, 13]	–	–	–	dec.	125–130	[12]
Isobutyl	–	–	[12]	liq.	–	[12]	–	–	–	112–113	160	[12]
Isoamyl	–	–	[12]	liq.	–	[12]	–	–	–	70	135–140	[12]
Cyclohexyl	–	180–190	[12]	148	140–148	[12]	–	–	–	152	155	[12]
Benzyl	dec.	70–110	[12]	dec.	77	[12]	–	–	–	dec.	122	[12]
Phenylethyl	–	–	[12]	112–115	105–115	[12]	–	–	–	–	–	–
Neopentyl	–	–	–	121–123	–	[9]	–	–	–	–	–	–

The equilibria of hydrolysis for this cation have been studied in detail [26a].

The IR spectra of dimethylgold bromide and dimethylgold iodide have also been recorded [25–27]. The energy threshold for internal rotation was determined from the dependence of the shape of the antisymmetric CH_3 deformation band in $(CH_3)_2AuI$ on temperature (90 to 298 °K), and was found to be approximately 770 cal/mole [27].

On the basis of UV spectroscopic studies on alkylgold compounds, *Chakravorty* [28] concludes that the alkyl groups produce a stronger ligand field than halide. Diethylgold bromide, unlike the tetrabromoaurate, is colorless. The energy of the $d_{x^2-y^2}$ orbital can therefore be assumed to be higher in the alkylgold compound than in the tetrabromoaurate.

An unknown volatile gold compound is formed when methyl chloride is blown through a molten euctectic gold-silicon alloy (380 °C) [29]; the crystals, which are colorless at −196 °C, decompose above −70 °C with deposition of gold.



≡$[R_2AuCN \cdot AuCN]_4$

Organogold compounds are also postulated as intermediates in the reactions of alkyllead compounds with gold trichloride [30], though they have not yet been isolated.

[26a] *S. J. Harris* and *R. S. Tobias*, Inorg. Chem. *8*, 2259 (1969).

[26b] *G. E. Glass* and *R. S. Tobias*, J. organometallic Chem. *15*, 481 (1968).

[27] *R. C. Leech*, *D. B. Powell*, and *N. Sheppard*, Spectrochim. Acta *21*, 559 (1965) *22*, 1931 (1966).

[28] *A. Chakravorty*, Naturwissenschaften *48*, 643 (1961).

[29] *E. W. Krahé* and *E. G. Rochow*, Inorg. nuclear Chem. Letters *1*, 117 (1965).

[30] *U. Belluco*, *L. Riccoboni*, and *G. Tagliavini*, Ricerca sci. *30*, 1255 (1960) Chem. Abstr. *55*, 7273 (1961) Ric. sci., Parte II, Sez. A *2*, 323 (1962) Chem. Abstr. *58*, 13976 (1963).

2.2.1.3. Thermal Behavior

Dialkylgold halides and cyanides are thermally unstable. Thus dimethylgold bromide decomposes when heated in boiling ether for 48 hours [8, 31], with formation of ethane, metallic gold, traces of methylgold dibromide, and gold tribromide.

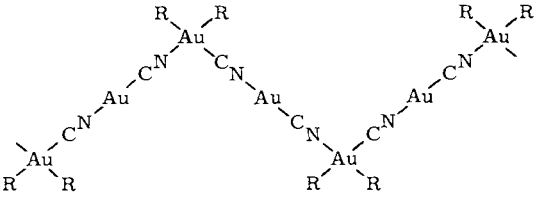
Diethylgold and dipropylgold cyanides decompose in a similar manner [23], the former slowly at room temperature, and the latter only in boiling benzene. The alkyl groups are removed stepwise.

$$[R_2AuCN]_4 \xrightarrow{\Delta} 2\,R_2Au_2(CN)_2 + 2\,R\text{–}R$$

$$2\,R_2Au_2(CN)_2 \xrightarrow{\Delta} 4\,AuCN + 2\,R\text{–}R$$

$$R = C_2H_5 \text{ or } n\text{-}C_3H_7$$

The dialkyldigold dicyanide formulated as an intermediate can be isolated. The following structures are particularly feasible for these compounds, which are insoluble in non-destructive solvents [32].



≡$[R_2AuCN \cdot AuCN]_n$

They correspond to coordination compounds of dialkylgold(III) cyanides and gold(I) cyanide.

2.2.2. Dialkylgold(III) Compounds Containing Gold-Oxygen Bonds

The structurally simplest of the known dialkylgold compounds containing the Au–O bond (see Table 3) is trimethylsiloxodimethylgold, which is formed from

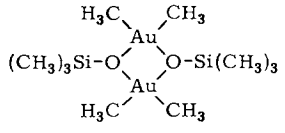
[31] *L. W. Woods*, Iowa State Coll. J. Sci. *19*, 61 (1944); Chem. Abstr. *39*, 693 (1949).

[32] *C. S. Gibson*, Proc. Roy. Soc. (London), Ser. A *173*, 160 (1939); Chem. Abstr. *34*, 1578 (1940).

dimethylgold bromide and sodium trimethylsilanolate [25].

$$[(CH_3)_2AuBr]_2 + 2\ NaOSi(CH_3)_3 \rightarrow [(CH_3)_2Au{-}OSi(CH_3)_3]_2 + 2\ NaBr$$

It can be concluded from the results of molecular weight determinations and from the NMR and IR spectroscopic data that trimethylsiloxodimethylgold exists in the dimeric state as a four-membered ring, and this again allows a square-planar arrangement of the ligands around the gold atoms. This assumption is confirmed by the diamagnetic behavior of the compound. The colorless crystals can be sublimed in a



high vacuum without decomposing. They decompose explosively at 120 °C, with deposition of a gold mirror on the walls of the vessel.

Dimethylgold hydroxide is particularly interesting. It is obtained from dimethylgold iodide and sodium hydroxide [26].

$$2\ [(CH_3)_2AuI]_2 + 4\ NaOH \rightarrow [(CH_3)_2AuOH]_4 + 4\ NaI$$

This compound is not dimeric, but *tetrameric* [33]. The ^{1}H-NMR spectrum shows two signals of equal intensity instead of the expected CH_3 singlet. A three-dimensional X-ray structural analysis [33] showed a puckered eight-membered Au–O ring system. The gold atoms in this ring nevertheless have the expected square arrangement of the ligands. In this structure (Fig. 1), the two methyl groups on each gold atom have structurally different environments, and are therefore magnetically nonequivalent. The isosteric $(CH_3)_2AuF$ should have a similar structure (see Section 2.2.1.1).

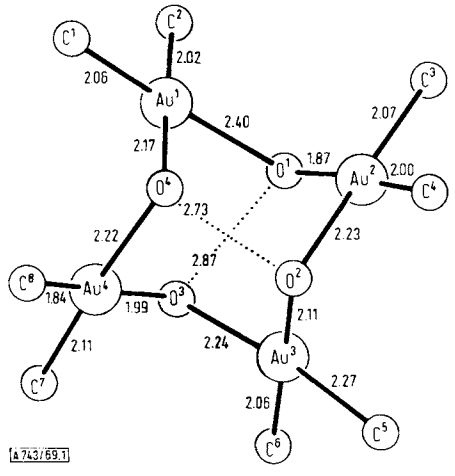


Fig. 1. Structure of cyclo-tetrakis(hydroxodimethylgold). (Bond lengths in Å.)

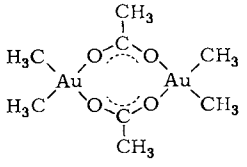
[33] *G. E. Glass, J. H. Konnert, M. G. Miles, D. Britton*, and *R. S. Tobias*, J. Amer. chem. Soc. *90*, 1131 (1968).

Trimethylplatinum hydroxide is also oligomeric; however, this compound forms tetramers having a cubane-like skeleton [34].

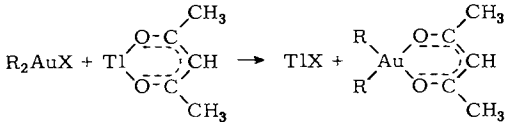
Colorless, crystalline dimethylgold acetate [35], which was only recently prepared from dimethylgold bromide and silver acetate in tetrahydrofuran, is again dimeric according to molecular weight determinations.

$$[(CH_3)_2AuBr]_2 + 2\ CH_3COOAg \rightarrow [(CH_3)_2Au{-}O(O)CCH_3]_2 + 2\ AgBr$$

The IR and NMR spectra confirm the assumption that the acetate groups act as bidentate ligands in the dimeric molecules. This leads to a structure with a planar eight-membered ring system and a coplanar arrangement (point group D_{2h}) of all the heavy atoms (Au, O, C). The extremely thin, plate-like appearance of the crystals and their diamagnetism agree well with this view.

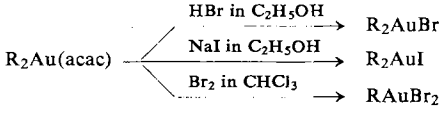


Dialkyl(2,4-pentanedionato)gold complexes (acetylacetonates) had been prepared much earlier from dialkylgold halides and 2,4-pentanedionatothallium [15,22].



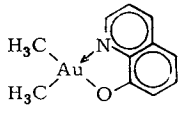
R = C_2H_5, CH_3; X = Br, I

The compounds are colorless, crystalline, and soluble in most organic solvents. They exhibit characteristic cleavage reactions:



According to IR studies [26], these complexes are typical chelates. Dimethylgold-2,4-pentanedionate has been the subject of studies of ligand exchange processes [26b]. The temperature dependence of NMR-spectra of its solution in 2,4-pentanedione provided the parameters of activation for a process in which ligands and solvent molecules compete for the central atoms.

8-Quinolinol also behaves as a bidentate, chelating ligand in corresponding compounds [36]:



[34] *R. E. Rundle* and *J. H. Sturdivant*, J. Amer. chem. Soc. *69*, 1561 (1947); see also [3a, b].

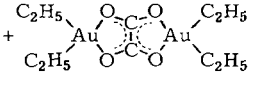
[35] *M. Bergfeld* and *H. Schmidbaur*, Chem. Ber. *102*, 2408 (1969).

[36] *E. Rivarola, G. C. Stocco, B. L. Pepe*, and *R. Barbieri*, J. organometallic Chem. *14*, 467 (1968).

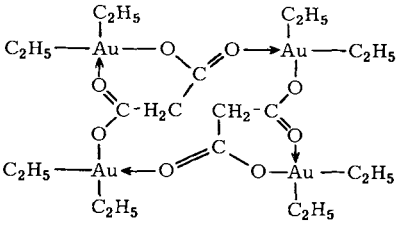
Table 3. Dialkylgold(III) compounds containing Au—O bonds.

	M.p. (°C)	Dec. (°C)	Ref.
$(CH_3)_2Au(C_5H_7O_2)$	84	—	[15]
(-2,4-pentanedionate)	80—81	—	[26, 26b]
$(C_2H_5)_2Au(C_5H_7O_2)$	9—10	—	[20]
$[(CH_3)_2AuOH]_4$	—	120	[26, 33]
$[(CH_3)_2AuOSi(CH_3)_3]_2$	39—40 subl. 40/ 0.1 torr	120	[25]
$(CH_3)_2Au(C_9H_6NO)$ (-8-quinolinolate)	131	—	[36]
$[(CH_3)_2Au(OOCCH_3)]_2$ (-acetate)	97—97.5	175	[35]
$\{[(C_2H_5)_2Au]_2SO_4\}_2$	96—97	96—97	[37, 38, 46]
$\{[(C_3H_7)_2Au]_2SO_4\}_2$	—	—	[37]
$[(C_6H_5CH_2CH_2)_2Au]_2SO_4$	—	108	[12]
$[(C_2H_5)_2Au]_2C_2O_4$ [-oxalate]	81	120	[37]
$Na[(C_2H_5)_2AuC_2O_4]$	—	—	[37]
$\{[(C_2H_5)_2Au]_2CH_2(COO)_2\}_2$ (-malonate)	136	—	[37]
$\{[(C_2H_5)_2Au]_2CH_3CH(COO)_2\}_2$ (-methylmalonate)	90—100	140	[37]
$[(C_2H_5)_2Au]_2C_nH_{2n}(COO)_2$			
$n = 2$ (-succinate)	145—146	—	[37]
$n = 3$ (-glutarate)	90	—	[37]
$n = 4$ (-adipate)	124—132	—	[37]
$n = 5$ (-pimelate)	97—81	100	[37]
$n = 6$ (-suberate)	86—88	110	[37]
Bis(diethylgold)saccharate	—	—	[37]
$[(C_2H_5)_2Au]_2C_6H_4(COO)_2$ (-phthalate)	—	120	[37]
$[(C_2H_5)_2Au]_2C_6H_3(COO)_2NO_2$ (-3-nitrophthalate)	—	—	[37]
$[(C_2H_5)_2Au]_2C_6H_4(COO)_2$ (-isophthalate)	—	—	[37]
$[(C_2H_5)_2Au]_2C_6H_3(COO)_2NO_2$ (-3-nitroisophthalate)	—	—	[37]
$[(C_2H_5)_2Au]_2C_6H_4(COO)_2$ (-terephthalate)	—	—	[37]
$\{[(C_2H_5)_2Au]_2O_3POC_6H_5\}_2$ (-phenylphosphate)	130	160	[39]
$\{[(C_2H_5)_2Au]_2O_3AsOC_6H_5\}_2$ (-phenylarsenate)	128	133	[39]
$[(C_2H_5)_2Au]_2Cr_2O_7$ (-dichromate)	186	—	[39]
$[(C_2H_5)_2AuO_2P(OC_6H_5)_2]_2$ (-diphenylphosphate)	70—71	—	[39]
$[(C_2H_5)_2Au]_3PO_4$	—	—	[33]
$[(n\text{-}C_4H_9)_2Au]_3PO_4$	145	—	[33]

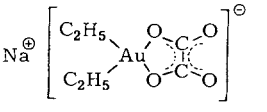
Dialkylgold compounds of dicarboxylic acids have been known for some time [37]. They are prepared by reaction of aqueous solutions of bis(dialkylgold) sulfates with the sodium salts of the corresponding dicarboxylic acids, *e.g.*:

$$[(C_2H_5)_2Au]_2SO_4 + \begin{matrix}COONa\\COONa\end{matrix} \rightarrow Na_2SO_4 + \text{  }$$

Bis(diethylgold) oxalate crystallizes in long, colorless needles. The results of molecular weight determinations are compatible with the indicated structure involving two five-membered rings. With malonic acid instead of oxalic acid, a fundamental change in structure is observed. Bis(diethylgold) malonate evidently contains not two, but four gold atoms per molecule; the compound is dimeric. The following structure is postulated:



The higher homologs also appear to be dimeric. Bis(diethylgold) oxalate dissolves in an aqueous solution of sodium oxalate, and a salt having the composition

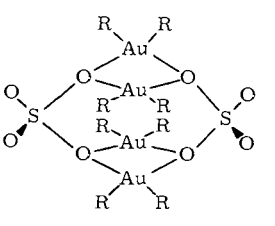


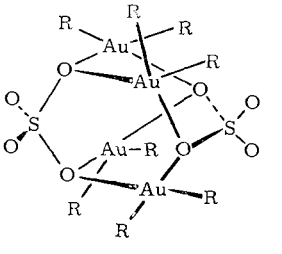
can then be isolated from the solution.

Bis(diethylgold) phthalate [37] probably has a structure similar to that of the oxalate. The isophthalic acid derivative is trimeric, while the terephthalic acid derivative is polymeric and insoluble. The reaction of dialkylgold bromides with silver sulfate in acetone yields bis(dialkylgold) sulfates [12].

$$2\,[R_2AuBr]_2 + 2\,Ag_2SO_4 \rightarrow [(R_2Au)_2SO_4]_2 + 4\,AgBr$$
$$R = C_2H_5 \text{ or } n\text{-}C_3H_7$$

The structure of the dimeric compounds is unknown; two suggested structures [38] are:

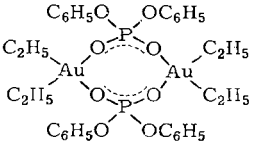




The first of these is less likely on steric grounds [38].

Bis(diethylgold) sulfate and 2,2'-bipyridyl react to form the complex salt $[(C_2H_5)_2Au \cdot bipy]_2^{\oplus}[(C_2H_5)_2Au(SO_4)_2Au(C_2H_5)_2]^{2\ominus}$, in which the anion presumably has a structure similar to that of diethylgold diphenyl phosphate (see below).

Related compounds have also been synthesized from the disilver salts of monophenyl phosphates and monophenyl arsenates [39]. These compounds are dimeric, like the sulfates, and probably have a similar constitution. Mention should also be made in this connection of the dimeric diethylgold diphenyl phosphate, which undoubtedly again has a structure involving an eight-membered ring system.



[37] *C. S. Gibson* and *W. P. Weller*, J. chem. Soc. (London) *1941*, 102.

[38] *R. V. G. Ewens* and *C. S. Gibson*, J. chem. Soc. (London) *1941*, 109.

[39] *M. E. Foss* and *C. S. Gibson*, J. chem. Soc. (London) *1949*, 3075.

Reactions of diethylgold and di-*n*-butylgold bromides with silver phosphate yield polymers having the composition $(R_2Au)_3PO_4$ that are sparingly soluble in all tested solvents [33].

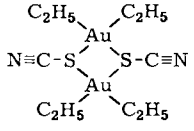
2.2.3. Dialkylgold(III) Compounds Containing Gold-Sulfur Bonds

Dimethylgold thiolates were mentioned earlier in connection with the reactions of trimethylgold (Section 2.1.3).

They can also be prepared from dialkylgold halides and thiols in the presence of bases [12]. Dimeric diethylgold thiocyanate is formed in the reaction of diethylgold bromide with silver thiocyanate [40].

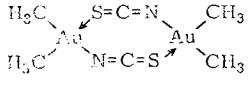
$$[(C_2H_5)_2AuBr]_2 + 2\ AgSCN \rightarrow [(C_2H_5)_2AuSCN]_2 + 2\ AgBr$$

Initially the evidence seemed to indicate that this molecule does not contain gold-nitrogen bonds; it was therefore thought to have the following structure:



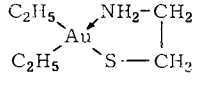
The compound decomposes above 80 °C with formation of gold(I) thiocyanate.

Recently di*methyl*gold thiocyanate has also been prepared and investigated [40a]. This compound is a dimer as well, but is said to have a double bridge structure of the following type:

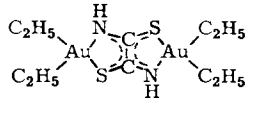


Only this formulation can explain the NMR-nonequivalence of methylgroups observed.

The reaction of diethylgold bromide with 2-aminoethanethiol yields a compound in which the nitrogen also has a donor function [41].



Bis(diethylgold) dithiooxamide [41] is formed on reaction of diethylgold bromide with dithiooxamide. This complex is isosteric with bis(diethylgold) oxalate, and probably has the structure:



[40] *W. L. G. Gent* and *C. S. Gibson*, J. chem. Soc. (London) *1949*, 1835.

[40a] *R. S. Tobias et al.*, unpublished; cited in [12a].

[41] *R. V. G. Ewens* and *C. S. Gibson*, J. chem. Soc. (London) *1949*, 431.

Dialkylgold compounds containing Au–S bonds (cf. Table 4) also include derivatives of monothiocarbonic and dithiocarbonic acids and of thioacetic acid:

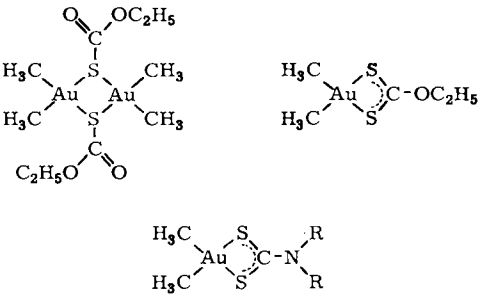


Table 4. Dialkylgold(III) compounds containing Au–S bonds.

	M.p. (°C)	Dec. (°C)	Ref.
$[(CH_3)_2AuSCN]_2$	—	—	[40a]
$[(C_2H_5)_2AuSCN]_2$	62–64	—	[40]
$(n\text{-}C_6H_{13})_2AuSC_6H_4COOH$	—	173–180	[12]
$(C_2H_5)_2AuSCH_2CH_2NH_2$	172–173	—	[41]
$[(C_2H_5)_2Au]_2C_2S_2(NH)_2$	142–143	—	[41]
$(CH_3)_2AuSC(S)N(C_nH_{2n+1})_2$ (—*N*,*N*-dialkyldithiocarbamate)			
$n = 1$	168	—	[42]
$n = 2$	90	90	[42]
$n = 3$	47.5	—	[42]
$n = 4$	41	—	[42]
$n = 9$	54–57	—	[42]
$(C_2H_5)_2AuSC(S)N(CH_3)_2$	59–62	—	[42]
$(C_2H_5)_2AuSC(S)N(C_4H_9)_2$	—	—	[42]
$(i\text{-}C_3H_7)_2AuSC(S)N(CH_3)_2$	87.5–89	—	[42]
$(C_6H_5CH_2)_2AuSC(S)N(CH_3)_2$	109–110	—	[42]
$[(CH_3)_2AuOC(S)OC_2H_5]_2$ (—*O*-ethylthiocarbonate)	—	115	[35]
$(CH_3)_2AuSC(S)OC_2H_5$ (—*O*-ethyldithiocarbonate)	3–4	—	[35]
$[(CH_3)_2AuSC(O)CH_3]_n$	—	90	[35]

The *N*,*N*-dialkyldithiocarbamates are also obtainable from gold(I) *N*,*N*-dialkyldithiocarbamates [42].

$$Au(S_2CNR'_2) \xrightarrow{Br_2} Br_2Au(S_2CNR'_2) \xrightarrow{RMgX} R_2Au(S_2CNR'_2)$$

Thioacetic acid and trimethylgold react to give polymeric dimethylgold monothioacetate [35].

$$(CH_3)_3Au + HS(O)CCH_3 \rightarrow CH_4 + [(CH_3)_2AuS(O)CCH_3]_n$$

2.3. Alkylgold(III) and Arylgold(III) Dihalides and Related Compounds

2.3.1. Alkylgold Dihalides

The alkylgold derivatives of the type $RAuX_2$ are remarkably unstable, and only alkylgold *dibromides* (see Table 5) are known at present. These are formed in the reaction of dialkylgold bromides with bromine in chloroform or carbon tetrachloride [7, 12, 14, 15, 21],

$$R_2AuBr + Br_2 \rightarrow RAuBr_2 + RBr$$

[42] *H. J. A. Blaauw*, *R. J. F. Nivard*, and *G. J. M. van der Kerk*, J. organometallic Chem. *2*, 236 (1964).

and also in small yields in the commutation reaction [14]

$$R_2AuBr + AuBr_3 \rightarrow 2\ RAuBr_2$$

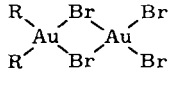
Table 5. Alkylgold and arylgold dihalides $RAuX_2$.

	Dec. (°C)	Ref.
$[CH_3AuBr_2]_2$	–	[15, 31]
$[C_2H_5AuBr_2]_2$	80–85	[7, 12, 14, 31]
$[C_6H_5CH_2AuBr_2]_2$	140	[12]
$[C_6H_5CH_2CH_2AuBr_2]_2$	150–160	[12]
$[n\text{-}C_3H_7AuBr_2]_2$	54 (m.p.)	[21]
$[n\text{-}C_6H_{13}AuBr_2]_2$	150	[12]
$C_6H_5AuCl_2$	73–75	[43]
$CH_3C_6H_4AuCl_2$	–	[43]
$C_6H_5C_6H_4AuCl_2$	65	[43]
$NCC_6H_4AuCl_2$	–	[44]

The compounds dissolve only very sparingly in organic solvents. Their high reactivity toward compounds containing olefinic double bonds and to benzene is particularly characteristic. Thus the reaction of ethylgold dibromide with benzene leads to bromobenzene, diethylgold bromide, and gold(I) bromide [14]. Ethylgold dibromide decomposes at 80–85 °C according to the equation

$$[C_2H_5AuBr_2]_2 \rightarrow 2\ AuBr + 2\ C_2H_5Br$$

Alkylgold dibromides, like dialkylgold halides, are *dimeric* [14, 21]. Their dipole moments are unusually high in comparison with those of the dialkyl compounds [21], the following unsymmetrical structure is therefore assumed.



The reaction behavior also points to a structure of this kind. For example, ethylgold dibromide reacts with an aqueous solution of KBr to give $K[AuBr_4]$ and $(C_2H_5)_2AuBr$ [14]. *n*-Donors such as ethylenediamine [14] and pyridine [21] react with alkylgold dibromides to form complexes of gold(III) bromide and of dialkylgold bromide.

2.3.2. Arylgold Dihalides

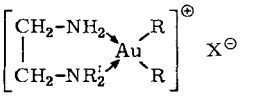
Benzene reacts vigorously with aqueous gold(III) chloride to form 1,2,4,5-tetrachlorobenzene; with a large excess of benzene, chlorobenzene and gold(I) chloride are formed. If this halogenation is stopped by addition of ether, acetic acid, ethyl acetate, or alcohol, phenylgold dichloride can be isolated in small yields [43]. This product is also thought to be formed as a preliminary stage in the reaction that has long been known as the "auration" of benzene [43].

Phenylgold dichloride is sparingly soluble in water and ether, and readily soluble in salt solutions and alcohol. Dihalogenogold derivatives have also been obtained with substituted benzenes [43,44]. However, these compounds have not yet been sufficiently studied. For this reason, Table 5 does not contain all the known examples.

Gold(III) chloride and pyrrole react to form a sparingly soluble black dye containing gold, the constitution of which is unknown [45].

2.4. Complex Organogold(III) Compounds with *n*-Donors

The pronounced tendency of trivalent gold atoms to form complexes is obvious even from the molecular structures of the functional organogold compounds. If a suitable strong donor is lacking, oligomerization or polymerization occurs. The constitution of the addition compounds formed in the presence of complexing agents was unknown for a long time, or was even given incorrectly; the necessary clarification was then provided by later investigations [46]. Contrary to the earlier views, many of the compounds have an ionic structure, particularly in the case of polydentate ligands. Typical examples are the ethylenediamine complexes of the dialkylgold halides:



R	R′	X	M.p. (°C)	Dec. (°C)	Ref.
C_2H_5	H	Br	–	182	[20]
C_3H_7	H	Br	–	190	[13, 21]
C_4H_9	H	Br	–	190	[13]
CH_3	H	I	168	–	[12a, 15, 26, 46]
C_2H_5	H	I	162	–	[20]
C_3H_7	H	$AuBr_2$	–	140	[21, 46]
C_2H_5	H	$(C_2H_5)_2AuBr_2$	–	113–114	[37, 46]
C_2H_5	H	$Au(CN)_2$	161–162	–	[23, 46]
C_3H_7	H	$Au(CN)_2$	151–152	–	[23, 46]
C_2H_5	C_2H_5	Br	83.5–84	–	[15, 46]
C_2H_5	H	$^1/_2\ [(C_2H_5)_2AuSO_4]_2$ [a]	–	147	[46]
CH_3	H	N_3	–	–	[12a]

[a] For structure see text.

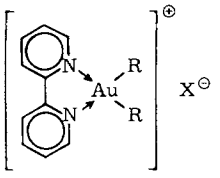
[43] *M. S. Kharasch* and *H. S. Isbell*, J. Amer. chem. Soc. *53*, 3053 (1931).

[44] *M. S. Kharasch* and *P. M. Beck*, J. Amer. chem. Soc. *56*, 2057 (1934).

[45] *G. Giuliani*, Gazz. chim. ital. *64*, 894 (1934).

[46] *M. E. Foss* and *C. S. Gibson*, J. chem. Soc. (London) *1949*, 3063.

The same is true of the 2,2′-bipyridyl complexes:

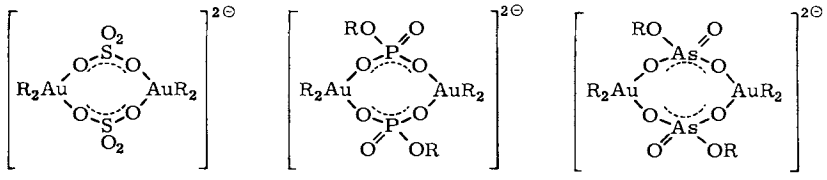


R	X	M.p. (°C)	Ref.
C_2H_5	NO_3	191–192	[46]
C_2H_5	Picrate	190–191	[46]
C_2H_5	$(C_2H_5)_2AuBr_2$	168 (121)	[15, 46]
C_2H_5	$AuBr_2$	169	[46]
C_2H_5	$^1/_2$ $[(C_2H_5)_2AuSO_4]_2$ [a]	162–163	[37, 46]
C_2H_5	$^1/_2$ $[(C_2H_5)_2AuO_3POC_6H_5]_2$ [a]	120	[39]
C_2H_5	$^1/_2$ $[(C_2H_5)_2AuO_3AsOC_6H_5]_2$ [a]	138	[39]

[a] For structure see text.

The bipyridyl may also be replaced by phenanthroline [46]. The evidence of the ionic character is based mainly on the results of conductivity measurements and of metathetical reactions in which the counterions are exchangeable.

Interesting organogold complex ions with sulfate, phenyl phosphate, and phenyl arsenate groups as bidentate ligands have been found in some cases as counterions:



The structural principles presumably correspond to that of the uncharged organogold sulfates, phosphates, *etc.* The large bond angles that are possible with a planar arrangement of the ring atoms appear to be preferred to those resulting from formation of four-membered rings. The eight-membered ring also avoids tricoordination of the oxygen atoms. Many parallels are to be found in the chemistry of inorganic heterocycles [47–52].

Table 6. Adducts of dialkylgold halides with monofunctional donors.

	M.p. (°C)	Ref.
$(C_2H_5)_2AuBr \cdot NH_3$	60 (dec.)	[7, 20]
$(C_2H_5)_2AuBr \cdot py$	59–60 (dec.)	[20]
$(C_3H_7)_2AuBr \cdot py$	61–62	[21]
$(C_2H_5)_2AuBr \cdot S(CH_2C_6H_5)_2$	91	[15, 53]
$(CH_3)_2AuBr \cdot P(C_6H_5)_3$	151	[10a]
$(CH_3)_2AuI \cdot S(CH_2C_6H_5)_2$	77–78 (dec.)	[15]
$[(CH_3)_2Au(OH_2)_2]NO_3$, ClO_4	–	[26, 54, 55]
$(C_6F_5)_2AuCl \cdot P(C_6H_5)_3$	150	[55a, 55d]
$C_6H_5AuBr_2 \cdot P(C_6H_5)_3$	199–201 (dec.)	[55c]

Diethylgold bromide also forms adducts with ammonia [7, 20], pyridine [20], and dibenzyl sulfide [15, 53]. The compositions of some of these complexes are given in Table 6. Their structure is unknown.

A triphenylphosphine complex of dimethylgold bromide is formed from $(CH_3)_3Au \cdot P(C_6H_5)_3$ and bromine or mercuric bromide [10a]. The complex $C_6F_5AuBr_2 \cdot P(C_6H_5)_3$ was obtained from $C_6F_5Au \cdot P(C_6H_5)_3$ and bromine [55c].

Triphenylphosphine also forms a 1 : 1 complex with bis-pentafluorophenylgold chloride, as described by *Nyholm* and *Royo* [55a]. "Oxidation" of $AuCl \cdot P(C_6H_5)_3$ by $(C_6F_5)_2TlCl$ according to

$$(C_6F_5)_2TlCl + AuCl \cdot P(C_6H_5)_3 \rightarrow (C_6F_5)_2AuCl \cdot P(C_6H_5)_3 + TlCl$$

yielded this first perfluoroarylgold(III) compound. Its reduction with hydrazine leads to $C_6F_5Au \cdot P(C_6H_5)_3$ – a compound which can also be obtained from $AuCl \cdot P(C_6H_5)_3$ and C_6F_5MgBr [55c].

The crystal structure of $(C_6F_5)_2AuCl \cdot P(C_6H_5)_3$ has been determined [55d]. The configuration of the gold atom is square planar with the phenyl rings in a *cis*-position. The Au–C distances of 2.12 and 2.18 Å are relatively short.

Dialkylgold halides are hydrated in water. A dihydrate $[(C_2H_5)_2Au(OH_2)_2]Br$ was postulated some time ago for diethylgold bromide [20]; these views have been confirmed by more recent investigations [25, 26, 26a, 54, 55]. The vibration-spectroscopic behavior, which was mentioned in Section 2.2.1.2, verifies the *cis* position of the ligands. Extensive experiments have now been carried out in an attempt to obtain information about the equilibrium constants of the solvation of dimethylgold cations and about the rate of exchange of the water molecules in the first coordination sphere of the gold atom on the basis of ^{17}O-NMR spectra [55]. The activation energy for the H_2O exchange is 8.4 ± 1.8 kcal/mole. This gives a mean residence time ("preexchange lifetime") of 2.2×10^{-5} s at 25 °C for the water molecules bound to gold. Both

[47] *H. Schmidbaur*, Allg. prakt. Chem. (Wien) *18*, 138 (1967); Fortschr. chem. Forsch., *13*, 167 (1969).

[48] *M. Schmidt* and *H. Schmidbaur*, Chem. Ber. *93*, 878 (1960); *94*, 2446 (1961).

[49] *H. Schmidbaur* and *H. F. Klein*, Chem. Ber. *101*, 2278 (1968).

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[51] *J. Goubeau*, Pure appl. Chem. *13*, 81 (1966).

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[54] *R. S. Tobias*, Organometallic Chem. Reviews *1*, 93 (1966).

[55] *G. E. Glass*, *W. B. Schwabacher*, and *R. S. Tobias*, Inorg. Chem. *7*, 2471 (1968).

[55a] *R. S. Nyholm* and *P. Royo*, Chem. Commun. *1969*, 421.

[55b] *A. Sacco* and *M. Freni*, Gazz. chim. ital. *86*, 195 (1956).

[55c] *L. G. Vaughan* and *W. A. Sheppard*, J. Amer. chem. Soc. *91*, 6161 (1969).

[55d] *R. W. Baker* and *P. Pauling*, Chem. Commun. *1969*, 745.

quantities have distinctly higher values for the analogous trimethylplatinum cation, the activation energy being 9.4 ± 1.0 kcal/mole and the preexchange lifetime 8.0×10^{-5} s, again at 25 °C. This difference is probably due to steric factors.

2.5. σ-Organogold(I) Compounds

2.5.1. Phosphine-Stabilized Alkylgold(I) and Arylgold(I) Compounds

σ-Alkyl and σ-aryl derivatives of Au^I, like those of Au^{III} appear to be capable of existing only in the presence of stabilizing complexing agents. In any case, all the known compounds of this type contain such ligands, particularly tertiary phosphines. Complexes of this nature were first prepared by *Coates et al.* [56] by reaction of organolithium compounds with the phosphine complexes of the gold(I) halides.

$$R'_3P{\rightarrow}AuX + LiR \rightarrow R'_3P{\rightarrow}Au{-}R + LiX$$

R = CH_3, C_2H_5, mesityl; X = Cl, Br; R′ = C_2H_5, C_6H_5

Some of the compounds that have been synthesized by this method are listed in Table 7. Some exhibit considerable thermal and chemical stability; they are soluble as the monomers in organic solvents, and are diamagnetic. Their dipole moments in the region of 5.4 to 5.6 D [57] indicate a relatively low polarity. IR spectroscopy met with difficulties because of the low intensity of some important bands, but nevertheless yielded some fundamental information [10].

These $RAu \cdot PR_3'$ compounds have recently gained new interest through mechanistic studies by *Ingold* and *Gregory* [10a]. As prototypes of compounds undergoing mono- and bimolecular electrophilic substitutions at carbon (S_E1 and S_E2, resp.) they have been shown to supplement the classical examples for this class of reaction mechanisms, the organomercurials. Kinetic studies of the reactions

$$RAu \cdot PR'_3 + HgX_2 \rightarrow RHgX + XAu \cdot PR'_3$$

R′ = C_6H_5; X = Cl, Br, I, CH_3COO, NO_3

have shown an S_E2 process for R = CH_3 and C_2H_5, but an S_E1 mechanism for
R = $C(CN)(C_4H_9)(OCOC_2H_5)$, in agreement with expectation.

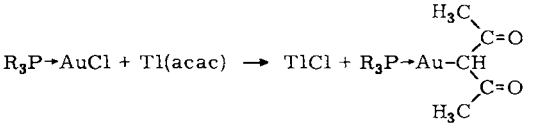
Substitutions in trialkylgold complexes $R_3Au \cdot PR_3'$ also occur with an S_E2 type mechanism [10a].

The structure of the compounds is assumed to be linear, corresponding to an sp-hybridized gold atom. Appreciable (d→d)π back-bonding components are probable for the Au–P bond [10, 57]. This approach or the SHAB [61, 62] principle offers possibilities of explaining the stabilizing effect of the phosphine ligands.

Table 7. σ-Alkylgold(I) and σ-arylgold(I) compounds.

	M.p. (°C)	Ref.
$CH_3Au \cdot P(C_2H_5)_3$	62	[56, 57]
$CH_3Au \cdot P(C_6H_5)_3$	175	[10, 56, 57]
	173–175	[10a]
$C_2H_5Au \cdot P(C_2H_5)_3$	51	[56, 57]
$C_2H_5Au \cdot P(C_6H_5)_3$	130	[56, 57]
	150–152	[10a]
$i\text{-}C_4H_9Au \cdot P(C_6H_5)_3$	0 (dec.)	[10a]
$(CH_3CO)_2CHAu \cdot P(C_6H_5)_3$	164–165	[10a]
$(CN)(C_4H_9)(C_2H_5OCO)CAu \cdot P(C_6H_5)_3$	131–132	[10a]
$(CN)(C_2H_5OCO)CHAu \cdot P(C_6H_5)_3$	253–255	[10a]
$(C_2H_5OCO)_2(C_4H_9)CAu \cdot P(C_6H_5)_3$	212	[10a]
$C_6H_5Au \cdot P(C_2H_5)_3$	68	[56, 57]
$C_6H_5Au \cdot P(C_6H_5)_3$	152 (164)	[56, 58]
$p\text{-}FC_6H_4Au \cdot P(C_6H_5)_3$	154	[55c]
$m\text{-}FC_6H_4Au \cdot P(C_6H_5)_3$	141	[55c]
$m\text{-}CF_3C_6H_4Au \cdot P(C_6H_5)_3$	150	[55c]
(mesityl)$Au \cdot P(C_6H_5)_3$	dec. 100	[56, 57]
(acac)$Au \cdot P(C_6H_5)_3$	—	[59]
C_5H_5Au	—	[60]
$C_5H_5Au \cdot P(C_6H_5)_3$	dec. > 100	[60]
$CH_3C_5H_4Au \cdot P(C_6H_5)_3$	—	[60]
$C_6F_5Au \cdot P(C_6H_5)_3$	dec. 160	[55a]
	171–172	[55c]

An interesting variant is found in the work of *Lewis et al.* [59]. The reaction of chlorotriphenylphosphinegold(I) with 2,4-pentanedionatothallium(I) yields a corresponding Au^I complex, in which, however, the heavy metal is bound to carbon and not to chelating oxygen atoms!



$R_3 = (C_6H_5)_3$, $(C_6H_5)_2C_2H_5$, or $(C_2H_5)_3$

NMR and IR spectra verify the composition and constitution. This preference for the C rather than for the O ligand is almost unique in the chemistry of metal acetylacetonates [63]. Significantly, parallels are found only with platinum [64] and rhodium [65].

2.5.2. Alkenylgold and Alkynylgold(I) Compounds

2.5.2.1. Cyclopentadienylgold(I) Derivatives

Hüttel et al. have described a compound having the composition C_5H_5Au [60], and so filled one of the last gaps in the field of cyclopentadienylmetal derivatives [66]. The reaction of certain olefin complexes of

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[63] *J. P. Collman*, Advances Chem. Ser. *37*, 78 (1963); Angew. Chem. *77*, 154 (1965); Angew. Chem. internat. Edit. *4*, 132 (1965).

[64] *A. G. Swallow* and *M. R. Truter*, Proc. Roy. Soc. (London), Ser. A *254*, 205 (1960).

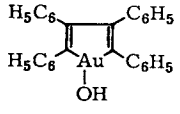
[65] *G. W. Parshall* and *F. N. Jones*, J. Amer. chem. Soc. *87*, 5356 (1965).

[66] See [3a], p. 90ff; *J. M. Birmingham*, Advances organometallic Chem. *2*, 365 (1964).

AuCl with NaC_5H_5 in tetrahydrofuran at −60 °C yields the desired compound as a very unstable yellow powder. A π-bonded structure of the ferrocene type and an ionic structure can be ruled out on the basis of spectroscopic studies; a constitution involving an Au–C σ-bond is therefore probable (monohapto). This view is strongly supported by the observations on the corresponding phosphine complexes, which are formed on reaction of $(C_6H_5)_3P \cdot AuCl$ with NaC_5H_5 or with C_5H_6 in the presence of bases, as well as from C_5H_5Au and $(C_6H_5)_3P$. It is soluble in organic solvents, and NMR spectroscopic measurements are therefore possible[60]. Only one signal was recorded for the C_6H_5 protons, as is typical of cyclopentadienylmetal compounds having a "non-stationary" M–C bond[67–73]. C_5H_5Au compounds thus appear to belong to the class of stereochemically dynamic organometallic compounds[67,68]. This is not contradicted by the NMR spectrum of the methylcyclopentadienyl derivative[60], which gives three groups of signals having the relative areas 2:2:3[71]. However, the very low temperature measurements required for final proof have not yet been carried out in either case.

2.5.2.2. Unsaturated Heterocycles Containing Gold

In the investigation of the reaction behavior of 1,2,3,4-tetraphenylbutadienylene-1,4-dilithium, *Braye et al.*[74] allowed this compound to react with gold trichloride. By a reaction course that is not entirely clear they obtained a yellow crystalline compound, m.p. = 190–195 °C (dec.), to which they assigned the structure of a 1-auracyclopentadiene:



Since there is no evidence for this structure, it is offered only with reservations.

2.5.2.3. Alkynylgold(I) Compounds

The general interest in metal acetylides[2,3] is evident even for gold in a number of extensive articles[75–78].

Ethynylenedigold(I) (gold(I) acetylide, carbide) has been known for a long time and feared for its high brisance[76,77]. According to *Nast*[76] a relatively stable ammonia adduct of Au_2C_2 is obtained from AuI and KC_2H in liquid NH_3. With an excess of KC_2H, complex potassium gold acetylides are formed, *e.g.* $K[Au(C{\equiv}CH)_2]$ and $K_2[HC{\equiv}CAuC{\equiv}CAuC{\equiv}CH]$, the latter being when acetylene is introduced at the same time (Table 8).

Table 8. Alkynyl and aralkynyl compounds of gold.

	M.p. (°C)	Dec. (°C)	Ref.
$Au_2C_2 \cdot (NH_3)_x$	—	expl.	[76, (77)]
$K[Au(C_2H)_2]$	—	—	[76]
$K_2[Au_2C_2(C_2H)_2]_2$	—	—	[76]
$[C_6H_5C{\equiv}CAu]_x$	—	105	[75, 76]
$[(CH_3)_3CC{\equiv}CAu]_4$	—	150	[75]
$(CH_3)_3CC{\equiv}CAu \cdot NH_3$	—	155	[75]
$(CH_3)_3CC{\equiv}CAu \cdot P(CH_3)_3$	194–195	—	[75]
$K[Au(C{\equiv}CC_6H_5)_2]$	...	...	[76]

The aralkynylgold compounds of the type $RC{\equiv}CAu$ and their complexes $RC{\equiv}CAu \cdot L$, which were first synthesized in 1962 by *Coates* and *Parkin*[75], are more stable (see Table 9).

Table 9. Complexes $C_6H_5C{\equiv}CAu \cdot L$ of phenylethynylgold.

L	M.p. (°C)	Dec. (°C)	Ref.
$(C_2H_5)_3P$	83–85	—	[75]
$(C_6H_5)_3P$	163–164	—	[75]
$(C_6H_5O)_3P$	113–114	—	[75]
$(C_2H_5)_3As$	67–68	—	[75]
$(C_2H_5)_3Sb$	96–97	—	[75]
Pyridine	—	80	[75]
Piperidine	111.5–112	—	[75]
NH_3	—	120	[75, 76]
$i\text{-}C_3H_7NH_2$	—	115	[75, 78a]
$C_5H_{11}NH_2$	124–125	—	[75]
$C_8H_{17}NH_2$	—	120	[75]
$C_9H_{19}NH_2$	117–118	—	[75]
$(C_4H_9)_2NH$	91–92 (dec.)	—	[75]
C_4H_9NC	40.5–41.5	—	[75]
$o\text{-}C_2H_5C_6H_4NC$	107–108	—	[75]
$p\text{-}CH_3C_6H_4NC$	176–177	—	[75]
$1/2\ [(C_6H_5)_2PCH_2]_2$	—	200	[75]

These compounds are formed on reaction of freshly reduced $AuCl_3$ with suitable alkali metal alkynides; the products are sparingly soluble yellow polymers. In the presence of donors (amines, phosphines, or arsines), however, low molecular weight complexes, which are mostly soluble as monomers in organic solvents, are formed. The *amine* complexes are not monomeric in organic solvents, presumably as a result of oligomerization due to hydrogen bonds, as is also shown by an X-ray structure analysis on isopropylaminephenylethynylgold(I)[78a]; even in the solid state, there is no π interaction of the gold atom with the electron system of the C≡C bond in this case, such as occurs in the corresponding compounds of copper and silver[78b,c]. This provides important evidence of the relatively lower tendency of gold to form metal-olefin π bonds (see Section 4).

The oligomerization observed in the case of the uncomplexed *tert*-butylethynyl compound cannot how-

[67] *S. J. Lippard*, Trans. New York Acad. Sci. *29*, 917 (1967); Chem. Abstr. *68*, 3862 (1968).

[68] *M. J. Bennett, F. A. Cotton, A. Davison, J. W. Faller, S. J. Lippard*, and *S. M. Morehouse*, J. Amer. chem. Soc. *88*, 4371 (1966).

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[73] *G. A. Shchembelov* and *Yu. A. Ustynyuk*, Doklady Akad. Nauk. SSSR *173*, 847, 1364 (1967).

[74] *E. H. Braye, W. Hübel*, and *I. Caplier*, J. Amer. chem. Soc. *83*, 4406 (1961).

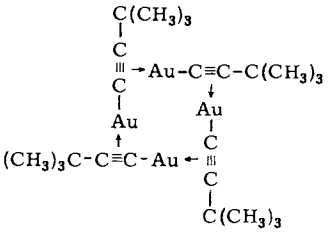
[75] *G. E. Coates* and *C. Parkin*, J. chem. Soc. (London) *1962*, 3220.

[76] *R. Nast* and *U. Kirner*, Z. anorg. allg. Chem. *330*, 311 (1964).

[77] *A. Matthews* and *L. L. Waters*, J. Amer. chem. Soc. *22*, 108 (1900), further literature cited therein.

[78] a) *P. W. R. Corfield* and *H. M. M. Shearer*, Acta crystallogr. *23*, 156 (1967); b) *20*, 502 (1966); c) *21*, 957 (1966).

ever be explained without the assumption of such bonds.



On the other hand, the fact that the IR absorption of the C≡C bonds are only slightly altered indicates that the interaction is weak [75, 76].

3. Isocyanide Complexes of Gold

Isocyanide complexes of gold(I) and gold(III) have been described by *Sacco* and *Freni* [55b]. In these compounds we meet again the gold-carbon σ-bond: R–N≡C→AuX.

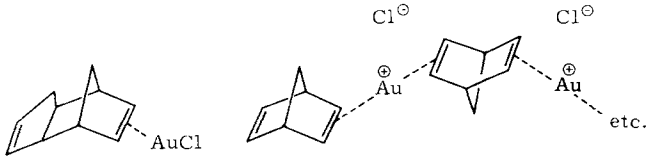
Reviving interest in this class of compounds is evident from a recent paper by *Vaughan* and *Sheppard* [55c], on organogold(I) complexes of isocyanides (Table 10). Information on the back-donation of electrons in the arylgold and isocyanidegold moieties was derived from ^{19}F-NMR-investigations of these compounds. ^{19}F chemical shifts are quite sensitive to all alterations in the state of bonding of the phenyl ring and are thus an excellent probe for this purpose.

Table 10. Isocyanide complexes of gold halides and organogold compounds (cf. also Table 9).

	M.p. (°C)	Ref.
$C_6H_5NC \cdot AuCl$	white	[55b]
p-$CH_3C_6H_4NC \cdot AuCl$	white	[55b]
p-$CH_3C_6H_4NC \cdot AuCN$	244 (dec.)	[55b]
p-$CH_3OC_6H_4NC \cdot AuCl$	—	[55b]
$[(C_6H_5NC)_4Au]Cl$	—	[55b]
$[(p\text{-}CH_3C_6H_4NC)_4Au]Cl$	190	[55b]
$[(p\text{-}CH_3C_6H_4NC)_4Au][B(C_6H_5)_4]$	175 (dec.)	[55b]
$[(p\text{-}CH_3OC_6H_4NC)_4Au]Cl$	—	[55b]
p-$CH_3C_6H_4NC \cdot AuCl_3$	yellow	[55b]
p-$CH_3OC_6H_4NC \cdot AuCl_3$	yellow	[55b]
p-$FC_6H_4NC \cdot AuCl$	247–148 (dec.)	[55c]
m-$FC_6H_4NC \cdot AuCl$	223–225	[55c]
p-$FC_6H_4NC \cdot AuC_6H_4(p\text{-}F)$	153–155 (dec.)	[55c]
m-$FC_6H_4NC \cdot AuC_6H_4(p\text{-}F)$	126–128 (dec.)	[55c]
p-$FC_6H_4NC \cdot AuC_6H_4(m\text{-}F)$	138–140 (dec.)	[55c]
m-$FC_6H_4NC \cdot AuC_6H_4(m\text{-}F)$	110–111 (dec.)	[55c]

4. Organogold Compounds Containing Gold-Carbon π Bonds

It is remarkable how recently the existence of simple olefin-gold complexes was verified when one thinks that the corresponding compounds of platinum (Zeise salt) are among the classical representatives of this class of compounds. Though compounds of this type were postulated as reaction intermediates a long time ago, they could not be isolated [79]. It was *Hüttel et al.* [80,82–85] and *Chalk* [81] who showed that gold is probably also capable of forming relatively stable π complexes. This is true in particular of Au^{I}, though less so of Au^{III}. The result is in agreement with the stability relations of the π complexes of Pt^{II} and Pt^{IV}. However, the stability even of Au^{I} complexes is still very low so that reversible addition or removal of olefin ligands is often possible. This in fact makes complexes of this type particularly interesting as intermediates in reactions of olefins in the presence of gold and its compounds as homogeneous or heterogeneous catalysts [86].



(Dicyclopentadiene · AuCl) (Norbornadiene · AuCl)

Table 11. Olefin complexes of gold chlorides.

L→AuCl	Dec. (°C)	Ref.
L = Cyclopentene	55–60	[80, 82]
Cyclohexene	55 (60)	[80, 82]
Cycloheptene	93–98	[82]
cis-Cyclooctene	81–85 (93–96)	[80, 82]
trans-Cyclodecene	75–80 (90–93)	[80, 82]
1-Octene	0	[83]
1-Decene	0	[83]
1-Dodecene	23–24	[83]
1-Tetradecene	33–35	[83]
1-Hexadecene	43–45	[83]
1-Octadecene	49–51	[83]
1,5-Cyclooctadiene	110–114	[82]
cis,trans-1,5-Cyclodecadiene	73–74	[82]
Norbornadiene	75–78	[82]
Dicyclopentadiene	90–95	[82, 85]
1,4-Hexadiene	50	[83]
1,5-Hexadiene	50	[83]
trans-1,4,9-Decatriene	58–60	[83]
cis,cis,trans-1,5,9-Cyclodecatriene	102–103	[82]
all-*trans*-1,5,9-Cyclodecatriene	98–100	[82]
$L_nAu_2Cl_4$		
L = Norbornadiene (n = 1)	50	[84, 85]
Norbornadiene (n = 2)	62–64	[84]
Norbornadiene (n = 3)	78–80	[84, 85]
Norbornene (n = 3)	65–70	[85]
cis-Butene (n = 3)	−10	[85]
1,5-Cyclooctadiene (n = 2)	98–102	[85]
Dicyclopentadiene (n = 3)	80–85	[85]
trans-Cyclodecene (n = 2)	30	[85]

[79] *F. H. Brain, C. S. Gibson, J. A. J. Jarvis, R. F. Phillips, H. M. Powell,* and *A. Tyalji,* J. chem. Soc. (London) *1952*, 3686.

[80] *R. Hüttel* and *H. Dietl,* Angew. Chem. *77*, 456 (1965); Angew. Chem. internat. Edit. *4*, 438 (1965).

[81] *H. J. Chalk,* J. Amer. chem. Soc. *86*, 4733 (1964).

[82] *R. Hüttel, H. Reinheimer,* and *H. Dietl,* Chem. Ber. *99*, 462 (1966).

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[85] *R. Hüttel, H. Reinheimer,* and *K. Nowak,* Chem. Ber. *101*, 3761 (1968).

[86] *S. Carra* and *R. Ugo,* Inorg. chim. Acta Rev. *1*, 49 (1967).

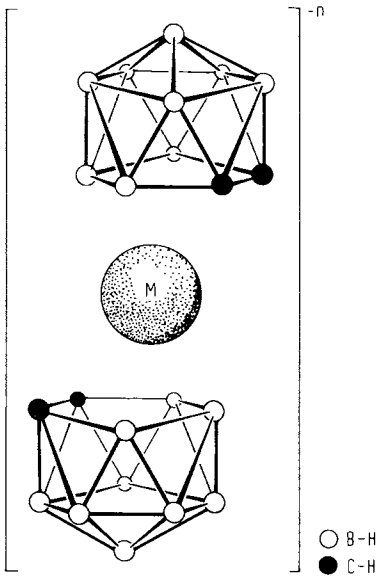
The known olefin-gold complexes have mostly been prepared by reaction of gold trichloride or tetrachloroauric acid or its salts with an olefin [80,81] (the first step being reduction to Au^{I}), or from AuCl and olefin [80,81]. The reaction is carried out at the lowest possible temperature (−60 to +20 °C). In the reduction of $AuCl_3$ it is possible under mild conditions or on addition of complexing agents to intercept intermediates in which both AuCl and $AuCl_3$ are coordinately bound [83–85]. Their overall composition is olefin·Au_2Cl_4; their diamagnetism (NMR), however, shows that these are not Au^{II} compounds but Au^{I}/Au^{III} compounds.

The bonding of the olefin ligands to gold is so weak in some cases that the dissociation of the hydrocarbon can be followed gravimetrically at room temperature [82], as *e.g.* in the case of cyclopentenechlorogold(I). The IR spectra show a characteristic shift of the C=C stretching vibration to lower wave numbers ($\Delta\tilde{\nu} \approx 120$–$140\ cm^{-1}$) as a result of complex formation; the NMR spectra of the olefins also change. However, all the structural details have not been verified in every case. X-ray studies in particular are still lacking. Consequently, Table 11 contains no structural information; the formulas given indicate the views that are held at present [80–85].

5. Gold-Carborane Compounds

It has been known for some years that anionic fragments of the carborane icosahedron can form stable complexes with transition metal ions that are completely novel from the standpoints of structure and of valence theory [87–92]. The development of this line of research has not even been halted by the noble metals gold and platinum [93,94]. The "gold dicarbollides" synthesized so far contain gold-carbon bonds of an entirely new type, and should therefore be mentioned before we conclude this article.

On the basis of X-ray structural investigations [94] on the isomorphous copper compound $(C_6H_5)_3PCH_3[Cu(C_2B_9H_{11})_2]$, the anion of the analogous gold compound must be assumed to have the constitution *(1)* (M = Au; $n = 1$).



(1)

This structure appears to be characteristic of d^8 and d^9 complexes in that the two carbollide caps in the structure are considerably displaced with respect to each other (a symmetrical arrangement is preferred in d^3 to d^7 complexes). *Wing* interprets this arrangement as a consequence of a π-allyl type interaction [94]. Other explanations are however possible [93].

The red $[Au(C_2B_9H_{11})_2]^{\ominus}$ ion containing Au^{III} can be reduced electrolytically to the corresponding deep blue paramagnetic Au^{II} complex, $[Au(C_2B_9H_{11})_2]^{2\ominus}$, which, *cum grano salis*, is the only "organometallic" gold(II) compound known at present.

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German version: Angew. Chem. *82*, 120 (1970)
Translated by Express Translation Service, London

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The Behavior of Acid Halides Toward Lewis Acids and Lewis Bases

By Ekkehard Lindner[*]

Reactions of some typical acid halides of carbonic and trithiocarbonic acids and of orthophosphoric and sulfuric acids with Lewis acids and Lewis bases are compared. Acylium, perfluoroacylium, thioacylium, and even sulfonylium ions are obtainable with Lewis acids. It is possible by conductivity measurements and by electronic and above all IR spectroscopic investigations to determine whether the 1:1 adducts of acid halides and Lewis compounds are acylium or sulfonylium salts or donor-acceptor complexes. In the reaction with Lewis bases, the halogen atom in the acid halide is replaced by the electron donor, generally with formation of nonpolar molecular compounds or complexes.

1. Introduction

This article presents a comparative report on the reactions of some typical acid halides that are formally derived from carbonic and trithiocarbonic acids and from orthophosphoric and sulfuric acids (RCOX, RCSX, OPX_3, R_2POX, and RSO_2X; R = organic or inorganic residue; X = halogen or acid residue) with Lewis acids and Lewis bases.

Particularly significant results were obtained from studies on the dependence of the C–O, C–S, P–O, or S–O bond on the acceptor or donor strength of the Lewis acid or base and on the electronegativity of the organic or inorganic residue bonded to the carbon, phosphorus, or sulfur. The ability of Lewis acids such as BF_3, PF_5, AsF_5, or SbF_5, whose central atoms have no free electron pairs, to accept the halogen atom of an acid halide depends on their acceptor strength. The coordination number of the Lewis acid rises to its maximum value, the Lewis acid being converted into an anion, while the acid halide forms an "electron-deficient" cationic system such as

$$R-\overset{\oplus}{C}=\ddot{O}: \leftrightarrow R-C\equiv\overset{\oplus}{O}:$$

The originally nonbonding electrons on the oxygen or on the sulfur make a considerable contribution to the resulting positive charge on the elements carbon, phosphorus, or sulfur, leading to additional π components in the C–O, C–S, P–O, and S–O bonds. The residue R also has an important influence on these bonds because of its inductive effect.

If, on the other hand, Lewis bases are allowed to act on acid halides, the halogen may also be split off as an anion. In this case, however, it is replaced by the electron donor, generally with formation of non-polar compounds. In contrast with the reactions with Lewis acids, the π components of the C–O, C–S, P–O, and S–O bonds are now decreased; the bond strength again depends on the donor strength of the Lewis base and on the electronegativity of the residue R.

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The phenomena just described can be followed particularly readily by methods based on vibration spectroscopy. In the IR spectra of the cationic systems formed from Lewis acids and acid halides, the frequencies of the element-oxygen or element-sulfur stretching vibrations increase considerably, pointing to correspondingly high force constants. In the reaction products of Lewis bases with acid halides, these stretching frequencies often show an extremely pronounced decrease; the force constants have therefore become extremely small.

2. Acyl Halides and Perfluorinated Acyl Halides

2.1. Reactions with Lewis Acids

Though acylium salts have been known for a long time[1], it was *Seel*[2] that first recognized them as "carboxonium" compounds and detected them. They are obtained *e.g.* by reaction of CH_3COF and BF_3 or CH_3COCl and $SbCl_5$ below 0 °C.

Their salt-like character has been confirmed by conductivity measurements in liquid SO_2

$$CH_3COF + BF_3 \underset{> 20\,°C}{\overset{< 20\,°C}{\rightleftharpoons}} [CH_3CO][BF_4]$$

Above the boiling point of CH_3COF (20.8 °C), the salt is largely dissociated into the two starting components.

Stable acylium salts were first reported by *Olah et al.*[3], who described them as "oxocarbonium" derivatives because of the positive charge on the carbonyl carbon atom. Two methods have become particularly widely used for the preparation of acylium salts[2,3]; these are the reaction of acyl fluorides with Lewis acids such as BF_3 or ElF_5 (El = P, As, Sb) and the reaction of acyl chlorides or bromides with the anhydrous silver complexes $Ag[BF_4]$ or $Ag[ElF_6]$ ("silver salt method")

[1] *F. Fairbrother*, J. chem. Soc. (London) *1937*, 503; *R. J. Gillespie, ibid. 1950*, 2997; *H. Burton* and *P. F. G. Praill, ibid. 1950*, 2034.

[2] *F. Seel*, Z. anorg. allg. Chem. *250*, 331 (1943); *252*, 24 (1944).

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in strongly polar solvents such as nitromethane or liquid SO_2:

$$RCOF + ElF_{n-1} \rightarrow [RCO][ElF_n]$$

or

$$RCOX + Ag[ElF_n] \rightarrow [RCO][ElF_n] + AgX$$

El = B, $n = 4$; El = P, As, Sb, $n = 6$; X = Cl, Br

The second method is often more favorable for preparative reasons. *Olah et al.*[3] isolated the thermally surprisingly stable, but extremely hygroscopic, acetylium, propionylium, and benzoylium cations as the salts $[RCO][ElF_n]$. The arsenic and antimony compounds, which are among the most stable of these, are almost completely in the form of the acylium salts *(1)* even at room temperature, whereas the PF_6^- derivative contains considerable quantities of a polarized donor-acceptor complex *(2)* under the same conditions.

$[R-C\equiv O:]\ [ElF_n]$ $\qquad$ $R-C(=O^{\delta\oplus}\cdots ElF_{n-1}^{\delta\ominus})-F$

(1) $\qquad$ *(2)*

The question whether a 1:1 adduct of the type $RCOF \cdot ElF_{n-1}$ is in the form of the acylium salt *(1)* or of a donor-acceptor complex *(2)* can be answered by conductivity measurements or by IR spectroscopic investigations[3,4]. Whereas the CO stretching absorption of *(1)* appears above 2290 cm^{-1}, *i.e.* in the CO triple bond region, the corresponding band for the compounds *(2)* lies below 1620 cm^{-1}; in other words, it has been shifted toward longer wavelengths relative to that of the free acid fluoride.

By X-ray studies on $[CH_3CO][SbF_6]$, *Boer*[5] was able to show the existence, in the solid state, of isolated linear $[CH_3CO]^+$ cations (symmetry C_{3v}), in which the C–H, C–C, and C–O distances are considerably shorter (d C–C = 1.378 Å, d C–O = 1.116 Å) than in aldehydes and ketones, owing to the positive charge on the carbonyl C atom. MO calculations gave the following charge distributions: –0.11 for the methyl carbon atom, 1.18 for the carbonyl carbon atom, –0.35 for the oxygen, and 0.09 for each hydrogen atom[5].

Acylium salts can also be detected chemically[3]. They react with benzene by a Friedel-Crafts mechanism to form the ketones. Only the salt form *(1)* has an acylating action, whereas *(2)* has not.

Electronegative ligands, such as perfluoroalkyl groups, have a considerable influence on the C–O bond. 1:1 complexes of perfluoroacyl fluoride with phosphorus, arsenic, or antimony pentafluoride can be prepared by the "silver salt method"[3] if liquid SO_2 is used as the solvent:

$$RCOBr + Ag[ElF_6] \rightarrow RCOF \cdot ElF_5 + AgBr$$

R = CF_3, C_2F_5; El = P, As, Sb

The advantage of acid bromides is obvious, since AgBr has a lower solubility product than AgCl. It has been found possible to prepare trifluoroacetylium hexafluoroantimonate(v) below –25 °C[6]. The conductivity diagram[7] (from measurements in liquid SO_2) shows a marked change of direction at the boiling point of CF_3COF (–57 °C). Below this temperature the specific conductivity increases very rapidly; $CF_3COF \cdot SbF_5$ is therefore best formulated as a 1:1 electrolyte $[CF_3CO][SbF_6]$ at these temperatures (equivalent conductivity at –60 °C: Λ_c = 83.6 Ω^{-1} $cm^2 mole^{-1}$).

Low-temperature IR studies revealed a band of medium intensity at 2371 cm^{-1}, which practically disappears at room temperature, and which is characteristic of a C≡O stretching vibration. From the occurrence of two other absorptions at 1780 and 1631 cm^{-1} (*i.e.* shifted to longer wavelengths in relation to CF_3COF) in the IR spectrum of $CF_3COF \cdot SbF_5$, which can be assigned to a keto (⟩C=O) stretching vibration, it is concluded that a considerable amount of the compound exists as a polarized donor-acceptor complex above –57 °C[6,7]. Whereas $CF_3COF \cdot AsF_5$ decomposes into CF_3COF and AsF_5 above –57 °C, and $CF_3COF \cdot PF_5$ cannot be isolated at all, the thermally more stable $CF_3COF \cdot SbF_5$ reacts with benzene at 6 °C to form $CF_3COC_6H_5$, which could be detected in small quantities when precipitated as the 2,4-dinitrophenylhydrazone.

The homologous 1:1 adduct $C_2F_5COF \cdot SbF_5$ exhibits no conductivity (in nitromethane) at room temperature and, as its IR spectrum shows, it is only partly in the form of the 1:1 electrolyte even below –30 °C. The action of C_6H_6 on $C_2F_5COF \cdot SbF_5$ does not yield the ketone[7].

2.2. Reactions with Lewis Bases

The behavior of aliphatic and aromatic acyl halides toward organometallic Lewis bases, particularly carbonylmetalates, was studied in detail several years ago[8–11].

$$RCOCl + Na[M(CO)_n] \xrightarrow{(C_2H_5)_2O} R-C(=O)-M(CO)_n + NaCl$$

e.g. R = CH_3, C_2H_5, C_6H_5, *etc.*; M = Mn, Re; $n = 5$; M = Co; $n = 4$, *etc.*

This reaction yields extremely reactive acylcarbonylmetal compounds, some of which are of industrial interest[10]. Derivatives are also known in which CO groups are replaced by other ligands, as in $CH_3COCo(CO)_3PR_3$[12] and π-$C_5H_5Fe(CO)_2COCH_3$[13], with the result that the stability is generally greatly

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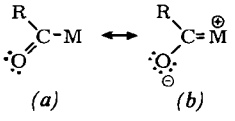
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increased [14]. It is interesting to note that only the *trans* complexes are obtained in the case of $RCO\text{-}Co(CO)_3PR_3$; the acyl residue and the phosphine ligand are arranged axially around the Co atom, and the three CO groups equatorially (pseudo-C_{3v}) [15]. On the other hand both *cis* and *trans* forms of the pseudo-octahedral Mn complexes of the type $RCOMn(CO)_4PR_3$ [16–18] have been isolated [17–19].

A characteristic of all acylmetal compounds is that owing to the strong donor properties of the metal, the keto (⟩C=O) stretching bands, in the sense of the polar limiting form *(b)* are strongly shifted toward longer wavelengths, pointing to a weakened C=O



(a) *(b)*

bond [11]. Carbonylacylmetal compounds eliminate CO when heated in the absence of air [8,9,11]. This reaction has been followed for acetylpentacarbonylmanganese with the aid of the isotopes ^{14}C [20] and ^{13}C [21]:

$$CH_3\overset{*}{C}OMn(CO)_5 \rightarrow CH_3Mn(CO)_4\overset{*}{C}O + CO$$

The CO removed was originally terminal, *i.e.* it did not come from the acetyl group. Conversely, no activity of the acetyl group can be detected in a reaction of $\overset{*}{C}O$ on $CH_3Mn(CO)_5$ under pressure [22]:

$$CH_3Mn(CO)_5 + \overset{*}{C}O \rightarrow CH_3COMn(CO)_4\overset{*}{C}O$$

Similar experiments with organocobalt derivatives led to the same results [15]. When partly halogenated acyl chlorides, such as CH_2XCOCl (X = F, Cl), are used, rotational isomers of the type $CH_2XCOMn(CO)_5$ are observed in the reaction with $[Mn(CO)_5]^-$, as is shown by NMR and IR data [23].

Perfluorinated acyl halides [24–27] or anhydrides of carboxylic acids [11,28,29] react with organometallic Lewis bases to give the carbonylperfluoroacylmetal compounds.

$$RCOX + Na[M(CO)_n] \rightarrow NaX + RCOM(CO)_n$$

R = CF_3, C_2F_5, C_3F_7 *etc.*; X = Cl, OCOR; M = transition metal

The stability of the metal complexes is considerably increased by the introduction of perfluoroalkyl groups, which relieve the metals of their negative charge. This is particularly noticeable in the case of cobalt; whereas $CH_3COCo(CO)_4$ [10,14] decomposes rapidly above −30 °C, $CF_3COCo(CO)_4$ [28] is stable up to 55 °C. Carbonylperfluoroacylmetal complexes can also be decarbonylated [26–29]; the products are the carbonylperfluoroalkylmetal complexes, which are thermally stable and resistant to atmospheric oxygen. The higher homologs $C_2F_5COCo(CO)_4$ and $C_3F_7COCo(CO)_4$ characteristically eliminate CO at much lower temperatures (>30 and >0 °C respectively) [29]. The carbonyl group between the metal and the perfluoroalkyl residue is thus evidently increasingly eliminated as the number of F atoms increases.

As expected, the electron-attracting perfluoroalkyl residues shift the keto (⟩C=O) stretching bands to higher frequencies in relation to those of the unfluorinated acylmetal compounds (cf. Table 1).

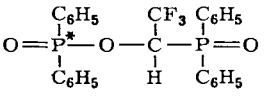
The behavior of acyl halides toward organophosphorus and organoarsenic compounds has also been studied. *Issleib* and *Priebe* [30] were the first to obtain $CH_3COP(C_6H_5)_2$ [from CH_3COCl and $LiP(C_6H_5)_2$], which can be readily oxidized with oxygen to $CH_3COPO(C_6H_5)_2$. Since Lewis basicity decreases in the order amines (though these occupy a special place because of the absence of energetically favorable d orbitals in nitrogen), phosphines, arsines, and stibines, it is particularly interesting to compare the properties of perfluoroacyldiphenylphosphines and perfluoroacyldiphenylarsines [31].

$$RCOX + MEl(C_6H_5)_2 \xrightarrow[THF]{-78\,^\circ C} RCOEl(C_6H_5)_2 + MX$$

R = CF_3, C_2F_5; X = Cl, Br, OCOR; M = Na, K; El = P, As

The colorless to orange-red liquids are extremely sensitive to air and moisture.

Contrary to expectations, oxidation of $CF_3COP(C_6H_5)_2$ with molecular oxygen leads, not to $CF_3COPO(C_6H_5)_2$, but by a complicated path that depends on the solvent (toluene or hexane) to 1-diphenylphosphoryl-2,2,2-trifluoroethyl diphenylphosphinate [31a] and CO_2. The



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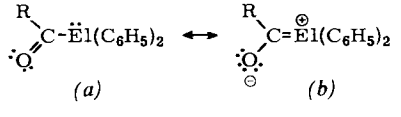
structure was demonstrated by alkaline decomposition to diphenylphosphinic acid and trifluoroethanol, and by mass spectroscopic (molecular mass line: 500), NMR (two ^{31}P signals), and IR studies. The proton on the asymmetric C atom gives the splitting scheme of first order coupling in the high-resolution ^1H-NMR spectrum, *i.e.* a doublet of quartets of doublets (coupling constants: $^2J_{HP} = 12.5$ Hz; $^3J_{HP^*} = 4.7$ Hz; $^3J_{HF} = 7.8$ Hz). The IR spectrum is characterized in particular by $\nu(C-H_{aliphat.})$ (2924 cm^{-1}) and ν_{as} $(P-O-C_{aliphat.})$ (1092 cm^{-1}) apart from the intense P–O and CF_3 stretching vibrations. The peculiar oxidation behavior of $CF_3COP(C_6H_5)_2$ is due to the electron-attracting CF_3 group and the lone pair of electrons on the phosphorus.

Whereas $CH_3COP(C_6H_5)_2$ and the perfluoroacyldiphenylarsines decompose when heated in the absence of air, perfluoroacyldiphenylphosphines, like the acylcarbonylmetal and carbonylperfluoroacylmetal compounds, quantitatively eliminate CO to form perfluoroalkyldiphenylphosphines. The removal of CO is evidently facilitated when the keto group is directly

$$RCOP(C_6H_5)_2 \xrightarrow{175\,^\circ C/190\,^\circ C} RP(C_6H_5)_2 + CO$$
$$R = CF_3,\ C_2F_5$$

flanked by a strong electron donor and an electronegative alkyl residue. $CF_3P(C_6H_5)_2$ can also be prepared from $(C_6H_5)_2PP(C_6H_5)_2$ and CF_3I [32].

An insight into the molecular structure and the difference in the chemical behavior of perfluoroacylphosphines and perfluoroacylarsines is provided above all by the IR spectra. The phosphines are characterized by the very low frequency (1702 cm^{-1}) of the keto (>C=O) stretching vibrations, whereas the corresponding band for the homologous arsines, in agreement with their weaker donor properties, is situated at a wave number about 55 cm^{-1} higher [31]. This is probably due to stronger participation of the limiting form *(6)* in the phosphorus compounds than in the arsenic compounds.



(a) *(b)*

The other IR data support this view, the CF_3 and P–C_{acyl} stretching vibrations being particularly characteristic.

Moreover, the behavior of $CF_3COSn(CH_3)_3$, which was recently isolated in the reaction of $LiSn(CH_3)_3$ with CF_3COCl, is quite comparable with that of $CF_3COAs(C_6H_5)_2$. Owing to tin's lack of donor properties, the colorless liquid does not eliminate CO when heated, and is even stable to dry oxygen. In agreement with this, the keto (>C=O) stretching vibration occurs at a very short wavelength [32a].

Table 1 shows a comparison of the C–O stretching frequencies and force constants of (trifluoro)acetyl fluoride and some derivatives.

Table 1. C–O stretching vibrations and estimated force constants of (trifluoro)acetyl fluoride and some derivatives.

Compound	$\nu(CO)$ (cm^{-1})	f_{CO} (mdyn/Å)	Ref.
CH_3COF	1848	13.79	[3]
CF_3COF	1901	14.59	[33]
$[CH_3CO]\,[PF_6]$	2297	21.30	[3]
$[CH_3CO]\,[SbF_6]$	2294	21.23	[3]
$[CF_3CO]\,[SbF_6]$	2371	22.70	[6, 7]
$CH_3COMn(CO)_5$	1640	10.86	[11]
$CH_3COCo(CO)_3P(C_6H_5)_3$	1666	11.22	[14]
$CF_3COMn(CO)_5$	1643	10.90	[11]
$CF_3COCo(CO)_3P(C_6H_5)_3$	1679	11.38	[28]
$CH_3COP(C_6H_5)_2$			[30]
$CF_3CON(C_6H_5)_2$			[34]
$CF_3COP(C_6H_5)_2$	1702	11.70	[31]
$CF_3COAs(C_6H_5)_2$	1758	12.48	[31]
$CF_3COSn(CH_3)_3$	1792	12.96	[32a]

3. Thioacyl Halides

A particularly interesting aspect in systematic studies is the behavior of thioacyl halides toward Lewis acids and Lewis bases. The only thioacyl halide that has been verified in every respect so far is thiobenzoyl chloride. *Staudinger* and *Siegwart* [35] obtained this compound as early as 1920 from dithiobenzoic acid and thionyl chloride. The preparation of CF_3CSCl [36] was also described for the first time in a patent a few years ago.

3.1. Reactions with Lewis Acids

As was seen in Section 2.1, the "silver salt method" is particularly suitable for the preparation of acylium salts. Stoichiometric quantities of C_6H_5CSCl and $Ag[SbF_6]$ react in liquid SO_2 at −40 °C to give an extremely hygroscopic, light brown complex, which is found even at room temperature to be the surprisingly stable thiobenzoylium hexafluoroantimonate(v) [37]:

$$C_6H_5CSCl + Ag[SbF_6] \xrightarrow[\text{liq. } SO_2]{-40\,^\circ C} [C_6H_5CS]\,[SbF_6] + AgCl$$

The ionic structure is shown by conductivity measurements (equivalent conductivity at −50 °C: Λ_c = 80.9 Ω^{-1} cm^2mole^{-1}), by IR studies [$\nu(C-S) = 1332$ cm^{-1}; $\nu(SbF_6^-) = 673$ cm^{-1} (T_{1u})], and by reaction with benzene:

$$[C_6H_5CS]\,[SbF_6] + C_6H_6 \rightarrow (C_6H_5)_2CS + H[SbF_6]$$

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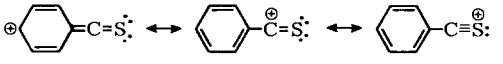
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Thiobenzophenone is formed in a yield of about 40 %. This was the first reaction to yield a thioacylium ion, and it was shown that thioacyl halides also react by the Friedel-Crafts mechanism. *Mayer* and *Scheithauer* [38] had previously obtained thiobenzophenone from thiobenzoyl chloride, benzene, and anhydrous Al_2Cl_6, and these authors also explained the reaction by a Friedel-Crafts mechanism.

According to the IR spectrum, the $[C_6H_5CS]^+$ cation can be essentially described by the limiting formulas *(1a)–(1c)*.

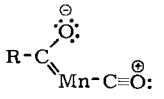


(1a) *(1b)* *(1c)*

3.2. Reactions with Lewis Bases

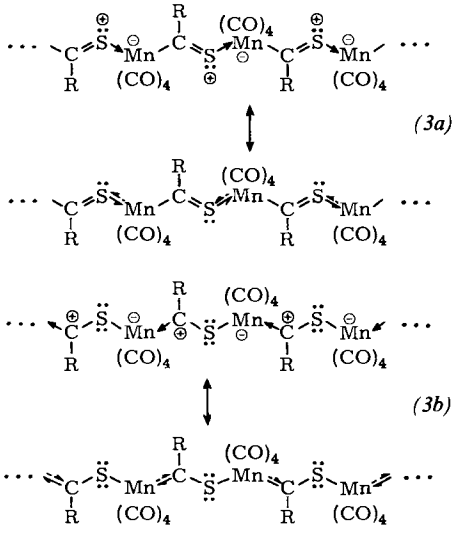
The reactions of thioacyl halides with organometallic Lewis bases are much more complicated than those of acyl halides, and are by no means uniform. Thus C_6H_5CSCl and $Na[Mn(CO)_5]$ react quantitatively at −78 °C in THF to give $C_6H_5CSMn(CO)_5$ [39]; however, this product eliminates one CO per Mn atom above −70 °C. In contrast with the reactions of the $[Mn(CO)_5]^-$ anion with acyl halides [11], carboxylic acid anhydrides [28,29], or even sulfonyl halides, in which the reaction product still contains an intact $Mn(CO)_5$ residue, no such product can be obtained in this case. The product isolated is instead a non-polar, chromatographically uniform brown compound that is inert to atmospheric oxygen, and which has the formula $[C_6H_5CSMn(CO)_4]_n$ (n is 3 or 4, depending on whether the reaction mixture is warmed rapidly or slowly to room temperature). It must be assumed from the solubility behavior of the "tetrameric" Mn compound that it is polymeric in the solid state, and breaks down into smaller fragments only on dissolution. It is interesting to note that the molecular weight of the "tetramer" falls to that of the "trimer" within a few days.

The coordination vacancy created on the manganese by the loss of CO is filled by the sulfur, as is shown in particular by IR data. The long wavelength of the ν(⟩C=O) band for the acylpentacarbonylmanganese compounds (cf. Section 2.2) points to appreciable participation of the polar limiting form *(2)*. Formal



(2)

replacement of the oxygen in the acyl residues by sulfur should lead to a decrease in the C–S bond order. Finally, the nucleophilic strength of the sulfur is understandable if one considers that sulfur is more readily polarizable than oxygen because of its greater atomic radius, and the nucleophilic strength is further increased by the negative charge carried by the sulfur in the polar limiting form. Intramolecular elimination of CO seems to be ruled out for steric reasons, so that only polymeric products are to be expected. One does in fact obtain a compound consisting of ···-$Mn(CO)_4$-C(R)–S–$Mn(CO)_4$–C(R)–S–··· units. The compound may be regarded either as a thioketone complex *(3a)* or as a carbene complex *(3b)* [40]; no distinction can be made on the basis of the IR spectrum.



(3a)

(3b)

It is interesting to note that there is no absorption between 700 and 1500 cm^{-1} that can be assigned to a C–S stretching vibration. However, a new band of medium to low intensity, which suggests a C–S vibration, appears at 630 cm^{-1} (cf. Table 2). In agreement with the proposed structures *(3a)* and *(3b)*, the spectrum also shows four C–O absorptions having very high wave numbers (*cis* position of the CO groups), *i.e.* 2100, 2020, 2011, and 1955 cm^{-1} for $n = 3$ and 2090, 2032, 2008, and 1956 cm^{-1} for $n = 4$. Only X-ray structural analysis can show whether structure *(3a)* or *(3b)* is present, since the Mn–C distance should be greater than 2 Å in a carbene complex [41].

The reaction of C_6H_5CSCl with the Lewis base $[Re(CO)_5]^-$ is fundamentally different from the reaction with $[Mn(CO)_5]^-$. All the results with $[Re(CO)_5]^-$ point to the formation of a dithiolate complex [42].

Table 2. C—S stretching vibrations and estimated force constants of C_6H_5CSCl and some derivatives.

Compound	ν(C—S) (cm^{-1})	f_{CS} (mdyn/Å)
C_6H_5CSCl	1250	8.03
$[C_6H_5CS][SbF_6]$	1332	9.12
$[C_6H_5CSMn(CO)_4]_n$	630	≈2.0

[38] *R. Mayer* and *St. Scheithauer*, J.prakt.Chem. *21*, 214 (1963).

[39] *E. Lindner*, Part of Habilitationsschrift, Universität Erlangen-Nürnberg 1967; *E. Lindner*, *H. Weber*, and *H.-G. Karmann*, J. organometallic Chem. *17*, 303 (1969).

[40] Cf. *e.g. E. O. Fischer* and *A. Maasböl*, Angew. Chem. *76*, 645 (1964); Angew. Chem. internat. Edit. *3*, 580 (1964).

[41] *O. S. Mills* and *A. D. Redhouse*, Angew. Chem. *77*, 1142 (1965); Angew. Chem. internat. Edit. *4*, 1082 (1965).

[42] *E. Lindner* and *H. Weber*, unpublished.

4. Phosphoryl Halides and Diorganophosphinyl Halides

4.1. Reactions with Lewis Acids

On reaction of phosphoryl halides (OPX_3; X = Cl, Br) with $Ag[SbF_6]$[39] in a polar solvent such as acetonitrile, though AgX separates out of the solution, no salt $[OPX_2]^+ [SbF_6]^-$ is formed. $Ag[SbF_6]$ evidently acts as a fluorinating agent in this case; OPF_3 ($\nu(P-O)$ = 1415 cm^{-1}) is formed quantitatively, irrespective of the stoichiometric ratio of the starting compounds

$$OPX_3 + 3\ Ag[SbF_6] \xrightarrow{20\,^\circ C} OPF_3 + 3\ AgX + 3\ SbF_5$$

The instability of phosphorylium ions is so severe that even organosubstituted derivatives $[R_2PO]^+$ cannot be stabilized. On reaction of bis(dimethylamino)phosphinyl chlorides or diphenylphosphinyl chloride on $Ag[SbF_6]$ in liquid SO_2 or acetonitrile in accordance with

$$R_2POCl + Ag[SbF_6] \xrightarrow[\text{liq. } SO_2/CH_3CN]{T > 0\,^\circ C} R_2POF{\cdot}SbF_5 + AgCl$$

R = $(CH_3)_2N$, C_6H_5

only donor-acceptor complexes of the form $R_2P(F)O^{\delta\oplus}\ldots SbF_5^{\delta\ominus}$ could be detected[42a].

4.2. Reactions with Lewis Bases

Hieber and *Duchatsch*[43] have shown that the phosphoryl halides $OPCl_3$ and $OPBr_3$ halogenate organometallic Lewis bases. Reaction with $[Co(CO)_3P(C_6H_5)_3]^-$ leads primarily to the halogen derivatives, which are

$$OPX_3 + Na[Co(CO)_3P(C_6H_5)_3] \xrightarrow{-70\,^\circ C} XCo(CO)_3P(C_6H_5)_3 + NaX + \{OPX\}$$

X = Cl, Br

thermally unstable and immediately change into the dicarbonyl compounds $XCo(CO)_2[P(C_6H_5)_3]_2$.

Toward neutral Lewis bases, such as triphenylphosphine or triphenylarsine, phosphoryl halides and thiophosphoryl halides act as excellent chalcogen transfer agents[44].

$$El'PX_3 + El(C_6H_5)_3 \rightarrow PX_3 + El'El(C_6H_5)_3$$

El' = O, S; X = Cl, Br; El = P, As

This reaction can be applied to any monodentate or polydentate organophosphine or organoarsine.

For phosphoryl halides (X = Cl, Br) in particular, the transfer of chalcogen to phosphines takes place *via* an extremely hygroscopic, thermally stable, isolable intermediate. This was found from concentration-dependent molecular weight determinations, conductivity measurements, IR studies, and its hydrolysis properties to be an ionic dihalogenophosphoryltriphenylphosphonium halide containing a P–P bond[45]:

$$OPX_3 + P(C_6H_5)_3 \xrightarrow{OPX_3} [(C_6H_5)_3PP(X_2)O]X$$

The observed chalcogen transfer occurs only in the presence of small quantities of moisture:

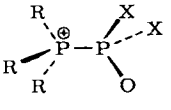
$$[(C_6H_5)_3PP(X_2)O]X \rightarrow OP(C_6H_5)_3 + PX_3$$

The salts may be regarded as substitution compounds of phosphoryl halides. Some time ago, *Gutmann*[46] described a crystalline adduct having the composition $OPCl_3{\cdot}2C_5H_5N$, which dissociates in $OPCl_3$ into the ions $[C_5H_5NP(Cl_2)O]^+$ and Cl^-. *Baaz* and *Gutmann*[47,48] later showed that tertiary aliphatic amines, as Lewis bases, also have a substituting action in $OPCl_3$ solution:

$$(C_2H_5)_3N + OPCl_3 + FeCl_3 \xrightarrow{OPCl_3} [(C_2H_5)_3NP(Cl_2)O][FeCl_4]$$

$As(C_6H_5)_3$, which is very readily soluble in $OPCl_3$, also reacts with the solvent[45]. However, the colorless $[(C_6H_5)_3AsP(Cl_2)O]Cl$ slowly loses $OPCl_3$ above room temperature, owing to the weaker donor properties of $As(C_6H_5)_3$.

The number of IR absorptions in the spectra of the compounds $[(C_6H_5)_3PP(X_2)O]X$ points to low symmetry [point group C_s, with $P(C_6H_5)_3$ as a point mass]. This leads to a pseudotetrahedral arrangement of the four ligands [2 X^-, $P(C_6H_5)_3$, and O] about the central phosphorus atom (Fig. 1).



R = C_6H_5

Fig. 1. Structural model of the cations $[(C_6H_5)_3PP(X_2)O]^+$.

As can be seen from Table 3, the P–O and P–Cl stretching vibrations in the phosphonium salts occur at higher frequencies than in the parent compounds

Table 3. P–O and P–Cl stretching vibrations of phosphoryl halides and their substitution products $[(C_6H_5)_3PP(X_2)O]X$.

Compound	Structure	ν(P–O) (cm^{-1})	ν(P–X) (cm^{-1})
$OPCl_3$	C_{3v}	1290 (A_1)	577 (E) 486 (A_1)
$OPBr_3$	C_{3v}	1261 (A_1)	488 (E) 340 (A_1)
$[(C_6H_5)_3PP(Cl_2)O]Cl$	C_s	1320 (A′)	587 (A′) 564 (A″)
$[(C_6H_5)_3PP(Br_2)O]Br$	C_s	1305 (A′)	492 (A′) 479 (A″)

[42a] *E. Lindner* and *K.-M. Matejcek*, Z. anorg. allg. Chem., in press.

[43] *W. Hieber* and *H. Duchatsch*, Chem. Ber. *98*, 2530 (1965).

[44] *E. Lindner*, unpublished.

[45] *E. Lindner* and *H. Schless*, Chem. Ber. *99*, 3331 (1966).

[46] *V. Gutmann*, Mh. Chem. *85*, 1077 (1954).

[47] *M. Baaz* and *V. Gutmann*, Mh. Chem. *90*, 276 (1959); *90*, 744 (1959).

[48] *M. Baaz*, *V. Gutmann*, and *L. Hübner*, Mh. Chem. *92*, 707 (1961).

OPX_3 corresponding to greater double-bond components in the P–O and P–Cl bonds, owing to the positive charge on the phosphorus of the PR_3 group. Dihalogenophosphoryltriphenylphosphonium halides can be converted specifically into 1:1 triphenylphosphine oxide-metal halide complexes containing a metal-oxygen-phosphorus bridge by reaction with metal halides. This reaction, which is of preparative interest, proceeds particularly well when the metal halides are soluble in an inert solvent (ether).

$$[(C_6H_5)_3PP(Cl_2)O]Cl + MCl_n \rightarrow (C_6H_5)_3POMCl_n + PCl_3$$

Many new 1:1 complexes have been obtained in this way [MCl_n = $TiCl_4$ (complex: yellow), $ZrCl_4$ (pale yellow), VCl_3 (pink), $FeCl_3$ (light yellow), and $CoCl_2$ (deep blue)]. The $AlCl_3$-[50] and $NbCl_5$ adducts[51] prepared by these reactions are already known.

The triorganophosphine oxide-metal halide complexes described many years ago by *Pickard* and *Kenyon*[52] have recently been subjected by numerous authors[51,53–56] to IR-[57] and UV spectroscopic studies[58].

While *Tyree et al.*[59], *Cotton et al.*[60], and *Merijanian* and *Zingaro*[61] also extended these studies to triorganoarsine oxides, *Tyree et al.*[58,62], *Gans et al.*[63], *Kohl*, *Lewis*, and *Whyman*[64], and *Hart* and *Newbery*[65] also reported on triphenylphosphine oxide-metal oxide halide complexes. The compounds can be prepared in general by direct action of triphenylphosphine oxide on the metal halide, and contain more $OP(C_6H_5)_3$ than they should for a ratio of 1:1. On the other hand, the formation of the few hitherto known 1:1 triarylphosphine oxide-metal halide adducts[50,51,66] was fortuitous.

The intense ν_{as}(P–O–M) bands[49] lie between 1160 and 950 cm^{-1} depending on the acceptor strength of the metal, and are shifted (considerably in some cases) toward longer wavelengths in relation to that of $OP(C_6H_5)_3$ (1191 cm^{-1}). Since each metal atom is bonded to only one phosphine oxide residue, the $(p\rightarrow d)_\pi$ back-bonding component of the O–P bond is greatly decreased. This can be illustrated by two titanium compounds; $2(C_6H_5)_3PO \cdot TiCl_4$[53]: ν(P–O) = 1130 cm^{-1}; $(C_6H_5)_3POTiCl_4$[49]: ν(P–O) = 1060 cm^{-1}.

The ν_s(P–O–M) stretching vibrations are more difficult to assign; this has been achieved with certainty for $(C_6H_5)_3POAlCl_3$[49,67] and $(C_6H_5)_3POCoCl_2$[49] (cf. Table 4). The simplified calculation of the force constants for the P–O and Al–O bonds on the basis of the three-particle model gives f_{PO} = 7.5 mdyn/Å and f_{AlO} = 1.7 mdyn/Å; the two P–O and Al–O oscillators are therefore strongly coupled with each other. By application of the Siebert approximation[68], bond orders of 1.7 and 0.3 are estimated for the P–O and Al–O bonds respectively. The relatively small force constant of the weak Al–O bond, which is characteristic of this addition complex, can be confirmed by experimental observations[49]. With the stronger acceptors $TiCl_4$, $ZrCl_4$, and particularly $NbCl_5$, the ν_{as}(P–O–M) stretching vibrations absorb at unusually low frequencies, corresponding to a stronger metal-oxygen bond. Finally, with $MoCl_5$ or WCl_6, the oxygen is actually displaced from the phosphorus to the metal[49,62,69,70].

Table 4. Some P–O–M stretching vibrations of 1:1-triphenylphosphine oxide-metal halide complexes.

Compound	ν_s(P–O–M) (cm^{-1})	ν_{as}(P–O–M) (cm^{-1})	Ref.
$(C_6H_5)_3POAlCl_3$	388	1156	[49, 50]
$(C_6H_5)_3POCoCl_2$	417	1152	[49]
$(C_6H_5)_3POTiCl_4$	–	1060	[49]
$(C_6H_5)_3POZrCl_4$	–	1054	[49]
$(C_6H_5)_3PONbCl_5$	–	939 953	[49, 51]

5. Sulfonyl Halides and Perfluorinated Sulfonyl Halides

5.1. Reactions with Lewis Acids

By reaction of *p*-$CH_3C_6H_4SO_2Br$ with $Ag[ClO_4]$, *Klages et al.*[71] were able to show that *p*-toluenesulfonylium ions probably exist in liquid SO_2 below –60 °C. If instead of $Ag[ClO_4]$ one uses $Ag[SbF_6]$, which has repeatedly given successful results in the past, only

[49] *E. Lindner*, *R. Lehner*, and *H. Scheer*, Chem. Ber. *100*, 1331 (1967).

[50] *M. J. Frazer*, *W. Gerrard*, and *R. Twaits*, J. inorg. nuclear Chem. *25*, 637 (1963).

[51] *D. Brown*, *J. F. Easey*, and *J. G. H. du Preez*, J. chem. Soc. (London) *A 1966*, 258.

[52] *R. H. Pickard* and *J. Kenyon*, J. chem. Soc. (London) *1906*, 262.

[53] *J. C. Sheldon* and *S. Y. Tyree*, J. Amer. chem. Soc. *80*, 4775 (1958).

[54] *D. M. L. Goodgame* and *F. A. Cotton*, J. chem. Soc. (London) *1961*, 3735.

[55] *K. Issleib* and *H. Reinhold*, Z. anorg. allg. Chem. *314*, 113 (1962).

[56] *H. Clees* and *F. Huber*, Z. anorg. allg. Chem. *352*, 200 (1967).

[57] *F. A. Cotton*, *R. D. Barnes*, and *E. Bannister*, J. chem. Soc. (London) *1960*, 2199.

[58] *S. M. Horner* and *S. Y. Tyree jr.*, Inorg. Chem. *2*, 568 (1963).

[59] *D. J. Phillips* and *S. Y. Tyree jr.*, J. Amer. chem. Soc. *83*, 1806 (1961).

[60] *D. M. L. Goodgame*, *M. Goodgame*, and *F. A. Cotton*, Inorg. Chem. *1*, 239 (1962); *G. A. Rodley*, *D. M. L. Goodgame*, and *F. A. Cotton*, J. chem. Soc. (London) *1965*, 1499.

[61] *A. Merijanian* and *R. A. Zingaro*, Inorg. Chem. *5*, 187 (1966).

[62] *S. M. Horner* and *S. Y. Tyree jr.*, Inorg. Chem. *1*, 122 (1962).

[63] *P. Gans* and *B. C. Smith*, J. chem. Soc. (London) *1964*, 4172.

[64] *F. J. Kohl*, *J. Lewis*, and *R. Whyman*, J. chem. Soc. (London) *A 1966*, 630.

[65] *F. A. Hart* and *J. E. Newbery*, J. inorg. nuclear Chem. *28*, 1334 (1966).

[66] *M. E. Peach* and *T. C. Waddington*, J. chem. Soc. (London) *1962*, 3450.

[67] *E. W. Wartenberg* and *J. Goubeau*, Z. anorg. allg. Chem. *329*, 269 (1964).

[68] *H. Siebert*, Z. anorg. allg. Chem. *273*, 170 (1953).

[69] *C. G. Barraclough*, *J. Lewis*, and *R. S. Nyholm*, J. chem. Soc. (London) *1959*, 3552.

[70] *F. A. Cotton* and *R. M. Wing*, Inorg. Chem. *4*, 867 (1965).

[71] *F. Klages* and *K. Hoheisel*, Chem. Ber. *96*, 2057 (1963); *F. Klages* and *F. E. Malecki*, Liebigs Ann. Chem. *691*, 15 (1966).

halogen exchange is observed at room temperature [72]. CF_3SO_2Cl and FSO_2Cl do not react with $Ag[SbF_6]$ [73]. Organosulfonylium ions cannot be stabilized even by strong Lewis acids unless the sulfur can transfer its positive charge to the organic residue, with participation of quinonoid limiting forms in the case of aromatic systems [72].

Thus the *p*-dimethylaminobenzenesulfonylium ions *(4)*, which (for El = Sb) are stable up to room tem-



(4a) *(4b)*

perature, but are very hygroscopic, can be prepared in accordance with

$$RSO_2Cl + Ag[ElF_6] \xrightarrow[\text{liq. } SO_2]{-25\,^\circ C} [RSO_2][ElF_6] + AgCl$$

$R = p\text{-}(CH_3)_2NC_6H_4$; El = Sb, As, P

from $p\text{-}(CH_3)_2NC_6H_4SO_2Cl$ [containing the $(CH_3)_2N$ residue, which acts as a strong electron donor] and the complexes $Ag[ElF_6]$ in liquid SO_2.

The participation of the quinonoid limiting form *(4b)* deepens the color of the complexes. This effect is particularly noticeable in *p*-dimethylaminobenzenesulfonylium hexafluoroantimonate(v), which is readily soluble in liquid SO_2, and whose deep orange color [$p\text{-}(CH_3)_2NC_6H_4SO_2Cl$ is lemon yellow] is a definite indication of the quinonoid form *(4b)*. Further evidence is provided by the electronic spectra. Whereas $p\text{-}(CH_3)_2NC_6H_4SO_2Cl$ has an intense maximum in the visible region at 24509 cm^{-1}, the band characteristic of the cation shows a bathochromic shift to 21 413 cm^{-1}. The ionic structure of the antimony complex is also shown by conductivity measurements in nitromethane (cf. Table 5).

Owing to the conjugation effect [limiting form *(4b)*], the symmetric and asymmetric SO_2 vibrations of $[p\text{-}(CH_3)_2NC_6H_4SO_2][SbF_6]$ absorb at higher frequencies than the corresponding vibrations in $p\text{-}(CH_3)_2NC_6H_4SO_2F$ (cf. Table 7). The stronger O–S double bond character [$(p\rightarrow d)_\pi$] and the intense absorption band at 662 cm^{-1} [$\nu(SbF_6^-)$ (T_{1u})] also point to the ionic structure. The stability of the $[p\text{-}(CH_3)_2NC_6H_4SO_2]^+$ cation decreases with decreasing acceptor strength of the Lewis acids AsF_5, PF_5, and BF_3. Table 5 shows a comparison of the properties of some *p*-dimethylaminobenzenesulfonyl and *p*-dimethylaminobenzenesulfonylium compounds.

Table 5. Properties of compounds of the type $p\text{-}(CH_3)_2NC_6H_4SO_2X$ and $[p\text{-}(CH_3)_2NC_6H_4SO_2]X$.

X	Color	Stability	Conductivity (Ω^{-1} cm^2 mole^{-1})
Cl	yellow	stable	–
F	beige	stable	–
SbF_6	orange	up to 30 °C	74.64
AsF	olive green	up to −20 °C	8.26
PF_6	light green	up to −25 °C	10.58
BF_4	–	not isolable	–

[72] *E. Lindner* and *H. Weber*, Chem. Ber. *101*, 2832 (1968).

[73] *E. Lindner*, unpublished.

5.2. Reactions with Lewis Bases

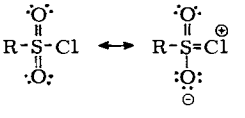
Organometallic sulfonyl or "*S*-sulfinato" complexes have been known only since 1964 [74]. They can be prepared by two basic methods:

a) by the action of sulfonyl halides or sulfonic acid anhydrides on organometallic Lewis bases, and

b) by insertion of SO_2 between the metal and the organic residue ("SO_2 insertion").

Neither process is generally applicable, but each complements the other.

Method a): The action of $p\text{-}CH_3C_6H_4SO_2Cl$ on the Lewis base $[Mn(CO)_5]^-$ leads not only to the expected pentacarbonyl-*p*-toluenesulfonylmanganese and $ClMn(CO)_5$, but also to a series of by-products, some of which are polymeric [75], and which prevent the preparation of pure $p\text{-}CH_3C_6H_4SO_2Mn(CO)_5$. The formation of $ClMn(CO)_5$ is based on the strongly electron-attracting effect of the *p*-toluenesulfonyl residue on the Cl atom; the halogen atom acquires a positive charge because of the inductive effect, with the result that the S–Cl bond assumes double bond character [76]. The instability of the $[p\text{-}CH_3C_6H_4SO_2]^+$ cation confirms these views.



If, however, $p\text{-}CH_3C_6H_4SO_2Cl$ is replaced by the anhydride $(p\text{-}CH_3C_6H_4SO_2)_2O$, heterolysis occurs in the presence of the carbonylmetalates of manganese, iron, and cobalt, which act as Lewis bases.

$$RSO_2\text{–}O\text{–}SO_2R \rightleftharpoons [RSO_2]^+ [RSO_3]^-$$

$R = p\text{-}CH_3C_6H_4$

The extremely unstable $[RSO_2]^+$ cation immediately reacts further with the anions mentioned [76], as follows:

$$[RSO_2]^+ + [\text{Lewis base}]^- \xrightarrow[THF]{-80\,^\circ C} RSO_2\text{Lewis base}$$

$[\text{Lewis base}]^- = [Mn(CO)_5]^-$, $[\pi\text{-}C_5H_5Fe(CO)_2]^-$, and $[Co(CO)_3P(C_6H_5)_3]^-$

Like the reaction of perfluorinated carboxylic acid anhydrides with carbonylmetalates, this reaction proceeds almost quantitatively [28,29]. The diamagnetic compounds [RSO_2Lewis base] are thermally very stable. The method is not applicable to other systems (*e.g.* $[Re(CO)_5]^-$ or $[\pi\text{-}C_5H_5Mo(CO)_3]^-$).

Unlike *p*-toluenesulfonic acid anhydride, $(CF_3SO_2)_2O$ is totally unsuitable for the introduction of a CF_3SO_2

[74] *J. P. Bibler* and *A. Wojcicki*, J. Amer. chem. Soc. *86*, 5051 (1964).

[75] *W. Beck*, private communication.

[76] *E. Lindner* and *H. Weber*, Z. Naturforsch. *22b*, 1243 (1967).

group; it oxidizes the carbonylmetalates to the neutral carbonylmetal compounds in every case[77]. The CF_3SO_2 derivatives were first isolated in yields of about 20 % on condensation of equimolar quantities of CF_3SO_2Cl with $[M(CO)_5]^-$ (M = Mn, Re), $[\pi\text{-}C_5H_5Fe(CO)_2]^-$, and $[Co(CO)_3P(C_6H_5)_3]^-$ in THF solution at −60 to −80 °C[77,78]:

$$CF_3SO_2Cl + [\text{Lewis base}]^- \rightarrow CF_3SO_2\text{Lewis base} + Cl^-$$

The perfluorinated compounds are thermally much less stable than the *p*-toluenesulfonyl derivatives (Table 6).

Table 6. Melting points and decomposition points of *p*-toluenesulfonyl and trifluoromethanesulfonyl complexes.

Compound	M.p. (°C)	Decomposition (°C)
$p\text{-}CH_3C_6H_4SO_2Mn(CO)_5$		150
$CF_3SO_2Mn(CO)_5$	83	120
$CF_3SO_2Re(CO)_5$	65	65
$p\text{-}CH_3C_6H_4SO_2(\pi\text{-}C_5H_5)Fe(CO)_2$		200
$CF_3SO_2(\pi\text{-}C_5H_5)Fe(CO)_2$		150
$p\text{-}CH_3C_6H_4SO_2Co(CO)_3P(C_6H_5)_3$		90
$CF_3SO_2Co(CO)_3P(C_6H_5)_3$		20
$CF_3SO_2(\pi\text{-}C_5H_5)NiCO$		−30

The principal products of the action of sulfonyl halides, and particularly of CF_3SO_2Cl, on carbonylmetalates are the carbonylchlorometal compounds, the yield of which largely depends on the electronegativity of the residue attached to the sulfonyl sulfur atom. It is significant that FSO_2Cl in which the CF_3 group has been replaced by the still more electronegative fluorine, reacts quantitatively with $Na[Mn(CO)_5]$ to give $ClMn(CO)_5$[78]

$$FSO_2Cl + Na[Mn(CO)_5] \xrightarrow[THF]{-80\,^\circ C} ClMn(CO)_5 + NaF + SO_2$$

and is therefore suitable for use as a mild halogenating agent. It would seem reasonable to prevent this undesirable reaction by the use of the sulfonyl fluorides instead of the chlorides, but this procedure has not acquired much importance, owing to the low yields[79]. The reaction of alkali metal organosulfinates with halogenated carbonylmetal compounds or halogenocarbonylmetalates has been used for the preparation of the Cr and W complexes $Na[M(CO)_5SO_2C_6H_5]$ (M = Cr, W)[80].

Finally, mention should also be made of the behavior of CF_3SO_2Cl toward carbonylmetal complexes with aromatic ligands ($[\pi\text{-}C_5H_5Fe(CO)_2]_2$[79] and $[\pi\text{-}C_5H_5NiCO]_2$[81]); the CF_3SO_2-iron and CF_3SO_2-nickel compounds listed in Table 6 are formed in yields of about 10%.

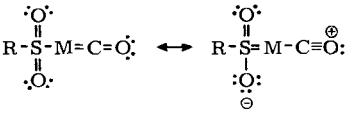
Method b): "SO_2 insertion" is particularly suitable for the preparation of carbonylalkanesulfonylmetal, carbonylbenzenesulfonylmetal, carbonyl-α-toluenesulfonylmetal, and carbonyl-*p*-toluenesulfonylmetal derivatives, which are formed in high yields and mostly without by-products[74,79,80,82], *e.g.*

$$RM(CO)_5 + SO_2 \rightarrow RSO_2M(CO)_5$$

Many sulfinato complexes derived from manganese[82], rhenium[80], and iron[79] have been obtained in this way: the compounds $RSO_2M(CO)_5$ (M = Mn, Re) and $\pi\text{-}C_5H_5Fe(CO)_2SO_2R$ (R = CH_3, C_2H_5, C_6H_5, $CH_2C_6H_5$, $p\text{-}CH_3C_6H_4$). Depending on the strength of the metal-carbon bond, liquid SO_2 is allowed to act on the organometallic compound (for example $\pi\text{-}C_5H_5Fe(CO)_2CH_3$[79]) either below the boiling point of SO_2 or under pressure at higher temperatures (about 40 °C) (*e.g.* $C_6H_5Mn(CO)_5$[80]). It is interesting to note that the SO_2 insertion cannot be applied to perfluorinated carbonylorganometallic compounds[80]. $CF_3Mn(CO)_5$ does not take up SO_2 even under extreme conditions; the metal-carbon bond is too strong, owing to the π-components.

The thermal behavior of the sulfonyl complexes described is quite different from that of the acyl compounds. No elimination of SO_2 was observed in any case[80]. The decomposition reactions are uncontrolled, and generally proceed with initial loss of CO.

The positions of the symmetric and asymmetric SO_2 stretching vibrations are strongly dependent on the nature of the residue X bound to the organosulfonyl group[76]. As can be seen from Table 7, their frequencies are highest for $p\text{-}CH_3C_6H_4SO_2F$, and, for the same organosulfonyl residue, they decrease with increasing donor strength of X; for the organometallic residues X = $Mn(CO)_5$, $\pi\text{-}C_5H_5Fe(CO)_2$, and $Co(CO)_3P(C_6H_5)_3$ in particular they fall by up to 200 cm^{-1}. This is also found in the trifluoromethanesulfonyl derivatives. The large decrease in the frequencies of the SO_2 bands is characteristic of organometallic sulfonyl compounds, and indicates the presence of strong bonds between the metal and the sulfur:



The electron-attracting CF_3 group causes a considerable increase in the frequencies of the SO_2 stretching vibrations. The low frequency $\nu_s(SO_2)$ and $\nu_{as}(SO_2)$ vibrations naturally mean that the C–O absorptions must occur at very short wavelengths, as was in fact found in every case. The spectra of the manganese and rhenium complexes are characterized by the presence of five absorptions in the terminal CO group region. The C_{4v} symmetry is so strongly perturbed because of the angular RSO_2 ligands that the B_1 vibration, which is forbidden in the IR, is in fact observed, and the band of the E vibration is also split.

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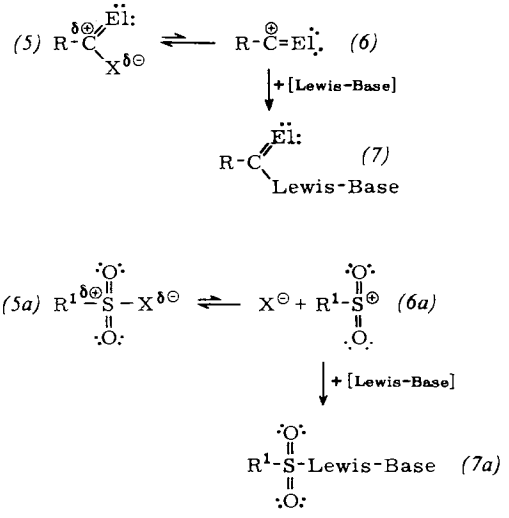
Table 7. Symmetric and asymmetric SO_2 stretching frequencies of some typical sulfonyl halides, sulfonylium compounds, and (perfluoro)-organosulfonylmetal complexes.

Compound	$\nu_s(SO_2)$ (cm^{-1})	$\nu_{as}(SO_2)$ (cm^{-1})	Ref.
p-$CH_3C_6H_4SO_2F$	1208 1218	1411	[76]
p-$CH_3C_6H_4SO_2Cl$	1177	1376	[76]
p-$(CH_3)_2NC_6H_4SO_2F$	1188	1393	[72]
p-$(CH_3)_2NC_6H_4SO_2Cl$	1160	1367	[72]
CH_3SO_2Cl	1192	1404	[83]
CF_3SO_2Cl	1128 1132	1440	[76, 77]
$[p$-$(CH_3)_2NC_6H_4SO_2]$ $[SbF_6]$	1195	1418	[72]
$CH_3SO_2Mn(CO)_5$	1053 1044	1201 1183	[82]
p-$CH_3C_6H_4SO_2Mn(CO)_5$	1045	1207	[76]
π-$C_5H_5Fe(CO)_2SO_2CH_3$	1061 1052	1194 1181	[79]
π-$C_5H_5Fe(CO)_2$—p-$SO_2C_6H_4CH_3$	1040	1192	[76]
$CF_3SO_2Mn(CO)_5$	1092	1220	[76]
π-$C_5H_5Fe(CO)_2SO_2CF_3$	1070	1232	[77]

6. Summary and Outlook

It was shown in Sections 2 to 5 that acylium, perfluoroacylium, thioacylium, and even sulfonylium ions are obtainable though only under extreme conditions in some cases. All the described reactions of acyl, perfluoroacyl, thioacyl, or sulfonyl halides and carboxylic acid or sulfonic acid anhydrides with organometallic, organophosphorus, or organoarsenic Lewis bases thus have fundamentally the same course. When a nucleophile dissolved in a polar medium approaches the acid halide or anhydride, the reaction proceeds uniformly *via* a transition state *(5)* or *(5a)* toward the limiting arrangement, the ions *(6)* or *(6a)* (heterolysis).

The intermediate cations *(6)* and *(6a)* can now react with the nucleophile, *i.e.* the Lewis base, to give the derivatives *(7)* and *(7a)* respectively. The rate-determining step is the heterolysis.



El = O; X = Cl, Br, OCOR; R = (perfluoro)organo group;
El = S; X = Cl; R = C_6H_5;
R^1 = p-$CH_3C_6H_4$, p-$(CH_3)_2NC_6H_4$; X = Cl, p-$OSO_2C_6H_4CH_3$

The surprising stability of the thiobenzoylium ion and the entirely novel polymeric tetracarbonylthiobenzoylmanganese compounds are of preparative interest. Thioacyl halides appear to be more reactive than other acid halides, as is shown by their behavior toward organometallic Lewis bases.

I am very grateful to my co-workers Dr. H. Kranz, Dr. H. Weber, Dr. G. Vitzthum, Dipl.-Chem. H.-G. Karmann, Dipl.-Chem. U. Kunze, Dipl.-Chem. H.-D. Ebert, and Dipl.-Chem. K.-M. Matejcek, who have played a vital part in these investigations, and to H. Schless, R. Lehner, and H. Scheer, who also made valuable contributions. Sincere thanks are due to Professor Dr.-Ing. H. Behrens for his interest in this work and for his generous support. I also thank the Verband der Chemischen Industrie, Fonds der Chemischen Industrie, and the Deutsche Forschungsgemeinschaft for their financial support.

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Structure of the Solvation Shell of Dissolved Particles

By H. G. Hertz[*]

The first part of the article deals with the structure of the solvation shell of simple ions, particularly those with the inert gas structure, in aqueous and non-aqueous solution. It is nowadays possible in favorable cases, to determine the solvation number or the coordination number in the first sphere. The solvation shells appear to be "more liquid" than was formerly believed. The hydration of neutral inert particles in aqueous solution is discussed in the second part. Caution is advised in the postulation of particular structural arrangements in the solution.

1. Introduction

An attempt is made to present some of the existing knowledge about the structure of the solvation shells of dissolved particles. It is not surprising that different views exist on a subject as complicated as this. Nevertheless, there should be no doubt about the experimental facts and their interpretation in the first part of the article. Toward the end of the article, on the other hand, it will be necessary to cover ground about which there is less certainty.

The results to be described here will be discussed from the points of view of the "molecular structures" of the liquids, the discussion being confined to liquid solutions in the narrowest sense. The essential nature of a liquid is best understood by considering it as a very large "heap" of molecules [1]. Figure 1 shows part of a

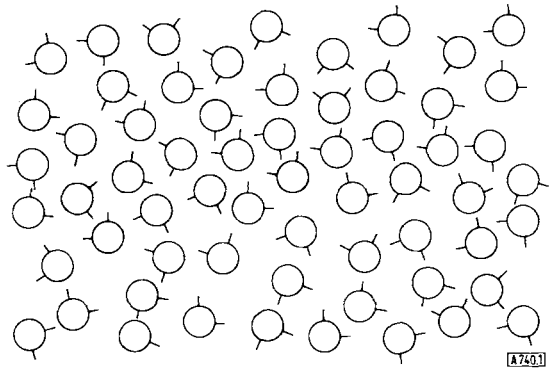


Fig. 1. Two-dimensional molecular model of a liquid.

two-dimensional analog of such an "heap". The molecules bear a certain resemblance to water molecules, but this is of no importance to the following discussion. The structure of this liquid can be described by the probability of finding certain intermolecular distances and orientations relative to an arbitrarily chosen molecule. This is described quantitatively by the molecular *distribution functions*, which generally contain several maxima and minima as a characteristic property of the *structure of the liquid* [2].

Figure 1 should be regarded as a "snapshot" showing the situation at one particular instant. For a low molecular weight liquid at room temperature, the picture of the liquid will have changed to such an extent after 10^{-11} to 10^{-10} sec, as a result of molecular motion, that any correlations in the arrangement of neighboring individual particles are no longer recognizable.

Introduction of foreign particles into the liquid leads to a change in its structure, and new molecular motions appear. The structural peculiarities that exist in the neighborhood of the dissolved particles and the nature of the molecular motions of solvent molecules, which are related to the dissolved particles form the subject of the present article.

Let us consider a few examples that illustrate the problem. Figures 2, 3, and 4 show possible effects of the dissolved particles on the structure of the solvent.

The classical positive solvation or hydration of ions (Fig. 2) needs no explanation. Figure 3 shows a slight change in the solvent in addition to pure replacement of particles. Accurate analysis of the distribution of the particles and of their orientation in relation to the ions and to themselves, *i.e.* the study of the molecular

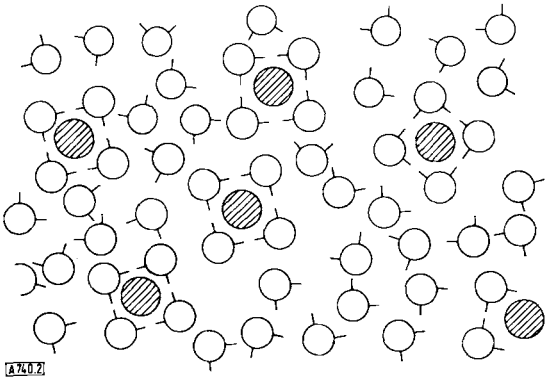


Fig. 2. Two-dimensional molecular model for strong solvation of dissolved particles in a liquid. In aqueous solution, the lines attached to the circles denote OH bonds for dissolved anions, and lone pairs of electrons for dissolved cations.

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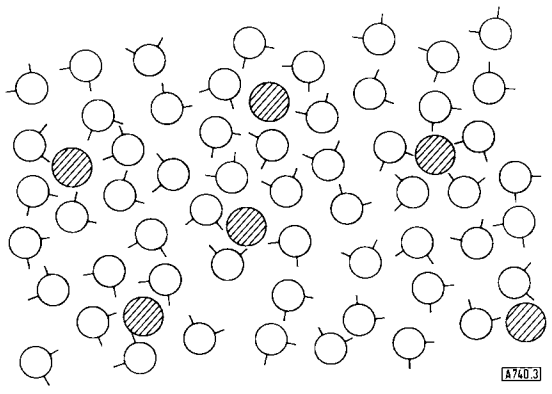


Fig. 3. Two-dimensional molecular model for weak solvation of dissolved particles in a liquid.

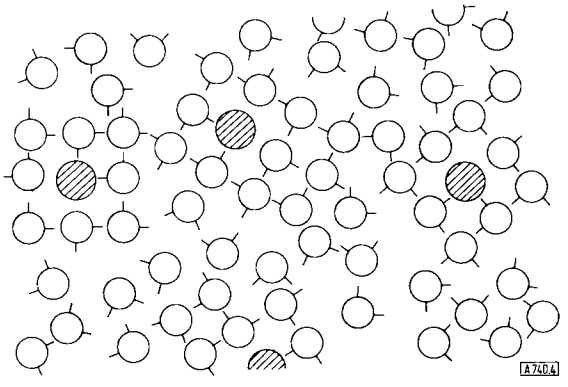


Fig. 4. Two-dimensional molecular model for solvation of "inert" dissolved particles with no fixed orientation between the molecules of the liquid and the dissolved particles.

distribution functions[2], would reveal that the ions act as centers of orientation, so that solvation of the ions is in fact present. In Figure 4 we see no orientation of a fixed molecular axis toward the center of the dissolved particle, but only orientation of the solvent molecules with respect to one another. It is to be expected that the linkage of two individual water molecules in the solvation shell of an ion in accordance with Figure 2 persists much longer than in pure water. The reorientation time of a molecule in the solvation shell will also be much longer than in pure water.

Figures 2, 3, and 4 provide some idea of what would be involved in a complete knowledge of the structural peculiarities of solvation. A precise analytical description would require a set of multi-dimensional molecular distribution functions[2], a requirement that is still far beyond our present capabilities. The gaps that remain will be pointed out in the following discussion. It will be seen that in addition to structural questions proper, molecular motions also play a part. The concept of solvation structure is accordingly extended to include molecular motions.

The discussion will however be confined to solvation phenomena connected with changes in the structure of the solvent around the *whole particle*. This excludes the wide field of specific interactions between molecules (or molecule-ions) in organic liquids. The following pages will thus be devoted to simple ions in aqueous and non-aqueous solvents and neutral particles in aqueous solution.

2. Solvation of Ions

2.1. True Solvation Structure

2.1.1. Aqueous Solutions

Let us first consider the old problem of hydration numbers. What are hydration numbers?

From the point of view of the structure, the question would have to be answered by considering Figure 2 or 3. As the situation passes from that of Figure 2 to that of Figure 3, however, it becomes increasingly difficult to specify a hydration number. It is generally necessary to decide arbitrarily which and how many water molecules are to be regarded as belonging to the hydration sphere. A reasonable procedure is to take the area under the first maximum or under the first two maxima of the radial probability distribution function for the pair ion-water molecule as a measure of the hydration number. For several reasons, hydration numbers defined in this manner will depend on the concentration.

Alternatively, we can try to define the hydration numbers from the point of view of the molecular motions. To do this, we follow the decay of the spatial correlation between the ion in question and the water molecules in its environment. If it is found, for example, that such a correlation exists for $n_h^{\pm}$ molecules, but not for any of the other molecules in the environment, then $n_h^{\pm}$ can be taken as the hydration number of the system. The result in this case will naturally depend on the time limit selected and the limit allowed for the breakdown of the correlations.

The conventional way to obtain the hydration number is as follows. One measures some physical quantity X, which is expressed in the form

$$X = X_0(1-x^+-x^-) + x^+X^+(n_h^+) + x^-X^-(n_h^-) \qquad (1)$$

x^+ and x^- are the mole fractions showing how many particles there are in the environment that is to be regarded as the hydration complex of the cation and of the anion respectively. $X^+(n_h^+)$, $X^-(n_h^-)$, and X_0 are the physical property in question for the hydration complexes of the cation and of the anion and for the unbound state. Both $x^{\pm}$ and $X^{\pm}$ can contain information about the hydration numbers $n_h^{\pm}$. This method is thus characterized by two points: The complicated molecular system of the solution is divided into discrete microscopic regions, and physical properties that are often rigorously defined only in macroscopic terms are assigned to these regions.

Comparison with Figure 3 in particular shows how rough this method can be. The hydration number obtained does not depend on our definition of the hydration sphere (first or second coordination sphere, residence time of the water molecules in the hydration sphere, *etc.*), but depends on the numerical values of the physical property that are assigned to the hydration complex. Thus different determination methods

often give qualitatively the same overall behavior for the hydration numbers, whereas distinct quantitative differences are obtained (see *e.g.* [3]). Hydration numbers of less than 4 for spherical ions are difficult to understand. The number of regions (first hydration sheath, second hydration sheath) in eq. (1) could naturally be increased, but the number of unknowns would then also increase.

The determination of the radial distribution function for ion/water systems by measurement of the areas of X-ray diffraction patterns of electrolyte solutions is in principle a satisfactory method of determining the hydration numbers (see *e.g.* [4]). Thus *Brady* [5] found a value of 6.3–6.5 for the hydration number of Er^{3+} in the first sphere (first coordination number) on this basis. This value must be treated as indicating six-fold coordination. Information about the second coordination sphere of Er^{3+} was also obtainable [5]; in the case of the erbium halides, however, this also contains two halide ions. Er^{3+} is a relatively small ion with a high charge, so that the situation corresponds to that of Figure 2. Difficulties arise with ions having larger radii or lower charges. Firstly, ions having low atomic numbers have low scattering powers for X rays, and so make only a small contribution to the overall diffraction picture. Secondly, all the pair distribution functions in the solution are superimposed in the primary result, so that the water-water distributions in the hydration shell and in the free water are involved as well as the cation-water and anion-water distributions. The corresponding distances are often similar. Several methods have been described [6–8] for the derivation of the desired hydration numbers (first coordination numbers) (see Table 1). The X-ray diffraction experiments were carried out at moderate concentrations (2–5 mole/kg of H_2O), so that the values for K^+ are probably not valid for infinite dilution. In the case of the Cs^+ ion, perturbation of the intact hydration shell by halide ions has been observed at moderate concentrations [8].

Table 1. Hydration numbers $n_h^{\pm}$ (coordination numbers in the first sphere) for some ions in water; concentration ranges 2–5 mole/kg.

Ion	Salt	$n_h^{\pm}$	Method	Ref.
K^+	KOH	4 (to 5?)	X-ray [a]	[6]
Er^{3+}	$ErCl_3$, ErI_3	6	X-ray	[5]
Cl^-	LiCl	6.2–7.3	X-ray	[8]
Br^-	LiBr	7.2–8.9	X-ray	[8]
I^-	LiI	8–9	X-ray	[8]
Al^{3+}	$AlCl_3$, $AlBr_3$, $Al(ClO_4)_3$	6	NMR	[11, 12, 19, 22]
Be^{2+}	$BeCl_2$, $Be(ClO_4)_2$	4	NMR	[12, 19, 22]
Ga^{3+}	$Ga(ClO_4)_3$	6	NMR	[12, 20, 21]
In^{3+}	$InCl_3$	4.7 [b]	NMR	[12]
Mg^{2+}	$Mg(NO_3)_2$, $Mg(ClO_4)_2$	6	NMR	[12, 15–17]
Cr^{3+}	$Cr(ClO_4)_3$	7 (6?) [c]	NMR	[22]
Ni^{2+}	$Ni(ClO_4)_2$	4 or 6	NMR	[25]
Co^{2+}	$Cr(ClO_4)_2$	6	NMR	[26]

[a] X-ray diffraction. [b] In water/acetone (1 : 3 v/v), $n_h^+ = 6$. [c] The difference from the expected value of 6 can be explained by the relaxation mechanism in the second coordination sphere of the (paramagnetic) Cr^{3+} ion.

X-ray diffraction experiments yield information on hydration numbers in the sense of the definition of the actual structure. We shall now discuss investigations that are closely related to the residence time of the water molecules in the hydration shell. These studies are based on NMR measurements. The condition for the occurrence of separate NMR lines in different chemical (*i.e.* different electronic) environments (see *e.g.* [9, 10]) is

$$\tau \gg (\Delta\omega)^{-1} \qquad (2)$$

τ is the average time spent by the nucleus in question in the particular electronic environment, and $\Delta\omega$ is the absolute value of the difference in the chemical shifts (in Hz) between the different environments through which the nucleus passes in the exchange process.

A typical case of the application of the inequality (2) is the exchange of the proton or water molecule between the hydration shells and the free water in electrolyte solutions. In diamagnetic electrolyte solutions at and above room temperature, the particle exchange between the various regions of the solution is always so fast that the inequality (2) is not satisfied. On the contrary, the relation

$$\tau \ll (\Delta\omega)^{-1}$$

is always valid, so that the solution water gives only one NMR signal. The position of this signal corresponds to the average of the shifts of all the environments through which the proton or the ^{17}O nucleus passes. By lowering the temperature, however, the residence time τ can be prolonged to such an extent, in suitable cases, that the inequality (2) is satisfied. Thus *Fratiello et al.* observed a separate NMR signal for the water of hydration in addition to the signal for free water in aqueous solutions of Al, Ga, Be, and In salts at about −50 °C [11, 12].

Two examples are shown in Figure 5. Measurement of the areas below the two absorption lines shows that for each dissolved Al^{3+} ion there are six water molecules (or more precisely their protons) in an environment in which the chemical shift in relation to the residual water is −272 Hz and in which the residence time is very much longer than $(272 \times 2\pi)^{-1}$ s $\approx 6 \times 10^{-4}$ s. A negative chemical shift of this order of magnitude is expected, according to the theory of

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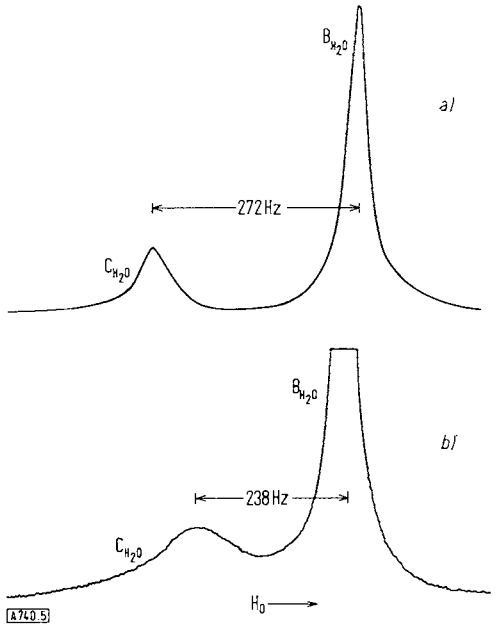


Fig. 5. Proton resonance spectra of aqueous solutions of Al and Ga salts. C_{H_2O} is due to the water in the hydration shell, and B_{H_2O} to that in the unbound state. (a) 1.59 mole of $Al(ClO_4)_3$ per kg of H_2O at −50 °C; (b) 2.42 mole of $GaCl_3$ per kg of H_2O at −58 °C. We thank Dr. *A. Fratiello* for these diagrams.

chemical shift [13,14], for the water protons in the electrostatic field of the cation. Since a strong electric field can exist only in the immediate vicinity of the ion, and since it is extremely unlikely that the same shift is produced by different field strengths, it is concluded that the six water molecules characterized by a long exchange time and a strong interaction are those of the first coordination sphere of *one* type of ion. The method thus leads directly to the hydration numbers in the first sphere. The results obtained so far are also collected in Table 1.

It can be seen in Figure 5b that the signal for the water of hydration in $GaCl_3$ solution is broader than that in $Al(ClO_4)_3$ solution. The coordination number for $GaCl_3$ is given by *Fratiello et al.* as only 5.7; a relatively fast exchange of the water protons, and possibly also of Cl^- ions, is already taking place. The figures given in Table 1 for the NMR results again refer to solutions of medium to high concentration (1.5–4.0 mole/kg of H_2O). In the case of In^{3+}, it is clear that the anions (Cl^-) have already occupied some sites in the hydration shell. The value given in parentheses for In^{3+} refers to a solution in a water-acetone mixture. The resolution of the lines is often much better in systems of this type [12]. Separate signals were originally obtained for the solvation shell in the case of Mg^{2+} only when an organic component (methanol [15,16], acetone [12,17]) was added to the aqueous solution. Later, however, separate (though broad) lines were obtained for the two residence ranges of water for concentrated solutions of $Mg(ClO_4)_2$ and $Mg(NO_3)_2$ (c = 3–4 mole/kg of H_2O) in water with no added organic component at −70 to −80 °C [17].

By means of a trick, separate NMR signals have even been observed for the water of hydration at room temperature with pure water as the solvent for the cations Al^{3+}, Ga^{3+}, and Be^{2+}. The trick consists in the addition of a paramagnetic ion, such as Co^{2+} or Dy^{3+}, in whose hydration shell very rapid water exchange takes place, to the solution of the ion under examination. This leads to a strong chemical shift of the water that is not contained in the hydration shell of Al^{3+}, with the result that the condition of the inequality (2) can be satisfied. Investigations of this type have been carried out for the ^{17}O resonance [18–21].

Similar experiments, again with the addition of paramagnetic ions, but which do not lead to the appearance of separate lines, also yield information about the hydration numbers in the first sphere [18–22]. No details can be given here. On the other hand, the measurements reported by *Swift* and *Sayre* [23] provide no reliable information about hydration numbers (see also [24]). A separate NMR signal has been found for the hydration shells of two paramagnetic ions (Ni^{2+}, ^{17}O resonance, room temperature [25]; Co^{2+}, proton resonance, about −60 °C [26]). The hydration number of Ni^{2+} may be either 4 or 6; the area measurement is very uncertain, but *Connick* and *Fiat* [25] favor a value of 4 on grounds of consistency with other NMR data. The coordination number in the first sphere of Co^{2+} is found to be 6 [26].

As was mentioned earlier, the hydration numbers provide information about the area under the first maximum of the (radial) pair distribution function for the particle pair ion-water. The next question is that of the shape of this distribution function in the region of the first maximum. A very sharp, steep maximum would correspond to a hydration shell in which, as in the case of a rigid molecule, the distances of the particles lie within a very narrow range. A flat, broad maximum, on the other hand, would indicate a relatively wide range of values for the distance between the ion and the water molecules, and would correspond roughly to the distribution of the intermolecular distances of pairs of particles in pure liquids. Pertinent

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[14] See *e.g. H. G. Hertz*, Ber. Bunsenges. physik. Chem. *67*, 311 (1963).

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[18] *J. A. Jackson*, *J. F. Lemons*, and *H. Taube*, J. chem. Physics *32*, 553 (1960).

[19] *R. E. Connick* and *D. N. Fiat*, J. chem. Physics *39*, 1349 (1963).

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[21] *T. J. Swift*, *O. G. Fritz jr.*, and *F. A. Stephenson*, J. chem. Physics *46*, 406 (1967).

[22] *M. Alei jr.* and *J. A. Jackson*, J. chem. Physics *41*, 3402 (1964).

[23] *T. J. Swift* and *W. G. Sayre*, J. chem. Physics *44*, 3567 (1966).

[24] *S. Meiboom*, J. chem. Physics *46*, 410 (1967).

[25] *R. E. Connick* and *D. N. Fiat*, J. chem. Physics *44*, 4103 (1966).

[26] *N. A. Matwiyoff* and *P. E. Darley*, J. physic. Chem. *72*, 2659 (1968).

information should again be obtainable by X-ray diffraction measurements. So far as we know, however, this problem does not appear to have been raised in the literature, and no investigations of the type required appear to have been carried out on electrolyte solutions. Owing to the overlap of distributions, as well as for other reasons, definite clarification of this structure problem will be possible only in a few favorable cases. However, the X-ray diffraction studies reported so far show that the maxima in the distribution functions, as expected, are very much sharper for the strongly hydrated Er^{3+} [5] than for solutions of KOH [6], KCl [6], LiCl [7], NaCl [8], and CsCl [8]. The sharpness for these last-named solutions is roughly the same as that for pure water. Because of the low scattering power of Li^+, however, no contribution can be expected for this ion.

Let us now turn to the question of the orientation of the water molecules in the hydration shell. The hydration energy of the ions is based mainly on ion-dipole interaction. It has always been regarded as obvious that at least one of the protons of the water molecule points toward the anion, whereas in the case of a cation, the water protons are directed away from the ion. Experimental evidence has been presented only in very rare cases, since it was accepted that none was necessary. There is in fact no doubt that such an arrangement of the water molecules exists in cases of strong hydration (cf. Fig. 2). The nuclear magnetic relaxation rate, which describes how quickly the (macroscopic) nuclear magnetization reaches its equilibrium value, depends in electrolyte solutions on how quickly the hydration complex reorients itself in the course of thermal motion, and is determined by the interaction of the water protons with their environment [9, 10, 27–29].

These two contributions can be observed separately with some paramagnetic ions. The interaction part here involves the distance of the protons in the first hydration shell from the center of the ion. Evaluation of the measurements gives roughly the distance expected for the proton directed away from the ion in the cases of Mn^{2+} [28, 30, 31], Cu^{2+}, and Cr^{3+} [31]. For the diamagnetic ions F^- [32, 33] and Li^+ [34, 35], only the product of the reorientation time of the hydration complex and the interaction factor can be determined experimentally from the relaxation rate of the ionic nucleus. Since the reorientation time is roughly known (see below), however, it can again be shown that the interaction term corresponds, on the whole, to the expected arrangement of the water protons in relation to the ion in question.

A question frequently discussed in the literature is whether the water molecule in the hydration shell of the anion is arranged symmetrically (center of the ion on the dipole axis, *i.e.* the bisector of the angle HOH) or unsymmetrically (center of the ion on the projection of one of the two O–H directions) [33, 36–40]. We cannot yet give a definite answer to this question [*].

While there is no doubt about the substantial nature of the orientation of the water molecules with strongly hydrated ions, the situation is not so clear with weakly hydrated ions, the behavior of which is illustrated diagrammatically in Figure 3. This is because of a special effect that occurs with large inorganic ions in aqueous solution, and which has been referred to as the structure breaking effect [42] and as negative hydration [43] (see also Section 2.2.3). The water in these solutions behaves spectroscopically and in its mobility as water whose temperature is higher than the true value. For example, the fluidity and the self-diffusion coefficient as well as the reorientation rate of the water molecule in a concentrated aqueous solution of potassium iodide are higher than in pure water at the same temperature. Because of this and other properties, the fairly large class of salts that exhibit this behavior are referred to as *structure breakers* [44], though nothing is known about the true change of structure in the solution. Conversely, salts with strongly hydrated ions are called structure formers. It is naturally questionable whether phenomena as complicated as changes in the structure of a solution can be adequately described by such simple terms [2]. Nevertheless, this terminology has become accepted as useful.

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[27] *R. E. Bernheim, T. H. Brown, H. S. Gutowsky,* and *D. E. Woessner,* J. chem. Physics *30,* 950 (1959).

[28] *N. Bloembergen* and *L. O. Morgan,* J. chem. Physics *34,* 842 (1962).

[29] See also *H. G. Hertz,* Progr. Nuclear Magnetic Resonance Spectroscopy *3,* 159 (1967).

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[35] *H. G. Hertz* and *H. Versmold,* unpublished.

[36] *J. D. Bernal* and *R. H. Fowler,* J. chem. Physics *1,* 515 (1933).

[37] *D. D. Eley* and *M. G. Evans,* Trans. Faraday Soc. *34,* 1093 (1938).

[38] *E. J. W. Verwey,* Recueil Trav. chim. Pays-Bas *61,* 127 (1942).

[39] *A. D. Buckingham,* Discuss. Faraday Soc. *24,* 151 (1957).

[40] *J. S. Muirhead-Gold* and *K. J. Laidler,* Trans. Faraday Soc. *63,* 944 (1967).

[*] An attempt has recently been made to determine the orientation of the water molecules in the system $F^-(H_2O)_4$ directly by a quantum mechanical *ab initio* calculation [41]. According to this calculation the unsymmetrical arrangement of the water molecules has the lower energy. However, the behavior at large ion-water molecule distances does not agree with that expected on the basis of the ion-dipole interaction. Moreover, the value found for the H_2O–H_2O interaction between two isolated water molecules with the same set of functions is much too high. This state of affairs greatly reduces the value of these calculations.

[41] *H. Versmold, R. Janoschek, W. Kraemer, G. Diercksen,* and *H. Preuss,* Report, Quantum Chemistry Group, Max-Planck-Institut für Physik und Astrophysik, No. 9, 76 (1968).

[42] *H. S. Frank* and *M. W. Evans,* J. chem. Physics *13,* 507 (1945).

[43] *O. Y. Samoilov,* Discuss. Faraday Soc. *24,* 141 (1957); Structure of Aqueous Electrolyte Solutions and the Hydration of Ions. Consultants Bureau Enterpr. Inc., New York 1965.

[44] *G. Engel* and *H. G. Hertz,* Ber. Bunsenges. physik. Chem. *72,* 808 (1968), and literature cited therein.

The hydration energy is naturally negative even for the structure-breaking ions, and depends on the ion-dipole interaction. The hydration energy is determined mainly by the difference in the amounts of work required to charge the ion in water and *in vacuo*. This is a consequence of the fact that the water dipoles in the environment of a dissolved particle assume a more favorable orientation when the particle is charged (ion-dipole interaction; for the orientation of the water molecules around a neutral particle, see Section 3). It should be mentioned now that a specific hydration of neutral apolar particles is nowadays assumed for water. *Frank* and *Evans*[42] called this effect "iceberg formation"; in the present article we shall use the somewhat neutral expression "hydration of the second kind". In the hydration of the second kind, there is a certain molecular orientation of water with respect to a neutral particle, *e.g.* a Xe atom. This orientation very probably becomes unfavorable when the Xe atom is replaced by an I^- ion. The electric field due to the charge calls for a more favorable orientation of the water dipoles. However, the field strength, which depends on the size of the particle and the magnitude of the charge, is not enough to bring the dipoles fully into the ideal orientation, *e.g.* as shown in Figure 2. Many of the dipoles thus remain in the "half-way" position and a relatively isotropic orientation of the water molecules occurs around a structure-breaking ion. It can be shown from thermodynamic data that the entropy[42] and the energy[44] increase when structure-breaking particles (large ions having the inert gas structure) become charged; the disorder in the solution, extending into the first coordination sphere of the ion[45] (see later), thus increases.

There are thus physical arguments that suggest the possibility of a relatively isotropic orientation distribution of the water molecules in the first coordination sphere of structure-breaking ions. Definite information is not yet available. However, there is a clue that could lead to further knowledge on this subject. The chemical shifts of the ionic nuclei ^7Li, ^{23}Na, and ^{27}Al (structure formers) in solutions in D_2O are extremely small in comparison with those in H_2O[46,47]. On the other hand, replacement of H_2O by D_2O leads to appreciable chemical shifts for the anionic nuclei ^{19}F, ^{35}Cl, $^{79,81}Br$, and ^{127}I[46,48,49], while replacement of $H_2{}^{16}O$ by $H_2{}^{18}O$ leads to practically no shift in the ^{19}F resonance (structure former). This shows qualitatively that the hydrogen nuclei are evidently nearer to the anion than to the cation. Measurements for the structure-breaking anions Cl^-, Br^-, and I^- in $H_2{}^{18}O$ have unfortunately not been reported, but the ^{133}Cs resonance (structure breaker) is displaced only slightly (if at all) more in D_2O than in $H_2{}^{18}O$[46].

The following rough calculation also points to incomplete orientation in the hydration shell. The average residence time of a water molecule in the hydration shell of the I^- ion is approximately $2 \times 10^{-12} - 4 \times 10^{-12}$ s (see below). Let us assume for simplicity that the molecule reaches a site in the hydration shell by a brief free "flight". The mean "flight velocity" can be taken from the kinetic gas theory to be approximately 6×10^4 cm/s. The "flight distance" to the site and back is of the order of magnitude of the diameter of a water molecule, *i.e.* about 3×10^{-8} cm, and the "time of flight" in the first coordination sphere is thus about 0.5×10^{-13} s. About 12–25% of the time spent by the water molecule in the hydration shell is therefore spent in free flight, *i.e.* the molecule is disoriented during this time. The orientation distribution of the water molecules thus has a broadening of at least this order of magnitude.

2.1.2. Non-aqueous Solutions

According to the above discussion, the solvation structure of an aqueous electrolyte solution lies between the two limiting situations indicated in Figures 2 and 3. Particularly for aqueous solutions of structure-breaking salts, there is a possibility that the true structure will be very close to the situation illustrated in Figure 3. Solutions of electrolytes in non-aqueous solvents very probably approximate to the structure model shown in Figure 2, *i.e.* they should have a more highly structured solvation shell than we expect in aqueous solutions. This can be seen from thermodynamic data. The thermodynamic transfer quantities are the changes in the free enthalpy of solvation (ΔG_t^0), the enthalpy of solvation (ΔH_t^0), and the entropy of solvation (ΔS_t^0) on transfer of a salt (or ion) from water into the non-aqueous solvent. The final state to which the operator Δ refers is thus the solution in the non-aqueous solvent. The experimental values found for the standard enthalpies of transfer ΔH_t^0 of some simple electrolytes such as alkali metal halides, nitrates, and perchlorates in solvents such as methanol, ethanol, formamide, *N*-methylformamide, *N*,*N*-dimethylformamide, acetone, and dimethyl sulfoxide are predominantly *negative*[50–58]. The free enthalpies

[45] *R. W. Gurney*: Ionic Processes in Solution. McGraw Hill, New York 1953.

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[54] *R. P. Held* and *C. M. Criss*, J. physic. Chem. *69*, 2611 (1965).

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[58] *Y. C. Wu* and *H. L. Friedman*, J. physic. Chem. *70*, 501, 2020 (1966); *71*, 1723 (1967).

of transfer of these simple salts are all positive [59–63], though negative values are assumed for certain cations after separation into ionic components [59,60]. In solvents such as ethanol and acetone, for which no experimental ΔG_t^0 values are available, it can again be concluded that $\Delta G_t^0 > 0$ from the decrease in solubility as compared with that in H_2O. From $\Delta G_t^0 > 0$ and $\Delta H_t^0 < 0$, since

$$T\Delta S_t^0 = \Delta H_t^0 - \Delta G_t^0$$

we find $\Delta S_t^0 < 0$. This is a particularly clear result: The (standard) entropy of solvation is more negative, *i.e.* the degree of order in the solvation structure is higher, in non-aqueous solvents than in water. Figure 6 shows the ionic standard entropies for a number of

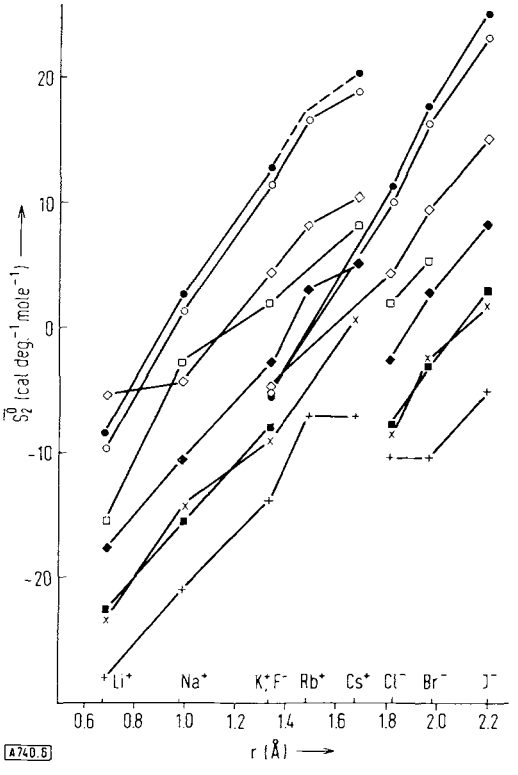


Fig. 6. Partial ionic entropies of some ions in various solvents (◇ = formamide, □ = *N*-methylformamide, × = *N,N*-dimethylformamide, ◆ = methanol ■ = ethanol ○ = H_2O, ● = D_2O, ÷ = NH_3) according to *C. M. Criss, R. P. Held,* and *E. Luksha* [64].

ions in various solvents (after *Criss, Held,* and *Luksha* [64]; the standard state is mole fraction x = 1). The standard entropy of transfer of a given ion is the difference between one of the numerical values of Figure 6 and that for the solvent H_2O. The entropies of transfer for a solvent become increasingly negative with decreasing characteristic structure of the solvent in the pure state [64].

The stronger solvation of ions in non-aqueous solvents is particularly clear from the fact that the ionic electric conductivities at infinite dilution are lower than in water, particularly when they are adjusted to take the viscosity of the solvent into account [65]. The hindrance of the movement of the ions by the adhering solvent molecules is thus greater in non-aqueous solvents.

So far as we know, however, no X-ray diffraction studies that directly show the sharper solvation structure have been reported as yet. Any diffraction diagrams that have been made for such systems appear more complicated than those of aqueous electrolyte solutions, owing to the greater number of intramolecular and intermolecular interatomic distances. An example is the investigation [66] of potassium iodide in formamide, which gave a value of 4.6 for the first coordination number of K^+ at a relatively low concentration (0.714 mole/kg of solvent); the coordination number decreases at higher concentration as a result of the increased ion association.

Since ions in non-aqueous solvents are generally more strongly solvated than in water, it is to be expected that the average residence time of a solvent molecule in the solvation shell will be longer. It should therefore be easier to observe separate NMR signals for the molecules in the solvation shell. Experience has shown that, even in non-aqueous solvents, the solvation complex is sufficiently long-lived only in exceptional cases. These exceptions are naturally again the small, highly charged ions. Thus a coordination number of 6 was found at room temperature for Al^{3+} in dimethyl sulfoxide [67], *N,N*-dimethylformamide [68–71], and acetonitrile [72], as well as for Ga^{3+} in *N,N*-dimethylformamide [69]. The chemical shift between the protons in molecules of the solvation shell and the free solvent molecules is about 20–50 Hz, depending on the nature of the system. Complications result from the fact that involved complexing equilibria can now occur with the anions [68,69,72]. At lower temperatures (<0 °C), Be^{2+} in dimethylformamide [73], $n_h^+ = 6$, Mg^{2+} in methanol [16], $n_h^+ = 6$, and ammonia [74], $n_h^+ = 5$ (?),

[59] *H. Strehlow* in *J. J. Lagowski*: The Chemistry of Non-Aqueous Solvents. Academic Press, New York 1967, Vol. 1, p. 129.

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[71] *W. G. Movius* and *N. A. Matwiyoff*, J. physic. Chem. *72*, 3063 (1968).

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[73] *N. A. Matwiyoff* and *W. G. Movius*, J. Amer. chem. Soc. *89*, 6077 (1967).

[74] *T. J. Swift* and *H. H. Lo*, J. Amer. chem. Soc. *89*, 3988 (1967).

and the paramagnetic ions Co^{2+}, $n_h^+ = 6$, and Ni^{2+} (n_h^+ not determinable) in methanol [75] and dimethylformamide [76] also give separate lines for bound and free solvent. The chemical shift in the sites of the solvation shell is about two orders of magnitude greater for paramagnetic than for diamagnetic ions. No separate signal was observed for the solvation shell in methanolic solutions of $LiClO_4$, $Ca(ClO_4)_2$, and $Ba(ClO_4)_2$, even at −110 °C; the exchange with the free solvent must therefore still be too fast in these cases [15, 16].

If the molecules of an organic solvent contain protons in non-equivalent positions, the signals of these protons will be displaced to different extents by the ion in relation to the signals of the free solvent [17, 68, 76]. This yields information about the arrangement of the molecules in the solvation shell. Thus it has been shown that coordination of dimethylformamide to the cation very probably occurs *via* O, and not *via* N [71, 73]. It can be seen from Figure 7 that in the case of Mg^{2+} in methanol [17], the cation has a relatively large influence on the OH proton, but only a small influence on the methyl protons [16] (for Mn^{2+} in methanol and in formic acid, see [77] and [78] respectively). Figure 7

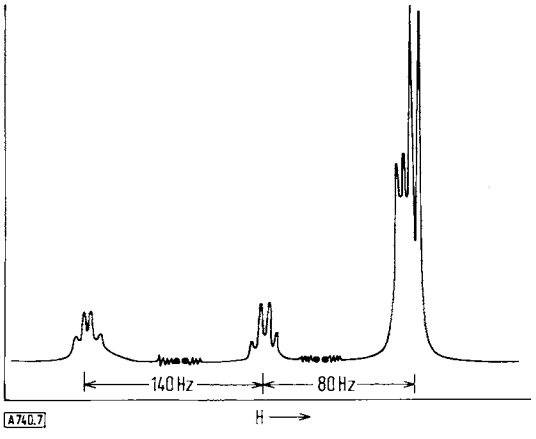


Fig. 7. Proton resonance spectrum of methanol in a solution of $Mg(ClO_4)_2$ in methanol and acetone at −60 °C. The applied magnetic field strength increases from left to right. The OH or methyl signal at lower field strengths corresponds to the methanol molecule in the solvation shell. The composition of the solution (in moles) is: $Mg(ClO_4)_2$ 0.55; CH_3OH 6.72; $(CH_3)_2CO$ 11.65; after *N. A. Matwiyoff* and *H. Taube* [17].

relates to a ternary mixture; in this case acetone is also added to the solution. The attainability of low temperatures, the magnitude of the chemical shift, and the solubility are often appreciably influenced by mixed solvents [17, 78–81].

[75] *Z. Luz* and *S. Meiboom*, J. chem. Physics *40*, 1058, 1066 (1964).

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[80] *R. G. Wawro* and *T. J. Swift*, J. Amer. chem. Soc. *90*, 2792 (1968).

[81] *A. Fratiello*, *R. E. Lee*, *V. M. Nishida*, and *E. Schuster*, J. chem. Physics *47*, 4951 (1967).

2.2.1. Aqueous Solutions, General

We now ask what conclusions can be drawn from the molecular motions concerning the structure of the hydration shell. Figures 1–4 all show the situation at one particular constant, and the positions of all the points shown will change with time. For reasons that will appear shortly, the time range in which we are interested lies between 10^{-14} and 10^{-10} s, *i.e.* it extends over four orders of magnitude. The fast motions are intramolecular and intermolecular periodic motions. However, the periodicity of these motions is no longer rigorous, since the potentials that determine the intramolecular and intermolecular vibrations have changed relative to a coordinate system fixed in space after about 10–1000 periods. This is a consequence of the (in contrast with the periodic motions) disordered thermal motion of the molecules and ions, *i.e.* Brownian motion. This "disordered" motion includes both the translational motion of the particles, which leads to normal diffusion, and the rotational diffusion motion, *i.e.* the reorientation of the (non spherically symmetrical) particles. These disordered thermal motions are slow in the time range chosen. Still slower motions ($t > 10^{-10}$ s for certain exchange processes) need not be considered.

2.2.2. "Fast" Motions in Aqueous Solution

Let us consider in more detail the fast periodic motions, the *intramolecular* vibrations of the water molecule with vibration periods in the range 1×10^{-14}–2×10^{-14} (wave numbers $\tilde{\nu}$ between 3500 and 1500 cm^{-1}) (Fig. 8). One might imagine that these vibrations

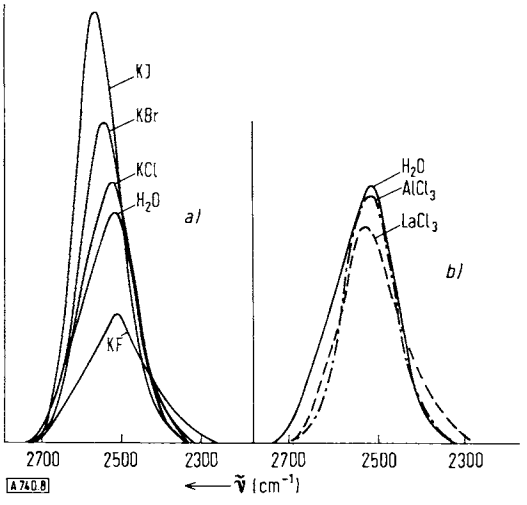


Fig. 8. The OD stretching vibration of HOD in the Raman spectra of some electrolyte solutions in water containing 5 mole-% of D at 27 °C, after *T. T. Wall* and *D. F. Hornig* [82].

would have different frequencies in the hydration shells of the ions and in the unbound water, and that separate intramolecular IR or Raman lines would

[82] *T. T. Wall* and *D. F. Hornig*, J. chem. Physics *47*, 784 (1967).

therefore be observed for the corresponding regions in electrolyte solutions. Surprisingly, however, no such line splitting has yet been observed, even with strongly hydrated ions such as Al^{3+} and La^{3+} [82] (see Fig. 8b). Other ions also generally fail to exhibit splitting; the only exception known at present is the splitting of the (symmetrical) OH stretching vibration in the IR spectrum of a solution of $NaClO_4$ in heavy water (containing HOD) [83,83a], for which no satisfactory interpretation has yet been found. In general, therefore, the difference in the frequencies of the intramolecular vibrations in the water of hydration and in the unbound water is small in relation to the bandwidth of these vibrations. Only a small frequency shift is observed for the symmetrical stretching vibration and the bending vibration of the overall solution [82–91]. With alkali metal halides, hydration has the same effect as a temperature rise (see Fig. 8a), *i.e.* the stretching vibration moves to higher frequencies and the bending vibration to lower frequencies. KF, however, exhibits the reverse behavior [82,83,88]. Anions have a stronger influence than cations, so that even the more highly charged strongly hydrated cations cause only a rather small overall displacement of the bands, corresponding in direction to a temperature decrease [82] (Fig. 8b). The effects are often on the very limit of the attainable accuracy of measurement, and the number of systems that have been studied is still relatively small. The chemical shifts of the proton resonance of the solution water show a similar behavior, though the tendency to negative shifts with strongly hydrated ions, again corresponding to a temperature decrease, is greater [14]. The frequency shift of the intramolecular vibrations is evidently connected with the breakdown of the structure of the water on the one hand and with the hydration of the ions on the other.

The Raman intensities of the stretching and bending vibrations do not exhibit the behavior expected from the parallelism with rising temperature. The halide anions exhibit a considerable increase in intensity in the order $F^- < Cl^- < Br^- < I^-$ [86–88], which is attributed to a decrease in the polarity of the O–H bond [80] and to a specific interaction with these ions as a result of their low electronic excitation states [82,92].

Intermolecular vibrations of pure water are the torsional or librational vibrations, which are due to the restricted rotation of the water molecule in relation to its neighbors. The periods of the vibrations are around 4.3×10^{-14} and 7.4×10^{-14} ($\tilde{\nu}$ = 780 and 450 cm^{-1}). Translational vibrations of the water molecule in the potential of its nearest neighbors are found at still lower frequencies ($\tilde{\nu}$ = 175 and 60 cm^{-1}; all the bands are very broad); the periods are 1.9×10^{-13} and 5.6×10^{-13} s. A rigid hydration complex as shown in Figure 2, which is a true "new molecule", should naturally exhibit new vibrations. In the limiting case of weak hydration (Fig. 3), the intermolecular vibrations of the water are also expected to change; owing to the greater disorder, these vibrations should be less well developed than in pure water, and the corresponding absorption bands should be broadened and displaced to lower frequencies. The existing experimental data are not very extensive. New absorptions corresponding to the case of Figure 2 for strongly hydrated cations have occasionally been observed in the Raman spectrum as broad, weak bands, *e.g.* for Zn^{2+} [93–95] and In^{3+} [96]. The frequencies roughly agree with those of the corresponding solid crystal hydrates [93–95].

The far IR spectra of alkali metal halides in aqueous solution [97] show, on the whole, the expected behavior with regard to the effects of structure formation or structure breaking (see Fig. 9).

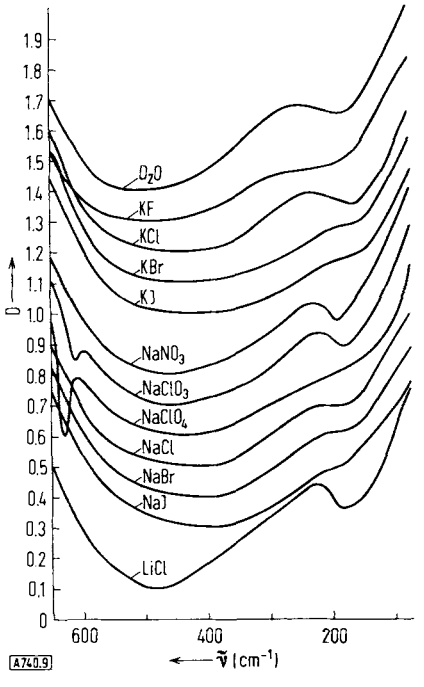


Fig. 9. Normalized IR transmittance D of D_2O solutions of some electrolytes in the low wave number range. The concentration is 4 mole/l in every case. For clarity, the curves are displaced vertically in relation to one another. The interval between lines on the ordinate is always 0.1; after *D. A. Draegert* and *D. Williams* [97].

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Of the salts in Figure 9, KF and LiCl contain structure-forming ions. In the presence of these salts, the frequencies of the torsional and translational bands of the D_2O used as the solvent change only slightly; KF causes broadening of the bands, while LiCl makes them sharper. The other salts, apart from NaCl, are typical structure breakers. These always displace the torsional bands to lower frequencies, with simultaneous broadening. The translational band is displaced only slightly and in both possible directions, and is almost completely absent in the case of iodides. No further details can be given here.

A particularly strong influence of the anions, especially of the halide ions, is seen in the Raman spectra [98,99]. In the presence of Cl^- and the structure breaker Br^-, the torsional band at 780 cm^{-1} is strongly displaced, and that at 450 cm^{-1} less strongly, to lower frequencies, again in agreement with the above predictions. The change in the purely dynamic vibration picture is masked, however, by the strong increase in the Raman scattering intensity, which is again due to a decrease in the polarity of the bond or the specific interactions with Cl^- and Br^- (and also I^-). This effect, which exhibits a remarkably small temperature dependence [98,99], is not yet understood in detail. *Walrafen* believes that strong hydration of these anions can be deduced, particularly since the displaced frequencies agree with those in crystal hydrates of chlorides and bromides [98–100]. This would be contrary to our view that *e.g.* Br^- is a pronounced structure breaker.

The translational intermolecular bands disappear from the Raman spectrum in the electrolyte solutions studied so far. Finally, mention should also be made of the translational intermolecular bands in the Raman spectra of acetate and formate solutions, which must be assigned to the hydration shells of these ions [101].

More definite information about the intermolecular vibration spectrum is obtainable in principle from neutron scattering measurements which are based on the fact that inelastically scattered neutrons take up quanta of the lattice vibrations as kinetic energy. Since there are no complex effects of the electronic structure of the molecules, the contributions of the cations and of the anions are perfectly equivalent. With the strongly hydrated cations, one generally finds [102] new vibrations due to the hydration complex as well as the vibrations of pure water. Comparison with the vibration spectra of the corresponding crystal hydrates shows identity with the frequencies of the solution for certain vibrations, whereas other details may differ in the solid state and in the solution. Large, singly charged ions, on the other hand, produce only small deviations from the vibrations of pure water; their effect appears to consist essentially in broadening and weakening of the water bands [102]. To sum up, we can say that investigations on the vibration picture of electrolyte solutions have led to certain conclusions regarding the structure problem, but the information obtained is often very limited.

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2.2.3. "Slow" Motions in Aqueous Solution

Having discussed the "fast" motions, we must now consider the "slow" motions. Let us start with the rotational diffusion motion of a rigid cationic hydration complex having the hydration number $n_h^+ = 6$ and with an octahedral arrangement of the six water molecules around the central ion. The reorientation time of this hydration complex in water is approximately 10^{-10} s at 25 °C. This time is known from proton relaxation measurements on aqueous solutions of doubly and triply charged paramagnetic ions (*e.g.* Mn^{2+}, Cu^{2+}, V^{2+}, Gd^{3+} [27–29, 103]).

The concept of the reorientation time can be grasped intuitively, but let us be more precise here. The reorientation time, whose order of magnitude is as given above, is the time in which the correlation of the vector R in Figure 10 relative to a given initial direction is lost. For the isotropic rotational motion of a

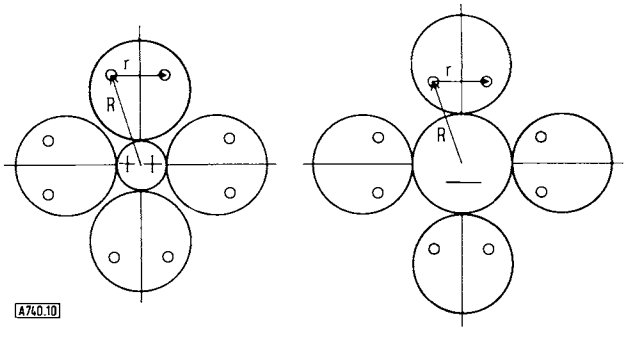


Fig. 10. Schematic section through the hydration complex of a cation and anion to illustrate the vectors R and r in the complex.

rigid hydration complex, this is also the reorientation time found for any vector in the complex, *e.g.* for the vector r joining the two protons of a water molecule (Fig. 10). Thus if measurement of the proton relaxation rate leads to the same reorientation time as above for this vector, the hydration complex is a rigid system; if on the other hand the values obtained are distinctly smaller, it must be concluded that the hydration complex is not rigid. In the latter case, *e.g.* rotation of the water molecules occurs about the axis shown, with the result that the directional correlation for the vector r decays more rapidly.

Knowledge of the orientation time of the vector r thus enables us to decide whether or not the hydration complex is rigid. It is now clear why 10^{-10} s was chosen as the upper limit of the time range to be considered. It can also be concluded qualitatively that the shorter the reorientation time of the intramolecular vector r, and hence of the water molecule in the hydration shell, the more closely will the structure of the hydration resemble that in Figure 3. It must again be said, however, that there is as yet no definite proof of this conclusion. Table 2 shows some reorientation times of water molecules (vector r) in the hydration shell, $\tau_r^{\pm}$, which were obtained from proton relaxation times

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in diamagnetic electrolyte solutions [32]. The hydration numbers that were not known from Table 1 were estimated. The orientation time of the H_2O molecule in pure water at 25 °C is $\tau_r^0 = 0.4 \times 10^{-11}$–$0.8 \times 10^{-11}$ s [29]; this may be taken as a reference value.

Table 2. Reorientation times $\tau_r^{\pm}$ of water molecules in the hydration shells of some ions (25 °C) [a, b] [32, 34].

Ion	Hydration number n_h^+	τ_r^+ (10^{-11} s)	Ion	Hydration number n_h^-	τ_r^- (10^{-11} s)
Li^+	4	2.3	F^-	6	1.8
Na^+	4	1.4	Cl^-	8	0.7
K^+	5	0.7	Br^-	8	0.6
Rb^+	6	0.5	I^-	9	0.4
Cs^+	6	0.4	NO_4^-	10	0.6
Mg^{2+}	6	4.2	ClO_4^-	10	0.4
Ca^{2+}	6	2.8	CO_3^{2-}	10	1.9
Sr^{2+}	6	2.5	SO_4^{2-}	10	1.4
Ba^{2+}	6	2.2	HgI_4^{2-}	14	0.6

[a] These values are based on a value of $\tau_r^0 = 0.8 \times 10^{-11}$ s for pure water.

[b] As a consequence of the NMR method used to obtain these data, all the times may be smaller by a factor of up to 3. If the hydration numbers implied in the reorientational motion are greater than those given here, the values of $\tau_r^{\pm}$ tend toward the reorientation time of pure water.

Let us first consider the ions for which $\tau_r^{\pm} > \tau_r^0$, *i.e.* the structure forming ions. The values given here are maximum values (they may be smaller by a factor of 3 [32]). If the number of water molecules per ion that execute slower motions than the molecules of pure water is greater than the number $n_h^{\pm}$ given in Table 2, the times $\tau_r^{\pm}$ decrease still further and approach τ_r^0. We can now make the following important observation from Table 2: None of the reorientation times is as great as the value $\tau_r^{\pm} \approx 10^{-10}$ s proposed above for the rigid complex. Even for Mg^{2+}, τ_r^+ is smaller than this limiting value by a factor of 2. It is probable, therefore, that even the hydration shell of Mg^{2+} is not rigid, and the water molecules rotate about the axes in Figure 10.

It is also very unlikely, from nuclear magnetic relaxation measurements on the F^- ion, that the fluoride ion is surrounded by a rigid, long-lived hydration shell. The term "long-lived" here means that the residence time of a water molecule in the hydration shell is longer than 10^{-10} s. Taking into account the possible configurations of the hydration shell, the nuclear magnetic relaxation time of ^{19}F in aqueous KF solution gives a value of at most about 5×10^{-11} s for the reorientation time of the vector R [33]; this is smaller than the value expected for the rigid complex. If the hydration shell were rigid and long-lived despite this deviation, the reorientation time of the complex (vector R) and its concentration dependence should also be found in the reorientation time of the molecules of the water of hydration (vector r) and its concentration dependence; however, this is not so. The reorientation time of the water molecules is always found to be shorter [33].

The self-diffusion coefficient of water in a KF solution having a concentration of about 9 mole/kg of H_2O is about 30% greater than that of the F^- ion [33]. The motion of the water molecules can thus no longer be strongly correlated with that of the F^- ions. A concerted translational diffusion of the ion and the surrounding water is however feasible at low concentrations $c_{F^-} \to 0$. It seems reasonable to conclude that the residence time of the water molecules in the hydration shell of F^-, even at low concentrations is not much greater than the mean jumping time of a water molecule in the solution ($\approx 10^{-11}$ s) [33]. Similar situations are found with the Li^+ and Ca^{2+} ions [104, 105]. It has been shown that as in the case of F^-, internal rotational motions also occur in the hydration shell of Li^+ [35, 106, 107].

Thus the study of the slow motions in electrolyte solutions with structure-forming ions appears to lead to a structural model that tends toward weak ("liquid") structuring extending over a large area rather than to rigid, compact hydration complexes.

It can also be seen from Table 2 that the reorientation times of the H_2O molecule are shorter in the hydration shells of many ions than in pure water. These are the structure-breaking ions. The description "structure-breaking" is partly based on this increase in the mobility of water, which also includes the translational diffusion motion [32, 104, 105, 108–110].

A comparatively fast isotropic reorientation of the H_2O molecule in the hydration shell should make the residence time of the molecule in the hydration shell shorter than the residence time in an "equilibrium position" of pure water [111]. It is interesting to note that the structure breakers even include a few doubly charged ions such as HgI_4^{2-}, $Hg(CN)_4^{2-}$, and CdI_4^{2-} [44]. Smaller values are also found for the activation energies for the reorientation of water in the neighborhood of structure-breaking ions than in pure water [32].

Frank and *Wen* [112] proposed the following model for the hydration of a structure-breaking ion. Each ion is always surrounded by a rigid hydration shell (zone A), and outside this is a region (B) in which the mobility is higher than in water. For structure-breaking ions, the influence of zone B on the observed mean mobility is greater than that of zone A. Against this picture is the model in which the region of increased fluidity extends right to the surface of the structure-breaking ion [43, 45]. There is no direct experimental evidence of the correctness of the multi-zone model. The orientation time of the water molecules in the environment *e.g.* of the I^- ion at $c = 6$ mole/kg of H_2O is shorter than in pure water. It has not, however, been found that this reorientation time becomes longer as $c \to 0$, as would be required for the multi-zone model; if anything it becomes shorter.

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On the other hand, it is not absolutely certain that the increase in the reorientation time with decreasing concentration as required by the multi-zone model is not masked by the disappearance of phenomena due to the ion-ion interaction [113–117]. In our opinion, the probability of this is extremely small, and we therefore favor the view that the zone of increased fluidity extends all the way to the surface of the structure-breaking ion.

The hydration energy, which has appreciable values even for structure-breaking ions, is mainly based on ion-dipole interaction. How then can the mobility of the water be increased, in view of the orientation of the dipoles in the field of the ion? It was this very question that forced *Frank* and *Wen* [112] to postulate their model. The hydration energy is determined by the energy required for complete removal of the water molecule from the ion or for its complete disorientation. If, however, the hydration shell always contains a few disoriented water molecules, the reorientation of any molecule of water of hydration must require only a relatively small quantity of energy, since one of the disoriented molecules can simultaneously change into the energetically favorable orientation [44]. The presence of disoriented molecules is shown very clearly by the increase in entropy and in energy that accompanies the formation of the solvation shell of a charged particle from that of an uncharged particle (Section 2.1.1). It can be shown that the fluidity, which is lower at very weak electric field strengths than that of pure water, increases at first (with few exceptions) with increasing field strength of the ion (*i.e.* with decreasing radius for a given charge), passes through a maximum and decreases until it finally again falls below that of pure water [44]. *Samoilov* [43] has also given an explanation of negative hydration (but see [44]).

2.2.4. Non-Aqueous Solutions

No spectroscopic studies that might contribute information about the structure of the solvation shell appear to have been reported for the "fast" motions in non-aqueous electrolyte solutions. The slow motions of the solvent molecules in the solvation shell have been investigated for several electrolytes in methanol, ethanol, acetone, dimethyl sulfoxide, formamide, *N*-methylformamide, ethylene glycol, and glycerol. In the first six solvents no structural breaking effect, *i.e.* no increase in fluidity, occurs. The reorientation of the molecules thus takes longer in the solvation shell than in the pure solvent. This is in agreement with the view that the solvation in this case is structurally more strongly developed than in water. It is interesting to note that the fluidity of ethylene glycol and of glycerol is increased by large ions such as Cs^+, I^-, and Br^-, though to a smaller extent than in the case of water [44].

3. Hydration of Neutral Particles and Ions with Inert Groups

3.1. General

Let us confine our discussion initially to non-polar, inert particles such as inert gases, saturated aliphatic hydrocarbons (methane, ethane, *etc.*), and inert inorganic compounds (CF_4, NF_3, SF_6). These substances exhibit a striking anomaly in aqueous solution. The (standard) entropy difference

$$\Delta S^0 = \bar{S}_2^0 - S_{2g}^0$$

for the transfer of one mole of the inert gas from the gaseous state (S_{2g}^0) into the aqueous solution ($\bar{S}_2^0$) at room temperature is approximately 10 cal deg^{-1} · mole^{-1} more negative than that expected from experiments on non-aqueous solvents (Barclay-Butler rule) [42]. The entropy of transfer $\Delta\bar{S}_t^0$ from water into an organic solvent is therefore positive, and thus has the opposite sign to that for ions. According to our definition, therefore, solvation of the entire particle does not occur in non-aqueous solvents. At sufficiently low temperatures, the dissolution process is always exothermic [42,118]. The low solubility of these substances in water, *i.e.* the marked increase in the (standard) free enthalpy for the dissolution process, ΔG^0, is therefore an entropy effect according to

$$0 < \Delta G^0 = \Delta H^0 - T\Delta S^0$$

As was indicated earlier, the anomalous negative entropy effect disappears as the temperature approaches the boiling point of water. Thus ΔS^0 increases rapidly with rising temperature at or below room temperature, *i.e.* $d\bar{S}_2^0/dT$ has large positive values. The same is therefore also true of the partial molal specific heat $C_{p2}^0 = T(d\bar{S}_2^0/dT)$ [119].

Frank and *Evans* [42] interpreted this characteristic entropy effect as resulting from an "increase in structure" in the water due to the dissolved inert particles: Owing to the bond deficit in the vicinity of the dissolved particle, the bonds between the water molecules are strengthened. This would imply a special orientation of the water molecules that is not based on a strong interaction with the dissolved particle, and which evidently results from the peculiarity of the water molecules ("iceberg-formation" [42] or "hydration of the second kind" [2]).

An increase in structure according to *Frank* and *Evans* can only mean that the number of hydrogen bonds in

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[117] *H. G. Hertz*, *G. Stalidis*, and *H. Versmold*, J. Chim. physique Physico-Chim. biol., Numero Spezial Octobre 1969, p. 177.

[118] *G. Némethy* and *H. A. Scheraga*, J. chem. Physics *36*, 3401 (1962).

[119] See *e.g. D. M. Himmelblau*, J. physic. Chem. *63*, 1803 (1962).

these solutions is greater than in pure water. In this view, this is also the cause of the negative ΔH^0 values. Since only van der Waals interaction exists between the dissolved particles and the water molecules, the structure could be pictured *e.g.* as shown in Figure 4. *Frank et al.* did not tie themselves to any special geometrical form for the hydration structure.

The hypothesis of *Frank* and *Evans* for the hydration of inert particles has now become a fixed part of present-day ideas on aqueous solution systems. Nothing is known, however, about the true mutual arrangement of the water molecules in the nearer or more distant environment of the dissolved particles. The increase in structure due to apolar dissolved particles or groups, which is often accepted as a fact, cannot yet be conclusively verified. As was mentioned earlier, the concepts of an increase and a decrease in structure are too simple. What is certain is that changes in structure occur [2].

The energy and entropy effect in the dissolution of apolar particles in water has also been interpreted (though not entirely satisfactorily) without the use of the concepts of hydration and increase in structure. Since water has a very open structure, comparatively little energy and entropy are required, according to *Eley* [120], to incorporate the dissolved particles in the only slightly enlarged cavities. According to *Powell* and *Latimer* [121], the anomalous entropies of solution can be explained by a decrease in the free volume in the solution and consequent hindrance or stiffening of the intermolecular vibrations. A similar picture follows from *Everett*'s model [122], according to which making a hole in the network of H-bonded water molecules to accommodate a solute molecule leads to contraction of the network in the vicinity of the hole owing to the resulting disequilibrium, and this leads in turn to denser packing and a decrease in entropy. No quantitative treatments of these views have yet been carried out.

3.2. Other Experimental Observations

The discussion will now be extended to the solution behavior of molecules having polar groups or an electric charge in addition to the inert alkyl groups (alcohols, ketones, tetraalkylammonium salts, *etc.*). These are the systems used in many investigations, since the solubility is greater. Many of the typical phenomena of hydration of the second kind are undoubtedly retained with these dissolved particles, but it is necessary to consider overlap of the contributions of the polar and of the apolar groups [123].

Probably the most impressive evidence in favor of the formation of definite structures is the existence of solid gas hydrates [124, 125] and clathrates [126]. It seems reasonable to regard the increase in structure in the aqueous solution as preformation of the solid hydrated structure [127–131].

It is not known, however, to what extent structures that are stable in the solid state are retained in the liquid state. Caution is necessary in view of the fact that the solution effects in question occur with very many substances, whereas only a few examples are known of hydrate formation in the solid state (see also [2]).

The disappearance of the negative entropy effect with rising temperature, as was mentioned earlier, requires a large positive value for the partial molal specific heat of the solute. Positive (partial) molal specific heats have in fact been found for several organic molecules and ions with polar groups or an electric charge in addition to alkyl groups [112, 132–138]. C_{p2}^0 usually increases with the number of CH_2 groups. The partial molal volume of the solutes with alkyl groups is smaller at low concentration in aqueous solution than the corresponding molal volume in the pure liquid or in apolar solvents [118, 138, 139–142]. It can probably be concluded that the filling of holes in the water structure by dissolved particles is not accompanied by formation of an equivalent quantity of new holes by additional iceberg structures. The water molecules may be more densely packed in the solution than in pure water. The compressibilities of solutions of alcohols, acetone, and a

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few other organic liquids with high water contents are lower than that of water [143–145].

For aqueous solutions containing alcohols, lower fatty acids, salts of fatty acids, ketones, nitriles, and tetraalkylammonium salts at low concentrations, the viscosity [124, 146–148], the reciprocal self-diffusion coefficient of the water molecule [149–152], the dielectric relaxation time [153, 154], and the reorientation time of the water molecule as found from nuclear magnetic relaxation times [142, 155, 156] are greater than for pure water. It can be concluded in particular from the behavior of the last three quantities that a state with a closer resemblance to the solid occurs in the solutions than in pure water. The motion in the latter case is evidently opposed by larger forces and torques associated with definite solvation structures.

However, the postulated decrease in the rate of molecular reorientation appears to be relatively small; at best, the reorientation time in the hydration shell is 1.5 to 2 times the value in pure water [142]. It has also been shown experimentally that in the translational motion, the hydration shell *e.g.* of the tetraalkylammonium ions is not firmly linked to the ion [152]. One would also expect much lower values for the equivalent conductivities than those actually observed if these ions and their hydration shells were in fact joined to form a rigid complex [157]. From another point of view, however, *Kay* interpreted his conductivity measurements on tetraalkylammonium ions with long alkyl chains in terms of a "structure forming effect" [158, 159].

Results of X-ray diffraction experiments on aqueous alcohol solutions have occasionally been used as evidence of the true increase in structure in these systems [43, 138]. In our opinion, however, these results are not sufficient to clarify the question under discussion.

The chemical shift of the proton resonance of water in solutions of some organic substances containing non-polar (alkyl) groups at room temperature generally becomes more positive as the number of CH_2 groups in the dissolved particle increases [160–162]. Taken in conjunction with the other observations for H bonds [9, 10, 160], this means that the non-polar groups decrease the number of hydrogen bonds in the water, instead of increasing it as postulated by *Frank* and *Evans*. At least a type of H bond different from that occurring in the free water must be formed in solutions of this type (see also [103]). *Glew et al.* recently observed a negative chemical shift of the protons of the solution water relative to pure water for *tert*-butanol, tetrahydrofuran, and acetone (in decreasing order) at low concentrations [130]. These authors believe that they have found the reinforcement predicted by *Frank* and *Evans* for the H bond formation between the water molecules. No negative shift is found with propylene oxide or dioxane at the same temperature. The only possibility of explaining this apparent contradiction is by a careful check of which part of the total effect is due to the polar group and which to the inert molecular residue. This will require further measurements on homologous series at 0 °C.

The literature contains conflicting evidence on the question of the influence of alkyl groups on the intramolecular vibrations of water. The frequency of the OH stretching vibration in the IR spectrum has been found to increase with the length of the alkyl chain for tetraalkylammonium ions in D_2O [83]. The frequency of the same vibration in the Raman spectra of alkyl sulfates in H_2O is reported to decrease as the number of C atoms increases [163]. The first of these observations would indicate breakage of H bonds, while the second would indicate formation of new H bonds (cf. also [90]). The interpretation of the Raman measurements on the solutions of alkyl sulfates [163] is subject to the general uncertainty that even today hinders our understanding of Raman scattering intensities. (For further solution properties, see [2].)

Efforts have also been made to explain the increase in structure in aqueous solutions of non-polar particles on a purely theoretical basis [118, 164, 165]. One of these attempts was based on a one-dimensional model, for which rigorous calculation is possible. According to this calculation, it should in fact be possible, in agreement with the hypothesis of *Frank* and *Evans*, for

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additional structure aggregates ("clusters") to be formed by the water molecules. The problem is merely to what extent the models assumed correspond to the real systems.

4. Conclusions

An understanding of the solvation structure of dissolved particles depends mainly on the interpretation of the anomalous entropy and energy effects. The difficulty of this problem is shown by the pressure dependence of the entropy of pure water in the region of 20 °C. As the pressure is increased, the entropy (and initially also the viscosity) decreases, though the general view is that H bonds are broken.

The observations associated with the motion of the water molecules and the existence of solid hydrates appear to lend partial support to the hypothesis of the increase in structure, but the properties based directly on the electronic structure of the water molecule do not readily fit this hypothesis. If an increase in the structure of the water is in fact associated with the dissolution process, it is of a different type from the increase in structure that occurs when pure water is cooled. The packing of the water molecules in the solution is evidently different from that in pure water.

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Energy Production in Anaerobic Organisms[**]

By K. Decker, K. Jungermann, and R. K. Thauer[*]

Biological redox processes are required for the synthesis of "energy-rich" compounds which are in an enzyme-controlled equilibrium with the general energy carrier adenosine triphosphate (ATP). The basic mechanisms of biological energy transformation are substrate level (SLP) and electron transport phosphorylations (ETP). In anaerobic catabolism the numerous nutrients are channelled into only a few substrate level phosphorylations; the occurrence in chemotrophic anaerobes of energy conservation coupled to electron transport has not yet been demonstrated unequivocally. At present, the determination of the ATP turnover (Y_{ATP}) in growing cells appears to be a promising method of approaching this problem. The existing knowledge of oxygen dependent enzyme reactions and their molecular evolution provides the basis for a biochemical definition of aerobic and anaerobic organisms.

1. Introduction

Biological energy production was believed by *Lavoisier* to depend upon oxidations with atmospheric oxygen; this view was held for more than a century [1]. It is now known that about 3×10^9 years ago, when life first appeared on earth [2], energy could not have been produced by combustion reactions, since our planet was still surrounded by a reducing, oxygen-free atmosphere [2, 3]. It is therefore probable that the first living organisms were anaerobes.

"Life without oxygen" still occurs on earth; it is found wherever putrefactive processes or excessive oxygen consumption by aerobic cells gives rise to niches of oxygen deficiency. This anaerobic life is sustained either by the radiant energy of the sun (phototrophy) or by the chemical energy (chemotrophy) of oxygen-independent reactions. It is reasonable to assume that the photosynthetic apparatus is a relatively late acquisition of anaerobes, and that the energy was originally provided by a chemotrophic metabolism. Thus, the study of strict anaerobes has gained interest also in connection with the evolution of cellular chemistry.

In this paper the principles of biological energy transformation will be discussed first. In view of the very large number of potential nutrients, it will not be attempted to discuss all the known pathways of substrate utilization in anaerobes. Instead, some recently elucidated examples will be presented to show how the numerous substrates (carbohydrates, amino acids) are transformed and directed to a few substrate level phosphorylations. Since electron transport phosphorylations have so far been definitely detected only

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in chemotrophic aerobes (respiratory chain [6]) or in phototrophic cells [9], the question whether they can also occur in chemotrophic anaerobic metabolism is of great interest at the moment, and is therefore also an important aspect of the following discussions.

The importance of growth yield measurements for the determination of the *in vivo* ATP turnover and hence for an understanding of the relations between overall metabolism and cell growth will also be discussed. Finally, the molecular evolution of biological energy transformations, and thus the position of the anaerobes in phylogeny, will be considered. An attempt will be made to provide a biochemical basis for the physiological definition of anaerobic organisms and their distinction from facultative and obligate aerobes.

2. Biological Energy Transformation

The metabolism of living cells is an open system characterized by the constant input and output of matter and energy, and whose chemical reaction chains are in a steady state. It can be subdivided into catabolism ("Energiestoffwechsel"), which provides the molecular energy carrier adenosine triphosphate (ATP), and anabolism ("Baustoffwechsel"), which uses the energy of ATP for the synthesis of monomers, for polymerizations, and for active transport (Fig. 1).

The energy metabolism is an exergonic system of electron donating and accepting reactions or reaction

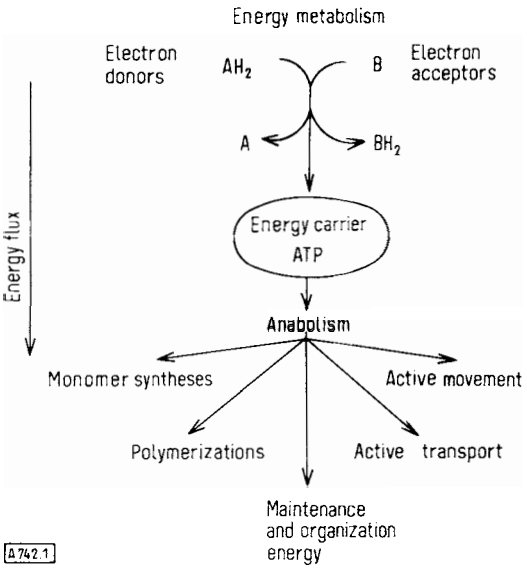


Fig. 1. The energy flux in metabolism.

conserved in the form of "energy-rich" compounds [4], which are in an enzyme-controlled equilibrium with the ATP system [eq. (a)]

$$ATP^{4\ominus} + H_2O \rightleftharpoons ADP^{3\ominus} + HPO_4^{2\ominus} + H^{\oplus}$$
$$(\Delta G_0' = -8.2 \text{ kcal/mole})[5, 5a][*] \quad \text{(a)}$$

Energy is transformed *via* the ATP* system [**] in two ways. *Substrate level phosphorylations (SLP)* convert the free energy of hydrolysis (the "group potential") [4]

		Electron donation (dehydrogenation)	Electron acceptance (hydrogenation)	$\Delta G_0'$ (kcal/reaction) [b] overall process
Chemotrophy [c]	Fermentation	glucose $\rightarrow$ (ATP) 2 pyruvate$^{\ominus}$ + 2 $H^{\oplus}$ + 4 [H]	4 [H] + 2 pyruvate$^{\ominus}$ $\rightarrow$ 2 lactate$^{\ominus}$	− 47.5
	Respiration	glucose + 12 H_2O $\rightarrow$ (ATP *(SLP)*) 6 $HCO_3^{\ominus}$ + 6 $H^{\oplus}$ + 24 [H]	24 [H] + 6 O_2 $\rightarrow$ (ATP *(ETP)*) 12 H_2O	−680.2
Photosynthesis [c]	Photosynthesis	H_2O $\xrightarrow{h\nu}$ 1/2 O_2 + 2 $H^{\oplus}$ + 2 $e^{\ominus}$	2 $e^{\ominus}$ + 2 $H^{\oplus}$ $\rightarrow$ (ATP *(ETP)*) 2 [H] *(NCPP)*	+ 56.7
		Chl $\xrightarrow{h\nu}$ Chl$^{\oplus}$ + $e^{\ominus}$	$e^{\ominus}$ + Chl$^{\oplus}$ $\rightarrow$ (ATP *(ETP)*) Chl *(CPP)*	0

[a] *SLP* = substrate level phosphorylation. *ETP* = electron transport phosphorylation. *NCPP*, *CPP* = noncyclic and cyclic photophosphorylation.
[b] Without ATP* formation and without radiant energy, see Tables 2 and 3.
[c] Chemosynthesis and chemotrophy are frequently used as synonyms in the English literature [8] and denote the biological production of energy from chemical reactions alone. The term chemosynthesis is therefore a more comprehensive term than fermentation and respiration. In the German literature, on the other hand, chemosynthesis refers only to the production of energy from redox processes between inorganic electron donors and electron acceptors, particularly oxygen. Chl = chlorophyll.

chains which are coupled by electron carriers. The donating part of the process comprises the flow of **electrons** from the donor substrate to the first **electron** carrier (usually NAD); the accepting part is the flow from the first electron carrier to the final acceptor.

The fraction of the total energy released by the redox processes that can be utilized by the cell is initially

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[*] $\Delta G_0' \equiv \Delta G_0$ at pH 7 (all other reactants 1 M, 25 °C).
[**] The symbol ATP* is used when only the turnover or the free energy of hydrolysis of the β,γ-pyrophosphate bond of adenosine triphosphate is meant.

Table 2. Dehydrogenations. Electron-donating, formally hydrogen-forming reactions of the energy metabolism.

Eq. no.	Substrates	Products	$\Delta G'_0$ (kcal/mole H_2) [a]	ATP* formed/reaction (SLP)	$\Delta G'_0$ (kcal/reaction) [a]	Route [b]	Ref.
	1. Carboxylic acids						
(1)	acetate$^{\ominus}$ + 4 H_2O (citrate cycle)	2 $HCO_3^{\ominus}$ + + 4 H_2	+ 6.4	0	+25.5		[5]
(2)	2 acetate$^{\ominus}$ + 2 H_2O (glyoxylate cycle)	1 $HCO_3^{\ominus}$ + pyruvate$^{\ominus}$ + 3 H_2	+12.6	−2	+37.7		[5]
(3)	acetate$^{\ominus}$ + H_2O	1 $HCO_3^{\ominus}$ + CH_4			− 6.8		[5]
(4)	propionate$^{\ominus}$ + 3 H_2O	1 $HCO_3^{\ominus}$ + acetate$^{\ominus}$ + $H^{\oplus}$ + 3 H_2	+ 5.9	1	+17.8		[10]
(5)	propionate$^{\ominus}$ + 7 H_2O	3 $HCO_3^{\ominus}$ + 2 $H^{\oplus}$ + 7 H_2	+ 6.2	0	+43.3	CC/OD	[10]
(6)	butyrate$^{\ominus}$ + 10 H_2O	4 $HCO_3^{\ominus}$ + 3 $H^{\oplus}$ + 10 H_2	+ 6.1	1	+61.3	CC	[5]
(7)	succinate$^{2\ominus}$ + 8 H_2O	4 $HCO_3^{\ominus}$ + 2 $H^{\oplus}$ + 7 H_2	+ 5.4	1	+38.1	CC/OD	[5]
(8)	butyrate$^{\ominus}$ + 2 H_2O	2 acetate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	+ 5.0	1	+10.1	BO	[5]
(9)	caproate$^{\ominus}$ + 4 H_2O	3 acetate$^{\ominus}$ + 2 $H^{\oplus}$ + 4 H_2	+ 5.0	2	+20.2	BO	[c]
	2. α-Keto acids						
(10)	pyruvate$^{\ominus}$ + 2 H_2O	acetate$^{\ominus}$ + $HCO_3^{\ominus}$ + $H^{\oplus}$ + H_2	−12.1	1	−12.1	OD	[5]
(11)	pyruvate$^{\ominus}$ + 6 H_2O	3 $HCO_3^{\ominus}$ + 2 $H^{\oplus}$ + 5 H_2	+ 2.7	1	+13.5	OD/CC	[5]
(12)	glyoxylate$^{\ominus}$ + 2 H_2O	formate$^{\ominus}$ + $HCO_3^{\ominus}$ + $H^{\oplus}$ + H_2	− 8.3	1	− 8.3	OD	[5]
(13)	glyoxylate$^{\ominus}$ + 3 H_2O (dicarboxylic cycle)	2 $HCO_3^{\ominus}$ + $H^{\oplus}$ + 2 H_2	− 4.1	1	− 8.2	OD	[5]
(14)	α-ketobutyrate$^{\ominus}$ + 2 H_2O	propionate$^{\ominus}$ + $HCO_3^{\ominus}$ + $H^{\oplus}$ + H_2	−12.1	1	−12.1	OD	[d]
(15)	α-ketoglutarate$^{2\ominus}$ + 2 H_2O	succinate$^{2\ominus}$ + $HCO_3^{\ominus}$ + $H^{\oplus}$ + H_2	−10.9	1	−10.9	OD	[5]
(16)	oxalacetate$^{2\ominus}$ + 3 H_2O	acetate$^{\ominus}$ + 2 $HCO_3^{\ominus}$ + $H^{\oplus}$ + H_2	−18.6	1	−18.6	OD	[5]
	3. α,β-Unsaturated acids, hydroxy acids						
(17)	lactate$^{\ominus}$ + 2 H_2O	acetate$^{\ominus}$ + $HCO_3^{\ominus}$ + $H^{\oplus}$ + 2 H_2	− 0.9	1	− 1.8	OD	[5]
(18)	malate$^{2\ominus}$ + 3 H_2O	acetate$^{\ominus}$ + 2 $HCO_3^{\ominus}$ + $H^{\oplus}$ + 2 H_2	− 3.6	1	− 7.2	OD	[5]
(19)	citrate$^{3\ominus}$ + 3 H_2O	succinate$^{2\ominus}$ + 2 $HCO_3^{\ominus}$ + $H^{\oplus}$ + 2 H_2	− 2.9	1	− 5.8	CC	[5]
(20)	isocitrate$^{3\ominus}$ + 3 H_2O	succinate$^{2\ominus}$ + 2 $HCO_3^{\ominus}$ + $H^{\oplus}$ + 2 H_2	− 3.7	1	− 7.4	CC	[5]
(21)	β-hydroxybutyrate$^{\ominus}$ + H_2O	2 acetate$^{\ominus}$ + $H^{\oplus}$ + H_2	− 9.9	1	− 9.9	BO	[5]
(22)	crotonate$^{\ominus}$ + 2 H_2O	2 acetate$^{\ominus}$ + $H^{\oplus}$ + H_2	− 8.1	1	− 8.1	BO	[e]
(23)	acrylate$^{\ominus}$ + 3 H_2O	acetate$^{\ominus}$ + $HCO_3^{\ominus}$ + $H^{\oplus}$ + 2 H_2	− 0.2	1	− 0.4	OD	[f]
(24)	fumarate$^{2\ominus}$ + 4 H_2O	acetate$^{\ominus}$ + 2 $HCO_3^{\ominus}$ + $H^{\oplus}$ + 2 H_2	− 4.0	1	− 8.0	CC/OD	[5]
(25)	glycolate$^{\ominus}$ + 2 H_2O	formate$^{\ominus}$ + $HCO_3^{\ominus}$ + $H^{\oplus}$ + 2 H_2	+ 3.3	1	+ 6.6	OD	[5]
	4. Aldehydes (aldoses, ketoses)						
(26)	formaldehyde + H_2O	formate$^{\ominus}$ + $H^{\oplus}$ + H_2	− 5.5	1	− 5.5		[5]
(27)	acetaldehyde + H_2O	acetate$^{\ominus}$ + $H^{\oplus}$ + H_2	− 8.5	1	− 8.5		[5]
(28)	glyceraldehyde + H_2O	glycerate$^{\ominus}$ + $H^{\oplus}$ + H_2	− 8.9	1	− 8.9	EM	[g]
(29)	glyceraldehyde	pyruvate$^{\ominus}$ + $H^{\oplus}$ + H_2	−15.5	1	−15.5	EM	[h]
(30)	glyceraldehyde + 2 H_2O	acetate$^{\ominus}$ + $HCO_3^{\ominus}$ + 2 $H^{\oplus}$ + 2 H_2	−13.3	2	−26.6	EM/OD	[h]
(31)	glyceraldehyde + 6 H_2O	3 $HCO_3^{\ominus}$ + 3 $H^{\oplus}$ + 6 H_2	− 0.3	2	− 1.9	EM/CC	[h]
(32)	3 ribose	5 pyruvate$^{\ominus}$ + 5 $H^{\oplus}$ + 5 H_2	−13.6	5	−67.8	TT/EM	[h]
(33)	ribose	acetate$^{\ominus}$ + pyruvate$^{\ominus}$ + 2 $H^{\oplus}$ + H_2	−39.1	2	−39.1	PK	[h]
(34)	glucose	2 pyruvate$^{\ominus}$ + 2 $H^{\oplus}$ + 2 H_2	−13.4	2	−26.8	EM	[h]
(35)	glucose + 4 H_2O	2 acetate$^{\ominus}$ + 2 $HCO_3^{\ominus}$ + 4 $H^{\oplus}$ + 4 H_2	−12.8	4	−51.0	EM/OD	[h]
(36)	glucose + 2 H_2O	acetate$^{\ominus}$ + pyruvate$^{\ominus}$ + $HCO_3^{\ominus}$ + 3 $H^{\oplus}$ + 3 H_2	−13.0	2	−39.0	PK/EM	[h]
(37)	glucose + 12 H_2O	6 $HCO_3^{\ominus}$ + 6 $H^{\oplus}$ + 12 H_2	0	4	0.3	EM/CC	[5]
(38)	3 heptose	7 pyruvate$^{\ominus}$ + 7 $H^{\oplus}$ + 7 H_2	−13.1	7	−91.8	TT/EM	[h]
(39)	gluconate$^{\ominus}$ + H_2O	acetate$^{\ominus}$ + pyruvate$^{\ominus}$ + $HCO_3^{\ominus}$ + 2 $H^{\oplus}$ + 2 H_2	−15.1	2	−30.3	PK/EM	[h]
(40)	gluconate$^{\ominus}$	2 pyruvate$^{\ominus}$ + $H^{\oplus}$ + H_2 + H_2O	−18.2	1	−18.2	ED	[h]
(41)	3 gluconate$^{\ominus}$ + 3 H_2O	5 pyruvate$^{\ominus}$ + 3 $HCO_3^{\ominus}$ + 5 $H^{\oplus}$ + 8 H_2	− 5.1	5	−42.0	TT/EM	[h]
(42)	6 gluconate$^{\ominus}$ [3 × eq. (37) + (38)]	11 pyruvate$^{\ominus}$ + 3 $HCO_3^{\ominus}$ + 8 $H^{\oplus}$ + 11 H_2	− 8.7	8	−95.6		[h]
	5. Alcohols						
(43)	methanol + H_2O	formate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	+ 2.6	1	+ 5.2		[5]
(44)	methanol + 2 H_2O	$HCO_3^{\ominus}$ + $H^{\oplus}$ + 3 H_2	+ 1.8	1	+ 5.4		[5]
(45)	ethanol + H_2O	acetate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	+ 0.8	1	+ 1.5		[5]
(46)	ethylene glycol	acetate$^{\ominus}$ + $H^{\oplus}$ + H_2	−19.6	1	−19.6		[10]
(47)	glycerol	pyruvate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	− 3.1	1	− 6.3	EM	[5]
(48)	glycerol + 2 H_2O	acetate$^{\ominus}$ + $HCO_3^{\ominus}$ + 2 $H^{\oplus}$ + 3 H_2	− 6.1	2	−18.4	EM/OD	[5]
	6. Amino acids						
(49)	2 glycine + 4 H_2O	acetate$^{\ominus}$ + 2 $HCO_3^{\ominus}$ + $H^{\oplus}$ + 2 $NH_4^{\oplus}$ + 2 H_2	− 6.0	1	−12.0	OD	[5]
(50)	glutamate$^{\ominus}$ + 3 H_2O	2 acetate$^{\ominus}$ + $HCO_3^{\ominus}$ + $H^{\oplus}$ + $NH_4^{\oplus}$ + H_2	−10.9	1	−10.9	OD	[5]
(51)	alanine + 3 H_2O	acetate$^{\ominus}$ + $HCO_3^{\ominus}$ + $H^{\oplus}$ + $NH_4^{\oplus}$ + 2 H_2	+ 0.5	1	+ 1.0	St	[5]
(52)	leucine + 3 H_2O	isovalerate$^{\ominus}$ + $HCO_3^{\ominus}$ + $H^{\oplus}$ + $NH_4^{\oplus}$ + 2 H_2	+ 0.5	1	+ 1.0	St	[i]
(53)	choline$^{\oplus}$ + H_2O	acetate$^{\ominus}$ + $H^{\oplus}$ + $(CH_3)_3NH^{\oplus}$ + H_2		1			
	7. Sulfonium compounds						
(54)	propiothetine + 3 H_2O	acetate$^{\ominus}$ + $HCO_3^{\ominus}$ + 2 $H^{\oplus}$ + $(CH_3)_2S$ + 2 H_2	− 5.1	1	−10.1	OD	[10]

Table 2 (continued)

Eq. no.	Substrates	Products	$\Delta G'_0$ (kcal/mole H_2) [a]	ATP* formed/reaction (SLP)	$\Delta G'_0$ (kcal/reaction) [a]	Route [b]	Ref.
	8. Inorganic electron donors						
(55)	$2\,NH_4^{\oplus}$	$N_2 + 2\,H^{\oplus} + 3\,H_2$	+6.3	0	+18.9		[5]
(56)	$NH_4^{\oplus} + 2\,H_2O$	$NO_2^{\ominus} + 2\,H^{\oplus} + 3\,H_2$	+35.0	0	+105.0		[5]
(57)	$NH_4^{\oplus} + 3\,H_2O$	$NO_3^{\ominus} + 2\,H^{\oplus} + 4\,H_2$	+35.9	0	+143.5		[5]
(58)	$NO_2^{\ominus} + H_2O$	$NO_3^{\ominus} + H_2$	+38.6	0	+38.6		[5]
(59)	H_2S	$S + H_2$	+6.6	0	+6.6		[5]
(60)	$H_2S + 4\,H_2O$	$SO_4^{2\ominus} + 2\,H^{\oplus} + 4\,H_2$	+9.2	0	+36.9		[5]
(61)	$S + 4\,H_2O$	$SO_4^{2\ominus} + 2\,H^{\oplus} + 3\,H_2$	+10.1	0	+30.3		[5]
(62)	$S_2O_3^{2\ominus} + 5\,H_2O$	$2\,SO_4^{2\ominus} + 5\,H_2$	+10.3	0	+51.5		[5]
(63)	$S_2O_3^{2\ominus} + 3\,H_2O$	$2\,SO_3^{2\ominus} + 3\,H_2$	+18.4	0	+55.2		[5]
(64)	$2\,Fe^{2\oplus} + 2\,H^{\oplus}$	$2\,Fe^{3\oplus} + H_2$	+54.8	0	+54.8		[13]

[a] The $\Delta G'_0$ values have been calculated from ΔG_0(f) values and are given to the first decimal place; they do not include formation or consumption of ATP*. [b] EM = Embden-Meyerhof pathway; OD = oxidative decarboxylation; CC = tricarboxylic acid cycle; BO = β-oxidation of fatty acids; ED = Entner-Doudoroff pathway; PK = phosphoketolase pathway; TT = transaldolase-transketolase pathway; St = Stickland reaction. [c] Analogous to eq. (8). [d] Analogous to eq. (10). [e] ΔG_0(f) of crotonate = −66.1 kcal/mole, calculated from ΔG_0(f) of butyrate [5] and E'_0 of butyrate/crotonate [11]. [f] ΔG_0(f) of acrylate = −68.4 kcal/mole, calculated from eq. (92) and ΔG_0(f) of propionate [10]. [g] Calculated by analogy with glyceraldehyde-3-P/3-P-glycerate [12]. [h] Calculated from the ΔG_0(f) values (kcal/mole) of the following groups: $-COO^{\ominus}$, −86.5; −CHO, −31.0; >CHOH, −37.0; $-CH_2OH$, −40.5; $>CH_2$, +1.2; $-CH_3$, −2.9. [i] Analogous to eq. (51).

of an "energy-rich" bond into a pyrophosphate bond of ATP; they occur in the electron-donating part of the overall redox process. *Electron transport phosphorylations (ETP)* [6, 7, 7a] convert the electrochemical potential between two redox partners in the electron-accepting part of the energy metabolism into an "energy-rich" (pyrophosphate) bond (see Table 1).

Only the complete elucidation of electron transport phosphorylation will show whether it is justified mechanistically to distinguish it from substrate level phosphorylation. Current views [6] suggest that electron transport phosphorylation is closely linked to physical processes (ion gradients, membrane potentials) at particulate cell elements, whereas substrate level phosphorylations are chemical processes catalyzed by soluble enzymes.

2.1. Biological Redox Processes

The metabolic processes that occur in nature are characterized by the diversity of the substrates that can be used for the production of energy. This is particularly true of the electron donors, but also to a considerable degree of the acceptors; they can be either organic or inorganic. The formal division of the energy metabolism into electron donating (Table 2) and electron-accepting (Table 3) reactions allows assembly of the many types of metabolism by combination of the much smaller number of partial processes.

Donor and acceptor processes differ in the mechanism of energy conservation. Donor processes are associated only with substrate level phosphorylations (Table 1); they are essentially the same for aerobic and for anaerobic organisms. In electron acceptor processes, aerobic organisms use oxygen as the terminal oxidant, while anaerobes use both organic (*e.g.* pyruvate, crotonate, acetaldehyde) and inorganic (*e.g.* $H^{\oplus}$, $HCO_3^{\ominus}$, $SO_4^{2\ominus}$) [*] electron acceptors.

The hydrogenation of oxygen in the respiratory chain is associated with a very efficient type of ATP* synthesis (*ETP*). The reduction of the anaerobic electron acceptors, on the other hand, does not appear to allow ATP* synthesis by ETP, since only a few electron acceptors have a sufficiently positive redox potential (Table 5).

Protons can also act as electron acceptors [eq. (113), Table 3] yielding molecular hydrogen. This increases the number of anaerobically possible electron donor processes, since the electrons can be removed *via* the hydrogenase system in any dehydrogenation. However, there is a thermodynamic price to pay for this advantage. The endergonic formation of hydrogen [eq. (113)] requires 4.6 kcal/mole, and this must also be supplied by the exergonic dehydrogenation step. Hydrogen formation has never been observed as the sole electron-accepting reaction of any energy metabolism.

Anaerobiosis also imposes restrictions on the electron-donating process. Thermodynamic considerations

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[*] Nitrate and nitrite should not be regarded in this context as typical anaerobic acceptor substrates, since they were probably formed geologically after the appearance of oxygen [15].

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Table 3, Hydrogenations. Electron-accepting, formally hydrogen-consuming reactions of the energy metabolism.

Eq. no.	Substrates	Products	$\Delta G'_0$ (kcal/mole H_2) [a]	ATP* required/ reaction	$\Delta G'_0$ (kcal/reaction) [a]	Ref.
	1. Carboxylic acids					
(65)	formate$^{\ominus}$ + $H^{\oplus}$ + H_2	formaldehyde + H_2O	+ 5.5	1	+ 5.5	[5]
(66)	formate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	methanol + H_2O	− 2.6	1	− 5.2	[5]
(67)	formate$^{\ominus}$ + $H^{\oplus}$ + 3 H_2	methane + 2 H_2O	−10.7	1 (?)	− 32.2	[5]
(68)	acetate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	ethanol + H_2O	− 0.8	1	− 1.5	[5]
(69)	2 acetate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	butyrate$^{\ominus}$ + 2 H_2O	− 5.0	1	− 10.1	[5]
(70)	acetate$^{\ominus}$ + propionate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	valerate$^{\ominus}$ + 2 H_2O	− 5.0	1	− 10.1	[b]
(71)	acetate$^{\ominus}$ + butyrate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	caproate$^{\ominus}$ + 2 H_2O	− 5.0	1	− 10.1	[b]
(72)	butyrate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	butanol + H_2O	− 2.0	1	− 3.9	[5]
(73)	propionate$^{\ominus}$ + $H^{\oplus}$ + 2 H_2	propanol + H_2O	− 1.2	1	− 2.5	[5, 10]
(74)	2 acetate$^{\ominus}$ + 2 $H^{\oplus}$ + 2 H_2	acetoin + 2 H_2O	+ 6.3	2	+ 12.5	[c]
(75)	2 acetate$^{\ominus}$ + 2 $H^{\oplus}$ + 3 H_2	2,3-butanediol + 2 H_2O	+ 2.0	2	+ 4.0	[c]
(76)	2 acetate$^{\ominus}$ + $H^{\oplus}$	acetone + $HCO_3^{\ominus}$		1	+ 8.8	[5]
(77)	2 acetate$^{\ominus}$ + $H^{\oplus}$ + H_2	isopropanol + $HCO_3^{\ominus}$	+ 2.8	1	+ 2.8	[5]
	2. α-Keto acids					
(78)	pyruvate$^{\ominus}$ + H_2	lactate$^{\ominus}$	−10.3		− 10.3	[5]
(79)	pyruvate$^{\ominus}$ + H_2O + H_2	ethanol + $HCO_3^{\ominus}$	−13.6		− 13.6	[5]
(80)	pyruvate$^{\ominus}$ + H_2	acrylate$^{\ominus}$ + H_2O	−11.7		− 11.7	[d]
(81)	pyruvate$^{\ominus}$ + 2 H_2	propionate$^{\ominus}$ + H_2O	−15.0		− 29.9	[5, 10]
(82)	2 pyruvate$^{\ominus}$ + 2 H_2O + H_2	2,3-butanediol + 2 $HCO_3^{\ominus}$	−20.2		− 20.2	[c]
(83)	2 pyruvate$^{\ominus}$ + H_2O + 2 H_2	2,3-butanediol + $HCO_3^{\ominus}$ + formate$^{\ominus}$	−10.2		− 20.4	[c]
(84)	2 pyruvate$^{\ominus}$ + H_2O + 2 H_2	butanol + 2 $HCO_3^{\ominus}$	−19.1		− 38.1	[5]
(85)	pyruvate$^{\ominus}$ + acetate$^{\ominus}$ + H_2	butyrate$^{\ominus}$ + $HCO_3^{\ominus}$	−22.2		− 22.2	[5]
(86)	pyruvate$^{\ominus}$ + $HCO_3^{\ominus}$ + H_2	malate$^{2\ominus}$ + H_2O	− 5.0	1	− 5.0	[5]
(87)	pyruvate$^{\ominus}$ + $HCO_3^{\ominus}$ + H_2	fumarate$^{2\ominus}$ + 2 H_2O	− 4.0	1	− 4.0	[5]
(88)	pyruvate$^{\ominus}$ + $HCO_3^{\ominus}$ + 2 H_2	succinate$^{2\ominus}$ + 2 H_2O	−12.3	1	− 24.6	[5]
(89)	α-ketobutyrate$^{\ominus}$ + 2 H_2	butyrate$^{\ominus}$ + H_2O	−15.0		− 29.9	[e]
(90)	oxalacetate$^{\ominus}$ + 2 H_2	succinate$^{2\ominus}$ + H_2O	−15.6		− 31.1	[5]
(91)	acetoacetate$^{\ominus}$ + H_2	β-hydroxybutyrate$^{\ominus}$	− 6.9		− 6.9	[12]
	3. α,β-Unsaturated acids, hydroxy acids					
(92)	acrylate$^{\ominus}$ + H_2	propionate$^{\ominus}$	−18.2		− 18.2	[f]
(93)	crotonate$^{\ominus}$ + H_2	butyrate$^{\ominus}$	−18.2		− 18.2	[g]
(94)	fumarate$^{2\ominus}$ + H_2	succinate$^{2\ominus}$	−20.5		− 20.5	[5]
(95)	lactate$^{\ominus}$ + H_2	propionate$^{\ominus}$ + H_2O	−19.6		− 19.6	[5, 10]
(96)	β-hydroxybutyrate$^{\ominus}$	butyrate$^{\ominus}$ + H_2O	−20.0		− 20.0	[5]
(97)	malate$^{2\ominus}$ + H_2	succinate$^{2\ominus}$ + H_2O	−19.7		− 19.7	[5]
(98)	glycolate$^{\ominus}$ + H_2	acetate$^{\ominus}$ + H_2O	−18.8		− 18.8	[5]
(99)	propiothetine + H_2	propionate$^{\ominus}$ + $H^{\oplus}$ + $(CH_3)_2S$	−27.9		− 27.9	[10]
	4. Aldehydes					
(100)	formaldehyde + H_2	methanol	−10.7		− 10.7	[5]
(101)	acetaldehyde + H_2	ethanol	−10.0		− 10.0	[5]
(102)	acetone + H_2	isopropanol	− 5.9		− 5.9	[5]
(103)	glyceraldehyde + H_2	glycerol	− 8.3		− 8.3	[c]
	5. Alcohols					
(104)	methanol + H_2	methane + H_2O	−27.0		− 27.0	[5]
(105)	ethanol + H_2	ethane + H_2O	−19.1		− 19.1	[c]
(106)	ethylene glycol + H_2	ethanol + H_2O	−21.1		− 21.1	[10]
(107)	glycerol + H_2	1,3-propanediol + H_2O	−19.7		− 19.7	[c]
	6. Amino acids					
(108)	glycine + H_2	acetate$^{\ominus}$ + $NH_4^{\oplus}$	−18.7		− 18.7	[5]
(109)	proline + H_2	δ-aminovalerate				
(110)	ornithine$^{\oplus}$ + H_2	δ-aminovalerate + $NH_4^{\oplus}$				
(111)	arginine$^{\oplus}$ + H_2	δ-guanidinovalerate + $NH_4^{\oplus}$				
(112)	tryptophan + H_2	indolepropionate$^{\ominus}$ + $NH_4^{\oplus}$				
	7. Inorganic electron acceptors					
(113)	$H^{\oplus}$ + NAD(P)H	H_2 + NAD(P)$^{\oplus}$	+ 4.6		+ 4.6	[5]
(114)	$HCO_3^{\ominus}$ + H_2	formate$^{\ominus}$ + H_2O	− 0.2		− 0.2	[5]
(115)	$HCO_3^{\ominus}$ + 2 H_2 + $H^{\oplus}$	formaldehyde + 2 H_2O	+ 2.7		+ 5.4	[5]
(116)	$HCO_3^{\ominus}$ + 3 H_2 + $H^{\oplus}$	methanol + 2 H_2O	− 1.8		− 5.4	[5]
(117)	$HCO_3^{\ominus}$ + 4 H_2 + $H^{\oplus}$	methane + 3 H_2O	− 8.1		− 32.3	[5]
(118)	2 $HCO_3^{\ominus}$ + 4 H_2 + $H^{\oplus}$	acetate$^{\ominus}$ + 4 H_2O	− 6.4		− 25.6	[5]
(119)	S + H_2	H_2S	− 6.5		− 6.5	[5]
(120)	S + H_2	$HS^{\ominus}$ + $H^{\oplus}$	− 6.6		− 6.6	[5]
(121)	$SO_3^{2\ominus}$ + 2 $H^{\oplus}$ + 2 H_2	S + 3 H_2O	−16.0	[h]	− 32.1	[5]
(122)	$SO_3^{2\ominus}$ + 2 $H^{\oplus}$ + 3 H_2	H_2S + 3 H_2O	−12.9	[h]	− 38.6	[5]
(123)	$SO_4^{2\ominus}$ + H_2	$SO_3^{2\ominus}$ + H_2O	+ 1.9	2 [h]	+ 1.9	[5]
(124)	$SO_4^{2\ominus}$ + 2 $H^{\oplus}$ + 3 H_2	S + 4 H_2O	−10.1	2 [h]	− 30.3	[5]
(125)	$SO_4^{2\ominus}$ + 2 $H^{\oplus}$ + 4 H_2	H_2S + 4 H_2O	− 9.2	2 [h]	− 36.8	[5]
(126)	$S_2O_3^{2\ominus}$ + 2 $H^{\oplus}$ + 4 H_2	2 H_2S + 3 H_2O	−10.3		− 41.3	[5]
(127)	$S_2O_3^{2\ominus}$ + 2 $H^{\oplus}$ + 2 H_2	2 S + 3 H_2O	−14.1		− 28.2	[5]

Table 3 (continued)

Eq. no.	Substrates	Products	$\Delta G_0'$ (kcal/mole H_2) [a]	ATP* required/ reaction	$\Delta G_0'$ (kcal/reaction) [a]	Ref.
(128)	$N_2 + 2\,H^{\oplus} + 3\,H_2$	$2\,NH_4^{\oplus}$	− 6.3		− 18.8	[5]
(129)	$2\,NO_2^{\ominus} + 2\,H^{\oplus} + 3\,H_2$	$N_2 + 4\,H_2O$	−63.7		−191.1	[5]
(130)	$NO_2^{\ominus} + 2\,H^{\oplus} + 3\,H_2$	$NH_4^{\oplus} + 2\,H_2O$	−35.0		−105.0	[5]
(131)	$NO_3^{\ominus} + H_2$	$NO_2^{\ominus} + H_2O$	−38.5		− 38.5	[5]
(132)	$NO_3^{\ominus} + 2\,H^{\oplus} + 4\,H_2$	$NH_4^{\oplus} + 3\,H_2O$	−35.9		−143.5	[5]
(133)	$2\,NO_3^{\ominus} + 2\,H^{\oplus} + 5\,H_2$	$N_2 + 6\,H_2O$	−53.6		−268.1	[5]
(134)	$O_2 + H_2$	H_2O_2	−32.7		− 32.7	[5]
(135)	$H_2O_2 + H_2$	$2\,H_2O$	−80.7		− 80.7	[5]
(136)	$O_2 + 2\,H_2$	$2\,H_2O$	−56.7		−113.4	[5]

[a] Cf. [a], Table 2. [b] Analogous to eq. (69). [c] Cf. [h], Table 2. [d] Cf. [f], Table 2. [e] Analogous to eq. (81). [f] Analogous to eq. (93). [g] Cf. [e], Table 2. [h] 2 ATP* are required for the activation of sulfate, whereas no ATP* appears to be necessary for the reduction of sulfite [14].

practically rule out saturated carboxylic acids as donor substrates, since their dehydrogenation [Table 2, eq. (8) and (9)] is so endergonic that any coupling with anaerobic acceptor processes with simultaneous ATP* synthesis seems hardly possible (but see [16,17]). Similarly, the dehydrogenating cycles [see Table 2, eq. (1), (2), and (13)] cannot serve as sources of energy under anaerobic conditions. Furthermore, the endergonic tricarboxylic acid cycle does not allow a net ATP* synthesis from C_2 units (acetate) by substrate level phosphorylation. Degradation of a substrate beyond acetate is therefore feasible for energy production only if the oxidation of the reduced coenzymes formed in the cycle can be linked to electron transport phosphorylation. This is not possible with the known anaerobic acceptor systems.

If no hydrogen is liberated in the energy metabolism of an anaerobic organism, the hydrogen balance must be compensated internally resulting in further restrictions on the possible metabolic pathways. Whereas aerobic metabolic processes are always intermolecular, the anaerobic energy metabolism must often also be intramolecular. In intermolecular redox processes the electron-donating and the electron-accepting steps (Table 1) are coupled only *via* the electron carrier, whereas in the intramolecular redox processes both the electron carrier and the electron acceptor act as coupling links (Fig. 2). Intramolecular redox processes consequently lose one "degree of freedom": the extent of possible dehydrogenations of the donor substrate and hence also the economic efficiency (Section 2.3) are limited by the need for compensation of the hydrogen balance *via* an intermediate formed from the donor (product coupling).

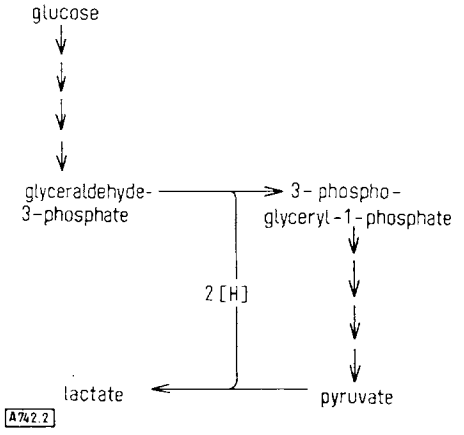


Fig. 2. Product coupling in glycolysis; pyruvate as product.

[16] *T. C. Stadtman* and *H. A. Barker*, J. Bacteriol. *61*, 67 (1951).
[17] *T. C. Stadtman* and *H. A. Barker*, J. Bacteriol. *61*, 81 (1951).

2.2. Energy-Rich Compounds

The "energy-rich" compounds formed in the redox processes of the cellular metabolism are characterized by their free energies of hydrolysis ("group potentials"), which lie in the range 6–15 kcal/mole. However, compounds leading to the formation of an "energy-rich" pyrophosphate bond but utilizing an electrochemical (with respect to a suitable electron acceptor) rather than a hydrolysis potential must also be regarded as "energy-rich" in the biochemical sense; these include substances such as NAD(P)H, $FADH_2$, $FMNH_2$, certain hydroquinones, and reduced cytochromes. In any case, the decisive factor is the ability of these compounds to serve for ATP* formation under the given conditions, *i.e.* that they exist in an enzymatic equilibrium with the ATP* system.

Compounds important for substrate level phosphorylations in anaerobic metabolism are listed in Table 4, while possible donors for electron transport phosphorylations are given in Table 5. It can be seen (particularly from Figure 3) that despite the large number of nutrients available to anaerobic organisms, there are only six to eight substrate level phosphorylation steps for energy conservation. Many anaerobic microorganisms must accomplish the entire ATP* formation by a single substrate level phosphorylation, whereas most aerobic cells have in addition to several substrate level phosphorylations also the very effective electron transport phosphorylation system of the respiratory chain.

2.3. Efficiencies

The production of "energy-rich" compounds, and hence the possibility of energy transfer to the master carrier ATP*, requires an overall metabolism that

Table 4. The "energy-rich" substrates of the ATP-synthesizing enzymes (substrate level phosphorylation).
ADP + substrate ~ P ⇌ ATP + substrate (137)
ADP + P_i + substrate ~ X ⇌ ATP + substrate + X (138)
P_i = inorganic phosphate.

Type of compound	Substrate ~ P or substrate ~ X in eq. (137) and (138)	$\Delta G_0'$ (kcal/mole)	Enzyme	Eq.
phosphoacyl anhydride	acetyl phosphate	−10.7 [10]	acetate kinase (E.C. 2.7.2.1.)	(137)
	carbamyl phosphate	−10.2 [a] [18]	carbamate kinase (E.C. 2.7.2.2.)	
	3-phosphoglyceryl 1-phosphate	−14.9 [a] [12]	3-phosphoglycerate kinase (E.C.2.7.2.3.)	
	propionyl phosphate	−10.7 [b]	propionate kinase (E.C. 2.7.)	
	butyryl phosphate	−10.7 [b]	butyrate kinase (E.C. 2.7.)	
phosphoenol ester	phosphoenol pyruvate	−13.9 [a] [12]	pyruvate kinase (E.C. 2.7.1.40.)	
acyl thioester	succinyl-coenzyme A	− 9.0 [5]	succinate thiokinase (E.C. 6.2.1.4.)	(138)
acyl anilide	N^{10}-formyltetrahydrofolate	− 6.2 [a] [19]	N^{10}-formyltetrahydrofolate synthetase (E.C. 6.3.4.3.)	

[a] Calculated from $\Delta G_0'$, of ATP* ≈ −8.2 kcal/mole [eq. (a)] and the $\Delta G_0'$ values of the kinase reactions.
[b] Analogous to acetyl phosphate.

Table 5. Possible "energy-rich" compounds for electron transport phosphorylation.

The redox potential of "energy-rich" compounds must be so much more negative than that of the respective electron acceptor at pH = 7 that the synthesis of one mole of ATP* becomes energetically possible. This means that in a two-electron transport $\Delta E_0'$ must be at least 200 mV ($\Delta G_0'$ = −9.2 kcal/mole) between two adjacent redox partners in an electron transport chain.

Electron donor	E_0' [a] (mV)	Electron acceptor	Ref.
acetate/*acetaldehyde*	−600		[5]
	−460	$SO_4^{2\ominus}/SO_3^{2\ominus}$	[5]
ferredoxin ox./*red.*	−420		[20]
	−420	CO_2/HCOOH	[5]
	−420	$H^{\oplus}/H_2$	
$NAD^{\oplus}/NADH + H^{\oplus}$	−320		[5]
	−280	S/H_2S	[5]
	−280	*acetoacetyl-CoA*/ β-hydroxybutyryl-CoA	[21]
	−280	$HCO_3^{\ominus}$/acetate	[5]
	−240	$HCO_3^{\ominus}/CH_4$	[5]
FAD/$FADH_2$ [b]	−220		[22]
	−220	$SO_4^{2\ominus}/H_2S$	[5]
	−200	*acetaldehyde*/ethanol	[5]
	−190	*pyruvate*/lactate	[5]
FMN/$FMNH_2$ [b]	−190		[22]
	−140	$SO_3^{2\ominus}/H_2S$	[5]
	− 70	$SO_3^{2\ominus}/S$	[5]
	− 10	*glycine*/acetate$^{\ominus}$ + $NH_4^{\oplus}$	[5]
	− 15	*crotonyl-CoA*/ butyryl-CoA	[11]
	+ 30	*fumarate*/succinate	[5]
	+170	*methanol*/methane	[5]
cytochrome c $Fe^{3\oplus}/Fe^{2\oplus}$	+220		[12]
	+340	$NO_2^{\ominus}/NH_4^{\oplus}$	[5]
	+420	$NO_3^{\ominus}/NO_2^{\ominus}$	[5]
	+815	O_2/H_2O	[5]
	+970	$NO_2^{\ominus}/N_2$	[5]

[a] $E_0' \equiv E_0$ (standard conditions) against the H electrode at pH = 7 and 25 °C. Calculated from the $\Delta G_0'$ values of Tables 2 and 3.

[b] The redox potentials of flavin enzymes may differ by as much as 200 mV from the values for the free coenzymes.

(formulated with the concentration of the exogenous substrates and of the products[*]) is sufficiently exergonic[**] [eq. (b)]:

$$\Delta G' = \Delta G_0' + 1.4 \log ([\text{products}]/[\text{exogenous substrates}]) \quad \text{(b)}$$

In order to synthesize an ATP* a free energy of −8.2 kcal/mole is needed for a reaction when carried out reversibly. The *thermodynamic efficiency* η [eq. (c)] of such an idealized *in-vitro* process is 100%.

$$\eta = \frac{n \times \Delta G_0' \text{ (ATP hydrolysis)}}{\Delta G_0' \text{ (overall process)}} \times 100\ (\%) \quad \text{(c)}$$

n = moles of ATP* formed per overall process

So high an efficiency cannot be reached in living cells, which are open systems with steady state equilibria, since not all the individual processes are reversible or even quasi-reversible. Moreover, the stoichiometric coupling of energy-supplying reactions and ATP* formation leads to a "quantization" of the energy transfer, with the result that only packets of 7–9 kcal/mole can be utilized for energy conservation. Exergonic processes yielding substantially smaller amounts of free energy in fact reduce the efficiency of the overall process; this is also true of the part of the energy of strongly exergonic reactions that exceeds 7–9 kcal/mole (Fig. 4).

A theoretical derivation of the upper efficiency limit for metabolic processes in living organisms has not yet been provided.

Experience has shown, however, that η values of more than 50% for overall processes are very unlikely. The

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[22] *W. M. Clark*: Oxidation Reduction Potentials of Organic Systems. The Williams and Wilkins Comp., Baltimore 1960, p. 444.

[*] They include the synthesized cell material which, in the case of anaerobes, can usually be disregarded as a product with little loss of accuracy (see Table 7)

[**] In microbiological cultures, the concentration ratio of products to exogenous substrates is generally $\geq 10^{-2}$ at the beginning of a growth phase and $\leq 10^2$ towards the end. The effectively utilizable energy of a metabolic process $\Delta G'$ thus deviates by at most ±2.8 kcal/mole from its standard free energy $\Delta G_0'$. It is therefore permissible to use $\Delta G_0'$ as the mean of $\Delta G'_{\text{initial}}$ and $\Delta G'_{\text{final}}$ for the assessment of the thermodynamics of an overall metabolism.

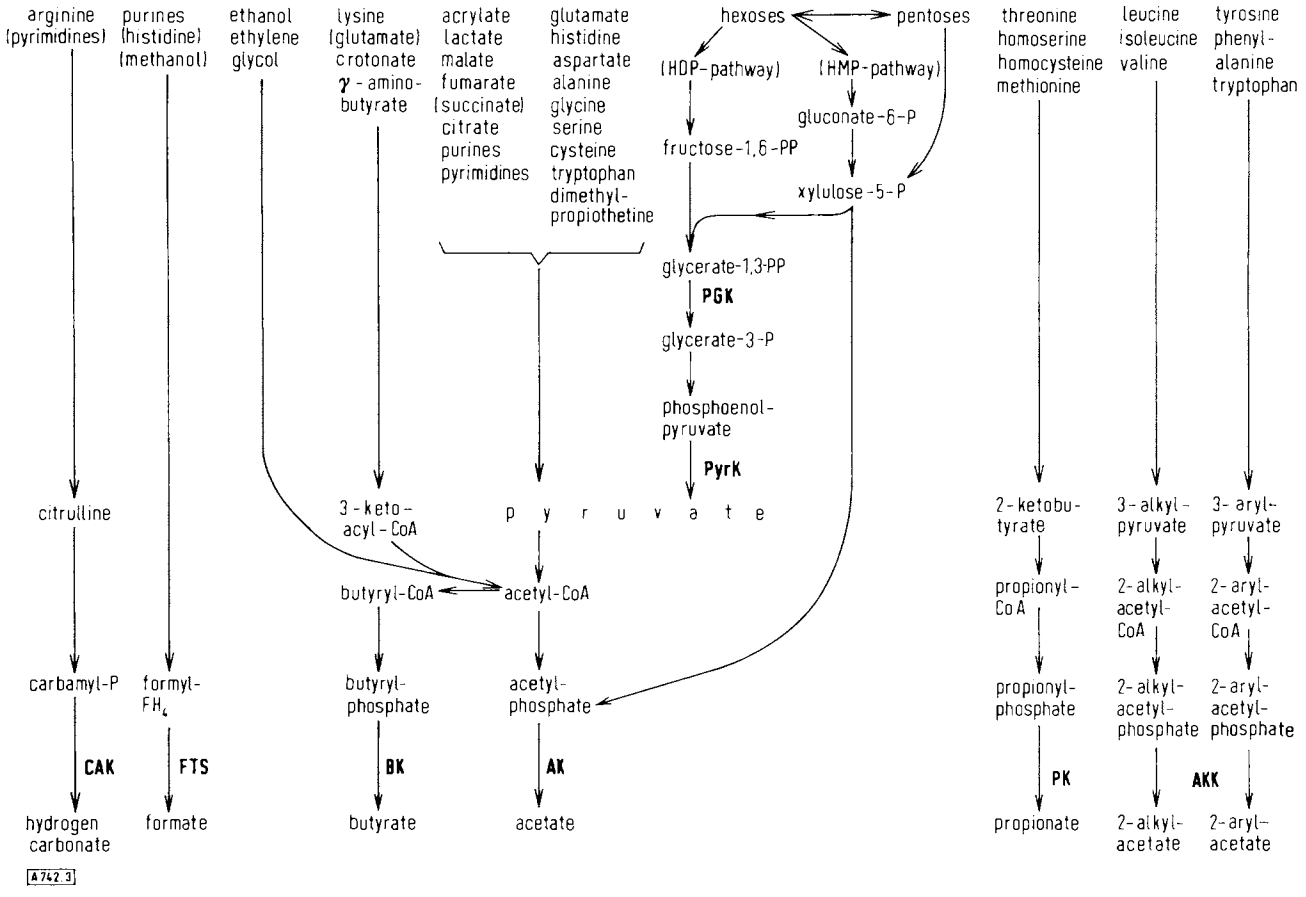


Fig. 3. Participation of the ATP*-synthesizing reactions in the catabolism (energy metabolism) of carbohydrates, amino acids, carboxylic acids, alcohols, and purine bases in anaerobes. HDP (hexose diphosphate) pathway; HMP (hexose monophosphate) pathway; CAK = carbamate kinase; FTS = formyltetrahydrofolate synthetase; AK = acetate kinase; PK = propionate kinase; BK = butyrate kinase; AAK = alkyl (aryl) acetate kinase; PGK = phosphoglycerate kinase; PyrK = pyruvate kinase.

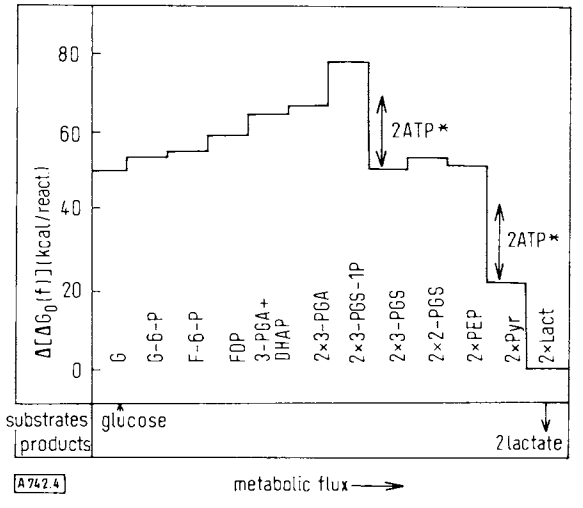


Fig. 4. Energy profiles of the metabolites of glycolysis. The free energies of formation ΔG_0 (f) of inorganic phosphate and of water are accounted for in the calculation of the differences. G = glucose; F = fructose; 3-PGA = 3-phosphoglyceraldehyde; DHAP = dihydroxyacetone phosphate; PGS = phosphoglycerate; PEP = phosphoenol pyruvate; Pyr = pyruvate; Lact = lactate.

majority of anaerobes work at efficiencies of 15 to 30%. With oxygen as an electron acceptor and a functional electron transport phosphorylation, the thermodynamic efficiency η is only slightly, the *economic efficiency* γ [eq. (d)]

$$\gamma = \frac{\text{moles of ATP* formed}}{\text{mole of substrate transformed}} \qquad \text{(d)}$$

of a cell considerably, improved (*e.g.* fermentation of glucose $\gamma = 2$, $\eta = 34\%$; respiration of glucose $\gamma \leqslant 38$, $\eta \leqslant 46\%$).

If the pathway of an energy metabolism is known, the η values can be calculated from eq. (c). For anaerobic lactic acid fermentation (Tables 2 and 3; eq. (34) + 2 × eq. (78)] they are found to be 34.5% (Embden-Meyerhof pathway, $\gamma = 2$) and 17.3% (Entner-Doudoroff pathway, $\gamma = 1$); the corresponding η values for the anaerobic alcohol fermentation [eq. (34) + 2 × eq. (79)] are 30.4% and 15.2% respectively. The relations between $\Delta G'_0$ of the catabolism, ATP* yield (γ), and cell synthesis, which are closely interrelated, will be discussed in detail in Section 2.4.

Certain predictions concerning the course of *in vivo* ATP* syntheses seem possible on the basis of thermodynamic data. The following rules are useful for the formulation and evaluation of the energy metabolism:

1. The effectiveness of the cell metabolism depends on its economic [γ in eq. (d)], rather than its thermodynamic efficiency [η in eq. (c)].

2. The thermodynamic efficiency of the metabolism of chemotrophic anaerobes does not exceed 50%, and is usually between 15 and 35%.

3. The transfer of energy by the ATP* system (substrate level and electron transport phosphorylations) is stoichiometrically related to the substrate turnover ("quantization" of energy).

4. If $\Delta G_0'$ of a catabolism allows the formation of only one "energy-rich" compound and if a substrate level phosphorylation is mechanistically feasible, it is more likely than a conceivable electron transport phosphorylation.

The application of these rules will be discussed in Section 3 in connection with some examples of anaerobic energy metabolism.

2.4. ATP* Turnover in Growing Cells

2.4.1. Limitation of Growth by Energy Metabolism

The central position of ATP* in metabolism relates the formation and consumption of this compound closely to the total free energy turnover in the cell. Since the intracellular concentration of ATP is of the order of 1–5 mmoles/l, and so represents a stationary ATP* energy of less than 0.04 kcal/g of fresh cells, the adenylic acid system obviously has a catalytic role. It can be calculated that ATP* must be consumed and resynthesized at least 4000 times[*] during the doubling of the cell mass in a growing bacterial culture. The function of ATP* as a switchboard for the energy turnover necessitates a kinetic equilibrium between ATP* producing and consuming reactions:

$$v_{\text{ATP* formation}} = v_{\text{ATP* consumption}} = v_{\text{growth}}$$

v = reaction rate

The process with the smaller capacity thus becomes the limiting factor for cell growth.

In aerobic organisms anabolism is generally rate-limiting. The energy-supplying processes can then be matched if (a) the increased ATP concentration or the decreased ADP (AMP) concentration have regulatory functions; (b) ATP* energy is diverted to the syntheses of storage material (polysaccharides, fats, poly-β-hydroxybutyric acid, *etc.*); (c) the energy-supplying processes are uncoupled or short-circuited: either less ATP* is formed or excess ATP* is split ("ATPases") with liberation of heat. In cases (b) and (c), which are found in aerobic bacteria, there is no proportionality between ATP* formation and cell synthesis.

In anaerobes the growth-limiting factor appears to be mainly the generation of ATP* in catabolism. This can be understood in view of the relation of the catabolic to the anabolic substrate supply in aerobic and anaerobic organisms.

This may be illustrated by the following example.

Consider an aerobic and an anaerobic cell that have the same enzymatic capacity and the same mechanisms (where relevant) of anabolism and of catabolism (*e.g.* formation from glucose of lactate or of CO_2); let the maximum anabolic capacity per cell be arbitrarily 30 C_3 units (*e.g.* pyruvate)/min, and the maximum catabolic capacity 100 C_6 units (*e.g.* glucose)/min.

An average of 8 ATP* are required for the conversion of one C_3 unit into cell material.

An aerobic organism can make use of its full anabolic capacity by complete degradation [eq. (37) and (136)] of $(8 \times 30)/38 = 6.3$ C_6 units for the supply of energy and $30/2 = 15$ C_6 units for the supply of anabolic precursors, *i.e.* using a total of only about 20% of its catabolic capacity.

The anaerobe on the other hand would have to use [eqs. (34) and (79)] $(8 \times 30)/2 = 120$ C_6 units for the production of energy alone, and a further 15 for the anabolic substrate, *i.e.* 135% of its actual catabolic capacity.

2.4.2. Growth yields (Y_S, Y_P, Y_{ATP})

The ATP* turnover in a living cell can be measured, if at all, only with great difficulty (*e.g.* by incorporation of ^{18}O from water into phosphate)[22a]. This important quantity must therefore be determined by measurement of the growth yields.

The growth yield Y_S or Y_P is defined as the number of grams Z of cell material (dry mass) formed on consumption of S moles of the energy substrate or with formation of P moles of product.

$$Y_S = \frac{Z\ [\text{g}]}{S\ [\text{moles}]} \qquad \text{(e)}$$

$$Y_P = \frac{Z\ [\text{g}]}{P\ [\text{moles}]} \qquad \text{(e')}$$

If the metabolism of the substrate, and particularly the phosphorylation reactions involved, is known, the net gain γ of ATP* (economic efficiency) can also be expressed in relation to the amount of substrate consumed S or product formed P.

$$\gamma_S = \frac{\text{moles of ATP* formed}}{\text{mole of substrate consumed}} \qquad \text{(d')}$$

$$\gamma_P = \frac{\text{moles of ATP* formed}}{\text{mole of product formed}} \qquad \text{(d'')}$$

The ATP growth yield (Y_{ATP}) is thus found to be

$$Y_{ATP} = \frac{Y_{S(P)}}{\gamma} \frac{[\text{g cells}]}{[\text{mole ATP}]} \qquad \text{(f)}$$

This quantity indicates how many grams of cell material are synthesized at the cost of one mole of ATP*. Y_{ATP} is thus the coupling factor between the ATP* turnover and the cell growth. If it were found to be a biological constant, conclusions about unknown metabolic pathways and in particular about the number of ATP*-forming steps (substrate level and electron transport phosphorylation) could be drawn from yield measurements.

Significant results can be obtained from yields methods only if very strictly defined experimental conditions are observed[23–26]. In particular, it is necessary to

[*] Assuming that 5 μmoles of ATP are present per g of wet cells and that the average growth yield (Y_{ATP}) is 10 g of dry cells (corresponding to 50 g of wet cells) per mole of ATP*, 20000 μmoles of ATP* are required for the synthesis of 1 g of wet cells. The ATP* pool must therefore have been turned over at least 4000 times during the doubling of the cell mass.

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[23] *W. W. Forrest* in: Microbial Growth, 19. Sympos. of the Society for General Microbiology, London 1969, Cambridge University Press, Cambridge 1969, p. 65.

[24] *T. Bauchop* and *S. R. Elsden*, J. gen. Microbiol. *23*, 457 (1960).

[25] *I. C. Gunsalus* and *C. W. Shuster* in *I. C. Gunsalus* and *R. Y. Stanier*: The Bacteria. Academic Press, New York 1961, Vol. 2, p. 1.

[26] *J. C. Senez*, Bacteriol. Reviews *26*, 95 (1962).

ensure that the growth is energy-limited (limited by the energy-substrate), that the measurements are carried out only during the active (logarithmic) growth phase, that the metabolic balance of the energy substrate is quantitatively obtained by measurement of Y_S and Y_P, and that additives to the nutrient medium, *e.g.* yeast extracts, are used for the anabolism rather than for the catabolism. The individual differences of various organisms as to nature, structure, and composition of the proteins, nucleic acids, and polysaccharides are compensated by the approximately equal ATP* requirements for their syntheses (Table 6).

Y_{ATP} values of about 10.5 are obtained when monomers (this refers mainly to the amino acids) are supplied for cellular synthesis in the form of protein hydrolyzates (complex medium). If no monomers are added (minimal medium), additional energy is required for their synthesis from the energy substrate; the Y_{ATP} values found under these conditions are consequently smaller (Table 7). The fact that the difference in the Y_{ATP} values obtained on minimal media is small as compared to complex media suggests that ATP* is necessary for the production of monomers even with supplemented media.

Whereas the ATP* requirement for monomer syntheses and polymerization can be calculated (Table 6), this is not possible at present for the other ATP*-consuming processes (Fig. 1), such as movement energy (particularly in ciliated cells), transport energy (active uptake of molecules or ions from the medium, active transport within the cell), "maintenance energy" [47–49] (resynthesis of cell components in connection with their "dynamic state") [50], and "organization energy" (negative entropy of cellular organization) [23, 26, 51].

It is assumed that the movement energy and in most cases (particularly in non-active uptake of the energy substrate) also the osmotic energy accounts for only a small part of the total energy expenditure; similarly, the turnover of the cell components in actively growing cells appears to be unimportant. The question how much energy a growing cell has to expend in the form of negative entropy of organization has been treated theoretically with varying results [23, 26]; little relevant experimental material appears to be available.

Though the above-mentioned experimental conditions were only partly observed in most cases (Table 7), the data obtained lead to the conclusion that a Y_{ATP} value of about 10.5 is generally valid for anaerobes under energy-limited conditions and for growth on

Table 6. ATP* requirement of the anabolism of *C. kluyveri* [27, 28].

			Protein	RNA	DNA	Lipids	Soluble fraction [a]
Contribution to dry weight (%)			68	7.6	1.4	5	20
ATP* required	mmoles/100 mg fraction [b]	monomer syntheses [c]	4.0	5.2	5.9	—	5.0
		polymerizations	2.7	0.6	0.7	7.2 [d]	—
		total	6.7	5.8	6.6	7.2	5.0
	mmoles/100 mg dry cells	monomer syntheses	4.2				
		polymerizations	2.3				
		total	6.5				
Y_{ATP}		polymerizations (calc.)	43.5				
		monomer syntheses + polymerizations (calc.)	15.4				
		total metabolism (exp.)	9.1				

[a] Extractable in 0.5 N $HClO_4$ at 4 °C. [b] From a component analysis and with the ATP* requirement of the biosyntheses. [c] Starting from CH_3COO^-, HCO_3^-, SO_4^{2-}, NH_4^+, HPO_4^{2-}. [d] Average ATP* requirement per monomer unit ($-CH_2-CH_2-$) = 2.

[27] *R. K. Thauer, K. Jungermann,* and *K. Decker,* Europ. J. Biochem. *1,* 482 (1967).

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Table 7. Survey of methods and results of growth yield determinations for unicellular organisms (bacteria and yeasts) under anaerobic and aerobic conditions.

Organism	Substrates	Y_S	Products	Y_P	γ (theor.)	Medium	T (°C)	Environment [d]	Culture [e]	E [f]	Determination [g]	Y_{ATP}	Ref.
Streptococcus faecalis	glucose	20	?		2/Gl.	semi-synthetic		an	b		turb.	10	[25]
	glucose arginine ribose	22 10.5 21	?		2/Gl. 1/Arg. 2/Rib.	1% casein hydrolyzate	37	an	b c b	1	turb.	11 10.5 10.5	[24]
	glucose glucose arginine	33.5 30.6 18.3	? ? measured		2/Gl. 2/Gl. 1/Arg.	1% casein hydrolyzate	37	an	b b c		turb.	16.7 15.3 18.3	[29]
	glucose [a] glucose [b]	32 21	up to 50% SVS [h] lactate		2/Gl.	2% yeast extract + 2% peptone	37	an	b		turb.	10.5	[30]
	glucose	33	SVS			1% casein hydrolyzate + 0.1% yeast extract + arginine	37	an	b		turb.		[31]
	glucose mannitol pyruvate glycerol	58.2 64.6 15.5 24.7	80% as acetate + CO_2		4/Gl. 4/Man. 1/Pyr. 2/Gly.	complex		ae ae ae ae	b	3	gr.	14.5 16.1 15.5 12.4	[32]
	glucose pyruvate	21.5 6.0	? ?		2/Gl.	complex		an an	b	2	gr.	10.7	
S. diacetilactis	glucose glucose galactose maltose glucose	33.7 32 36.4 64.5 43.4 [c]	?		2/Gl. 2/Gl. 2/Gal. 4/Malt. 2/Gl.	1% peptone + yeast extract or 0.5% casein hydrolyzate	32	an	b c b b c	3.3	turb.	16.8 16.0 18.2 16.1 21.7	[29]
S. lactis	glucose	40	?		2/Gl.		32	an	b		turb.	20	[29]
S. cremoris	glucose	32	?		2/Gl.		32	an	b		turb.	16	[29]
Lactobacillus delbrueckii	glucose	19.6	?		2/Gl.	complex		an	b			9.8	[25]
L. plantarum	glucose	18.8	?		2/Gl.	3% additives	30	ae	b		turb.	9.4	[34]
Leuconostoc mesenteroides	glucose arabinose	14.2 16.2	?			complex		an	b				[25]
Micrococcus lactilyticus	lactate	10.1	?					an	b				[25]
Propionibact. pentosaceum	glucose glycerol lactate	37.5 20 7.6	?			0.5% casein hydrolyzate	30	an	b		turb.		[24]
Pseudomonas lindneri	glucose	8.3	?		1/Gl.	complex	30	an	b		turb.	8.3	[24]
Pseudomonas $C_{12}B$	acetate 1-dodecanol	23.5 217	?			minimal	30	ae	b		gr. + turb.	10.7	[35]
Desulfovibrio desulfuricans	pyruvate + sulfate lactate + sulfate pyruvate + sulfite	9.4 9.9 9.5	?		 1/Pyr.	minimal	32	an	b			 9.5	[26]
Escherichia coli	glucose	25.8	measured	considered	3/Gl.		37	an	b			11.2	[33]
Ruminococcus albus	cellobiose	102	measured		9/Cb.	minimal		an	c		turb.	11.3	[36]
Selenomonas ruminantium	glucose	62				1.5% yeast extract		an	c		turb.		[37]
Bacteroides amylophilus	maltose glycerol	160 20	?		9/Malt. 2/Glyc.	complex		an	b + c		turb.	17.8 10	[38]
Clostridium tetanomorphum	glutamate	6.8	determined quantitatively	considered	0.62/Glu.	1% yeast extract	37	an	b		gr.	10.9	[39]
Clostridium aminobutyricum	hydroxybutyrate aminobutyrate	8.9 7.6	not determined quantitatively		0.5/Hb 0.5/Ab	0.4% yeast extract		an	b			17.8 15.2	[40]

Table 7 (continued)

Organism	Substrates	Y_S	Products	Y_P	γ (theor.)	Medium	T (°C)	Environment [d]	Culture [e]	E [f]	Determination [g]	Y_{ATP}	Ref.
Clostridium sp.	dimethylpropiothetine	3.3	not determined quantitatively		0.33/Dpt.		37	an	b			10.0	[10]
Clostridium glycolicum	ethylene glycol	7.7	determined quantitatively		0.5/Eth.	0.75% casein hydrolyzate	37	an	b			15.4	[41]
Clostridium kluyveri	crotonate	4.8	acetate butyrate $H^{\oplus}$	4.8 9.6 9.1	0.5/Crot. 1/$H^{\oplus}$		33	an	b	3.1	gr.	9.1	[42]
	ethanol acetate	1.5 n.s. [h]	H_2 $H^{\oplus}$ butyrate caproate	4.6 9.1 n.s. [h] n.s. [h]	0.5/H_2 1/$H^{\oplus}$	minimal	33	an	b	1.3	gr.	9.1	[42]
Methanosarcina barkeri	methanol	3.3	?		0.25/Meth.			an	b		gr.	13.2	[43]
Methanobacillus omelianskii	ethanol/CO_2	1	?					an	b		gr.		[43]
Gluconobacter liquefaciens	fructose	21.0	?		2/Fr.	complex	30	ae	b	14		10.5	[44]
Aerobacter aerogenes	glucose fructose	26.1 26.7	determined quantitatively			minimal	37	an	b	14.5		10.2 10.7	[45]
Saccharomyces cerevisiae	glucose	21	?			1% casein hydrolyzate	30	an	b			10.5	[24]
	glucose	89	CO_2		28/Gl.		38	ae	c	61.8		8.5	[46, 6]
Torulopsis utilis	glucose	108	CO_2		38/Gl.		38	ae	c	74.1		10.9	[46, 6]

[a] Logarithmically growing cells. [b] Linearly growing cells. [c] Corrected for maintenance energy and substrate incorporation. [d] an = anaerobic; ae = aerobic. [e] b = batch; c = continuous. [f] E = substrate incorporation in mole % of the substrate turnover. [g] Determination of the cell mass. turb. = turbidity measurements; gr. = gravimetric. [h] SVS = steam volatile substances; n.s. = non-stoichiometric.

complex media. A Y_{ATP} of about 15 has been calculated on the basis of a component analysis of *C. kluyveri* (Table 6) and of the known biosynthetic mechanisms [28]; this value may be taken as the upper yield limit when minimal media are used.

2.4.3. Measurement of Y_{ATP} in the Crotonate Metabolism of *Clostridium kluyveri*

The simplicity of the energy metabolism of *C. kluyveri* with crotonate and hydrogen carbonate as the sole carbon substrates [52] made this strict anaerobe [42] a good subject for the determination of Y_{ATP}. The experimental conditions mentioned in Section 2.4.2 could be maintained.

The anaerobic disproportionation of crotonate follows eq. (g) [sum of eqs. (22) and (93) in Tables 2 and 3]:

$$2\ \text{crotonate}^{\ominus} + 2\ H_2O \rightarrow \text{butyrate}^{\ominus} + 2\ \text{acetate}^{\ominus} + H^{\oplus} \quad (\Delta G_0' = -26.3\ \text{kcal/reaction}) \qquad (g)$$

It is clear from the scheme of the energy metabolism (Fig. 5) that this process is stoichiometrically coupled with a substrate level phosphorylation, and that one ATP* is formed by the acetate kinase reaction [eq. (h)] per proton produced.

$$\text{acetyl phosphate} + \text{ADP} \rightleftharpoons \text{acetate} + \text{ATP} \qquad (h)$$

[52] *R. K. Thauer, K. Jungermann, J. Wenning*, and *K. Decker*, Arch. Mikrobiol. *64*, 125 (1968).

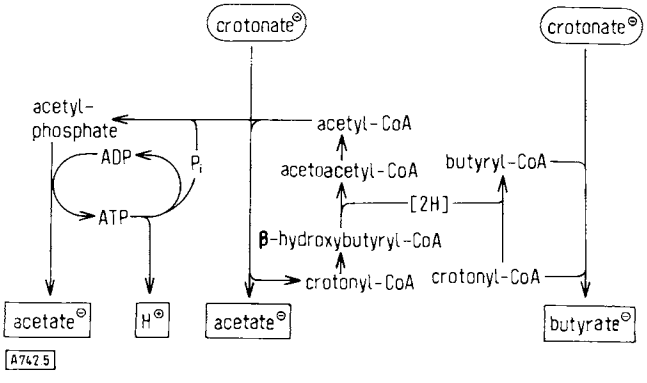


Fig. 5. Scheme of the crotonate fermentation in *Clostridium kluyveri*. P_i = inorganic phosphate.

γ is thus 0.5 with respect to crotonate and 1.0 with respect to $H^{\oplus}$. Identical Y_{ATP} values were calculated from measurements of the cell yield (Table 8) related

Table 8. Y_{ATP} values of the crotonate metabolism of *Clostridium kluyveri* [a].

Substrate or product [b]	$Y_{S(P)}$	γ	Y_{ATP}
crotonate	4.8	0.5	9.6
butyrate	9.6	1.0	9.6
acetate	4.8	0.5	9.6
$H^{\oplus}$	9.1	1.0	9.1

[a] One $H^{\oplus}$ is consumed during the reduction of acetate and CO_2 *via* pyruvate to the average oxidation state of the cell material. By measuring the growth yield per mole of $H^{\oplus}$, therefore, one obtains only the quantity of ATP* that is consumed in the synthesis of the cell material starting from pyruvate. Owing to the low incorporation (3.1%, see Table 7), the deviation lies within the limits of the experimental error. [b] See eq. (g).

to substrate consumption (Y_S) and to product formation (Y_P). The same result was obtained in corresponding experiments with ethanol + acetate + hydrogen carbonate as the growth substrates (Table 7).

3. The Energy Metabolism of Obligate Anaerobes

The most important growth substrates of anaerobic organisms are listed in Figure 3. Some classes of substances (*e.g.* saturated fatty acids, alkanes, and isocyclic aromatic compounds, see Section 2.1) cannot be utilized for the production of energy in the absence of oxygen for thermodynamic and mechanistic reasons. The nutrients of anaerobes are mainly alcohols or acids with additional functional groups which permit further dehydrogenation and hydrogenation reactions. Substrate level (and possibly electron transport) phosphorylations are inserted into the metabolism of these substrates in order to conserve their potential energy. In this section typical energy conserving processes in strict anaerobes are discussed (see Fig. 3 and Tables 2 and 3).

3.1. Substrate Level Phosphorylations

The number of enzymatic processes associated with substrate level phosphorylation has been found to be surprisingly small (Table 5). From the various different substrates[53,54], a few "energy-rich" intermediates (acyl-CoA, formyl-FH_4, carbamyl phosphate) are formed. In anaerobes the necessity to direct the growth substrates to one of these "energy-rich" metabolites with compensation of the H balance (product coupling) requires pathways of substrate conversion quite different from those found in aerobic organisms. Examples are the anaerobic degradation of glutamic acid[39,55,56], glycine[57–59], lysine[60–63], and the purines[64–67].

3.1.1. Acylate Kinases

The process catalyzed by the acylate kinases[39,65,68–70] [eq. (i)] is the most important reaction for the production of energy in anaerobes. It occurs in all Clostridia that utilize amino acids, purine bases, carbohydrates, and alcohols, as well as in sulfate-reducing bacteria. Its occurrence in methanobacteria has not been verified. The acylate kinases can therefore be regarded as typical enzymes of anaerobic life; their central function, as well as that of the associated α-keto acids (pyruvate), can be seen from Figure 3.

Acylate kinases are also found in facultative aerobes[71] (*e.g. E. coli*); they have never been definitely detected in strictly aerobic cells (plants, animals)[69,72].

$$\text{acyl phosphate} + \text{ADP} \rightleftharpoons \text{acylate} + \text{ATP} \qquad (\Delta G'_0 = -2.5 \text{ kcal/mole}) \qquad \text{(i)}$$

Acyl phosphates are formed mainly from acyl-CoA by phosphotransacylation [eq. (j); P_i = inorganic phosphate].

$$\text{acyl-CoA} + P_i \rightleftharpoons \text{acyl phosphate} + \text{CoASH} \qquad (\Delta G'_0 = +2.5 \text{ kcal/mole}) \qquad \text{(j)}$$

In systems whose purpose is the activation of an acid (acylate thiokinases, aminoacyl-t-RNA synthetases), the direction of the acyl~P (*e.g.* acyl adenylate) synthesis is thermodynamically favored since two pyrophosphate bonds [eq. (m)] of the ATP are involved.

$$\text{acylate} + \text{ATP} \rightleftharpoons \text{acyl adenylate} + \text{PP} \qquad \text{(k)}$$
$$\text{PP} + H_2O \rightarrow 2\,P_i \qquad \text{(l)}$$
$$\text{acylate} + \text{ATP} + H_2O \rightarrow \text{acyl adenylate} + 2\,P_i \qquad \text{(m)}$$

3.1.2. Formyltetrahydrofolate Synthetase

The formyltetrahydrofolate synthetase reaction[19,67,73–75] converts the bond energy of the N^{10}-formyl-FH_4 into a pyrophosphate bond of ATP [eq. (n)].

$$\text{formyl-}FH_4 + \text{ADP} + P_i \rightleftharpoons \text{formate} + \text{ATP} + FH_4 \qquad (\Delta G'_0 = +2.0 \text{ kcal/mole}) \qquad \text{(n)}$$

[53] *W. A. Wood* in *J. C. Gunsalus* and *R. Y. Stanier*: The Bacteria. Academic Press, New York 1961, Vol. 2, p. 59.

[54] *H. A. Barker* in [53], p. 151.

[55] *M. Sprecher*, *R. L. Switzer*, and *D. B. Sprinson*, J. biol. Chemistry *241*, 864 (1966); *R. L. Switzer* and *H. A. Barker*, *ibid. 242*, 2658 (1967).

[56] *A. H. Blair* and *H. A. Barker*, J. biol. Chemistry *241*, 400 (1966).

[57] *B. P. Cardon* and *H. A. Barker*, Arch. Biochem. *12*, 165 (1947).

[58] *M. L. Baginsky* and *F. M. Huennekens*, Biochem. biophysic. Res. Commun. *23*, 600 (1966); Arch. Biochem. Biophysics *120*, 703 (1967).

[59] *S. M. Klein* and *R. D. Sagers*, J. biol. Chemistry *241*, 197, 206 (1966); *242*, 297, 301 (1967); J. Bacteriol. *83*, 121 (1962).

[60] *L. Tsai* and *T. C. Stadtman*, Arch. Biochem. Biophysic *125*, 210 (1968).

[61] *T. C. Stadtman* and *P. Renz*, Arch. Biochem. Biophysics *125*, 226 (1968).

[62] *E. E. Dekker* and *H. A. Barker*, J. biol. Chemistry *243*, 3232 (1968).

[63] *R. C. Bray* and *T. C. Stadtman*, J. biol. Chemistry *243*, 381 (1968).

[64] *R. D. Sagers* and *J. V. Beck*, J. Bacteriol. *72*, 199 (1956).

[65] *R. D. Sagers*, *M. Benziman*, and *I. C. Gunsalus*, J. Bacteriol. *82*, 233 (1962).

[66] *J. C. Rabinowitz* and *H. A. Barker*, J. biol. Chemistry *218*, 161 (1956).

[67] *J. C. Rabinowitz* and *W. E. Pricer*, J. biol. Chemistry *237*, 2898 (1962).

[68] *E. R. Stadtman* and *H. A. Barker*, J. biol. Chemistry *184*, 769 (1950).

[69] *I. A. Rose* in *P. D. Boyer*, *H. Lardy*, and *K. Myrbäck*, The Enzymes. Academic Press, New York 1962, Vol. 6, p. 115.

[70] *J. Pawelkiewicz* and *A. B. Legocki*, Bull. Acad. polon. Sci. *11*, 569 (1963); Chem. Abstr. *60*, 12291 (1963).

[71] *I. A. Rose*, *M. Grunberg-Manago*, *S. R. Korey*, and *S. Ochoa*, J. biol. Chemistry *211*, 737 (1954).

[72] *K. Decker*: Die aktivierte Essigsäure. Enke, Stuttgart 1959, p. 151.

[73] *B. K. Joyce* and *R. H. Himes*, J. biol. Chemistry *241*, 5716 (1966); *241*, 5725 (1966).

[74] *L. Jaenicke*, Angew. Chem. *73*, 449 (1961).

[75] *H. R. Whiteley* and *F. M. Huennekens*, J. biol. Chemistry *237*, 1290 (1962).

The ATP* formation according to eq. (n) is an extremely specialized process confined to a few anaerobes (*e.g. C. acidi urici, C. cylindrosporum*)[66,67]. The "energy-rich" formyl or formimino group is formed on degradation of purines, and possibly also from methanol (*via* methyl-FH_4) [Section 3.2.4] and from histidine[54].

Formyltetrahydrofolate synthetase activity is however found not only in anaerobes but also in aerobic cells including the liver of animals[76], where it fulfills an anabolic function.

3.1.3. Carbamate Kinase

ATP* formation from carbamyl phosphate[18,77,78] [eq. (o)] is associated with the degradation of arginine (*S. faecalis*)[24,29] and possibly of pyrimidines (*Zymobacterium oroticum*)[54]. However, this reaction has not been found to be the sole ATP* source in any organism.

carbamyl phosphate + ADP $\rightleftharpoons$ ATP + carbamate ($\Delta G'_0 = -2.0$ kcal/mole) (o)

As in the case of acylate kinases [eq. (i)] and of the acyl thiokinases, a different pathway has also been provided in nature for the anabolic formation of carbamyl phosphate [eq. (p)].

The enzyme carbamyl phosphate synthetase requires *N*-acetyl glutamate and possibly biotin[79,79a] as cofactors, uses glutamine instead of NH_3, consumes two moles of ATP*, and so leads to the practically irreversible formation of carbamyl phosphate[79].

2 ATP + CO_2 + glutamine + 2 H_2O $\rightarrow$ carbamyl phosphate + glutamate + 2 ADP + P_i (p)

3.1.4. Phosphoglycerate Kinase and Pyruvate Kinase

In carbohydrate fermentations[53] the enzymes phosphoglycerate kinase (PGK) and pyruvate kinase (PyrK) participate in ATP* synthesis by substrate level phosphorylations [eq. (q) and (r)]. Pyruvate kinase does not lead to a "*de novo*" synthesis of ATP*; rather, the phosphate needed for carbohydrate activation (*e.g.* hexokinase reaction) and derived from ATP* is transferred back to ADP.

1,3-phosphoenolpyruvate + ADP $\rightleftharpoons$ 3-phosphoglycerate + ATP ($\Delta G'_0 = -6.7$ kcal/mole) (q)

Phosphoenolpyruvate + ADP $\rightleftharpoons$ pyruvate + ATP ($\Delta G'_0 = -5.7$ kcal/mole) (r)

Only these two enzymes of anaerobic carbohydrate catabolism still have an important role in aerobic energy metabolism.

[76] *L. Jaenicke* and *E. Brode*, Biochem. Z. *334*, 108 (1961).

[77] *M. E. Jones* and *F. Lipmann*, Proc. nat. Acad. Sci. USA *46*, 1194 (1960).

[78] *M. E. Jones*, Methods in Enzymol. *5*, 903 (1962).

[79] *V. P. Wellner, J. I. Santos*, and *A. Meister*, Biochemistry *7*, 2848 (1968).

[79a] *R. B. Huston* and *Ph. P. Cohen*, Biochemistry *8*, 2658 (1969).

3.2. Does Electron Transport Phosphorylation Occur in Chemotrophic Anaerobes

Though electron transport phosphorylation in chemotrophic anaerobes is theoretically feasible, its existence has not yet been convincingly demonstrated. Possible candidates are 1. *C. kluyveri, C. sticklandii*; 2. *Methanobacillus omelianskii* and *Methanosarcina barkeri*; 3. *Desulfovibrio* species. An attempt will be made to answer this question on the basis of the existing experimental data.

3.2.1. The Ethanol-Acetate Metabolism of *Clostridium kluyveri*. Reduction of Crotonyl-CoA to Butyryl-CoA

C. kluyveri grows on ethanol, acetate, and CO_2 with formation of butyrate, caproate, and hydrogen[80]. The condensation of ethanol and acetic acid to form butyric acid (and caproic acid) [eq. (45) + eq. (69) = eq. (s), and 2 × eq. (45) + eq. (69) + eq. (71) = eq. (t)] was long regarded as a process that should involve electron transport phosphorylation, in view of the absence of any recognizable substrate level phosphorylation[10,81,82].

ethanol + acetate $\rightarrow$ butyrate + H_2O ($\Delta G'_0 = -8.6$ kcal/reaction) (s)

2 ethanol + acetate $\rightarrow$ caproate + 2 H_2O ($\Delta G'_0 = -17.2$ kcal/reaction) (t)

Electron transport phosphorylation was thought to be coupled to the reductive formation of butyryl-CoA [eq. (u)].

crotonyl-CoA + H_2 $\rightarrow$ butyryl-CoA ($\Delta G'_0 = -18.6$ kcal/reaction) (u)

The electrons could be transferred to a flavoprotein *via* a pyridine nucleotide. Electron transport phosphorylation is theoretically conceivable in such a sequence, since the reduction of flavoproteins by pyridine nucleotides in the respiratory chain is also associated with phosphorylation. The detection of such a process would thus be of fundamental importance, particularly since the reduction of crotonyl-CoA has been found in a *soluble* enzyme system[82].

However, the discovery that the energy metabolism is associated with the formation of $H^{\oplus}$, H_2 gas, and ATP* in stoichiometric amounts [eq. (i) and (j)] and that this ATP* synthesis is sufficient for growth (see section 2.2) ruled out *C. kluyveri* as a candidate for electron transport phosphorylation[42].

The quantitative data on the ethanol-acetate fermentation, together with the results of the dispropor-

[80] *B. T. Bornstein* and *H. A. Barker*, J. biol. Chemistry *172*, 659 (1948).

[81] *H. A. Barker*: Bacterial Fermentations. Wiley, New York 1956, p. 95.

[82] *C. W. Shuster* and *I. C. Gunsalus*, Federation Proc. *17*, 310 (1958).

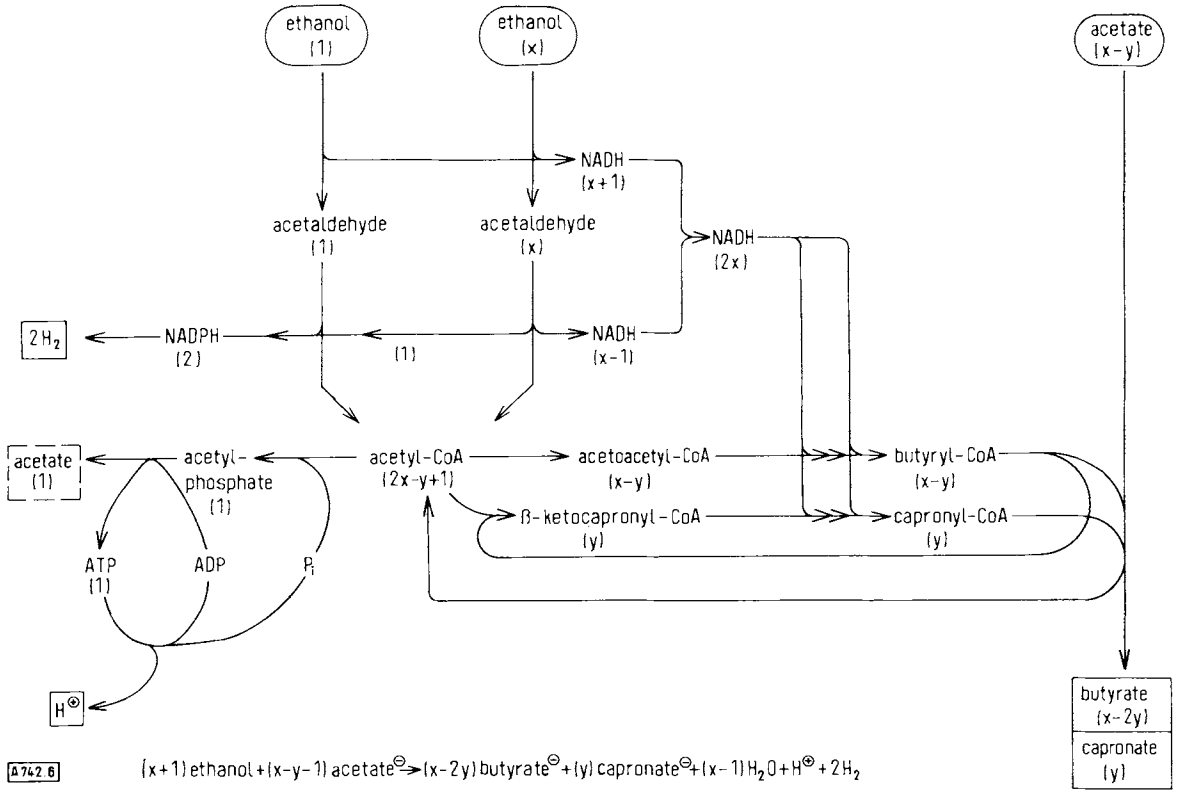


Fig. 6. Scheme of the ethanol-acetate fermentation in *Clostridium kluyveri*. The factors x and y take into account the non-stoichiometric coupling of fatty acid and ATP* synthesis and the growth phase dependent relation of butyrate and caproate formation [42]. At the beginning of the growth phase $x \approx 5$ and $y \approx 1$.

tionation of crotonate [eq. (g)], also allow an interpretation of the coupling mechanism between the energy-supplying and the ATP*-synthesizing processes, as well as an explanation of the acetate requirement of *C. kluyveri* [42,82a] (Fig. 6).

The dehydrogenation of acetaldehyde to acetyl-CoA is the only individual reaction of the catabolism that is linked to a *de novo* formation of an "energy-rich" bond. The right-hand part of Figure 6 shows, however, that the greater part of the "active acetate" is consumed in the butyrate synthesis.

The ATP* synthesis by substrate level phosphorylation can only be associated with the process shown in the left-hand part of Figure 6. However, there is no organic hydrogen acceptor available in this reaction sequence. The free energy of the dehydrogenation of acetaldehyde can therefore be converted into ATP* energy only if electrons react with protons to form hydrogen. Formation of H_2 from NADPH has been demonstrated in a soluble system of *C. kluyveri* (Fig. 8) [83,84].

It is not immediately obvious from Figure 6 why *C. kluyveri* cannot grow with the reactions in the left-hand half of the diagram alone, without the need for the extensive fatty acid formation. However, the formation of acetate and hydrogen from ethanol [eq. (45)] is endergonic, and alone cannot be associated with a net ATP* synthesis. The synthesis of butyrate (or caproate) from ethanol and acetate [eq. (s) and (t)], on the other hand, is exergonic, though not sufficiently so, when the η values are taken into account (see Section 2.3), for the stoichiometric formation of one ATP* per butyrate formed. The fatty acid synthesis must therefore be repeated several times, like a "pump mechanism", to provide sufficient free energy for an ATP* synthesis that is physiologically possible ($\eta \leqslant 35\,\%$). The CoA transferase system [eq. (v)] is responsible for this non-stoichiometric energy coupling.

$$\text{butyryl-CoA} + \text{acetate} \rightleftharpoons \text{butyrate} + \text{acetyl-CoA} \qquad (\Delta G_0' \approx 0) \qquad \text{(v)}$$

The higher group potential of the butyryl-CoA resulting from its exergonic formation is transferred to the acetyl-CoA pool by reaction (v) and so allows a thermodynamically feasible ATP* synthesis [eq. (w); cf eqs. (i) and (j)].

$$\text{acetyl-CoA} + \text{ADP} + P_i \rightleftharpoons \text{ATP} + \text{acetate} + \text{CoA} \qquad (\Delta G_0' \approx 0) \qquad \text{(w)}$$

Since the different group potentials of the CoA-thioesters are reflected in their steady state concentrations (Fig. 7), the non-stoichiometric relation of butyrate, caproate, and ATP* syntheses can also be explained by eq. (v). Under growth conditions, the "pump mechanism" is repeated approximately five times per mole of ATP*, leading to a thermodynamic efficiency of about 20 %.

[82a] *S. Schoberth* and *G. Gottschalk*, Arch. Mikrobiol. *65*, 318 (1969).

[83] *K. Jungermann, R. K. Thauer, E. Rupprecht, C. Ohrloff*, and *K. Decker*, FEBS Letters *3*, 144 (1969).

[84] *R. K. Thauer, K. Jungermann, E. Rupprecht*, and *K. Decker*, FEBS Letters *4*, 108 (1969).

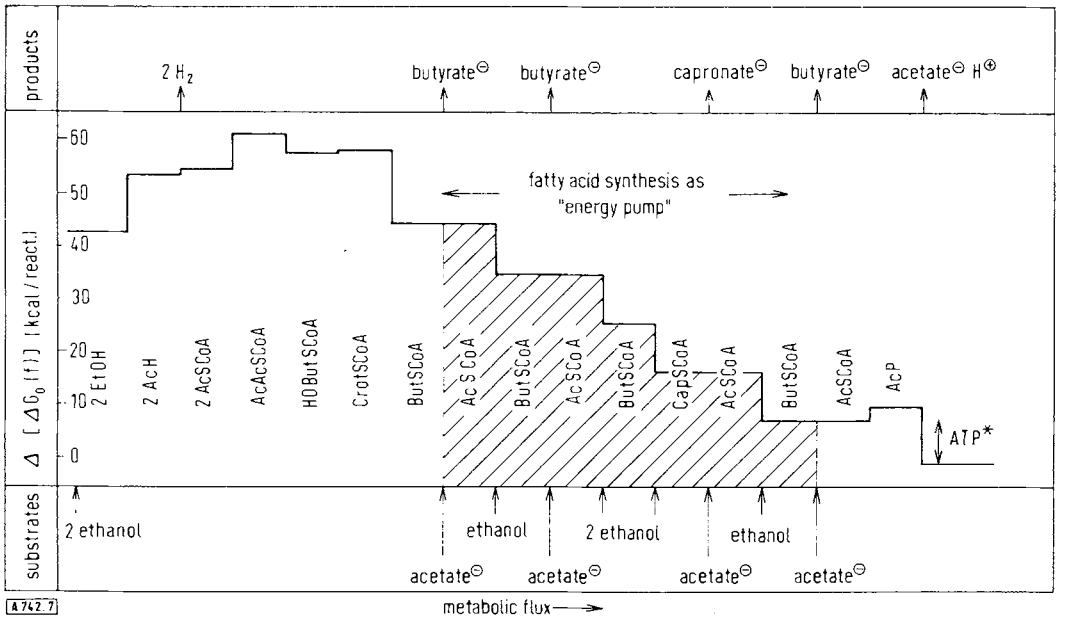


Fig. 7. Energy profile of the metabolites of the ethanol-acetate fermentation of *Clostridium kluyveri*. Note the increase in the group potential $\Delta G'_0$ of acetyl-CoA with each "cycle" of the fatty acid synthesis as result of the increase in the potential difference Δ [ΔG_0(f)] with respect to ethanol.
The free energies of formation ΔG_0(f) of coenzyme A, P_i, and H_2O are accounted for in the calculation of the differences.
EtOH = ethanol; AcH = acetaldehyde; Ac = acetyl; AcAc = acetoacetyl; HOBut = β-hydroxybutyryl; Crot = crotonyl; But = butyryl; Cap = caproyl. Overall metabolism:
6 ethanol + 3 acetate$^{\ominus}$ → 3 butyrate$^{\ominus}$ + 1 caproate$^{\ominus}$ + 4 H_2O + $H^{\oplus}$ + 2 H_2.

The necessity of synthesizing C_4 and C_6 fatty acids also explains why *C. kluyveri* requires acetate as a substrate and cannot grow on ethanol alone.

The main assimilatory reaction of *C. kluyveri* [52,85] is the ferredoxin (Fd)-dependent pyruvate synthesis [86,87] [eq. (x)] (see also Fig. 8).

$$\text{acetyl-CoA} + Fd^{2\ominus}_{red} + 2H^{\oplus} + HCO_3^{\ominus} \rightarrow \text{pyruvate}^{\ominus} + \text{CoA} + Fd_{ox} + H_2O \qquad (x)$$

This acetate and CO_2 assimilation has no effect on the total carbon balance (Table 7).

It is interesting to note that in *C. kluyveri*, the reduction of ferredoxin ($E'_0 = -420$ mV) is effected not by electron donors with a more negative redox potential but by pyridine nucleotides ($E'_0 = -320$ mV) (Fig. 8).

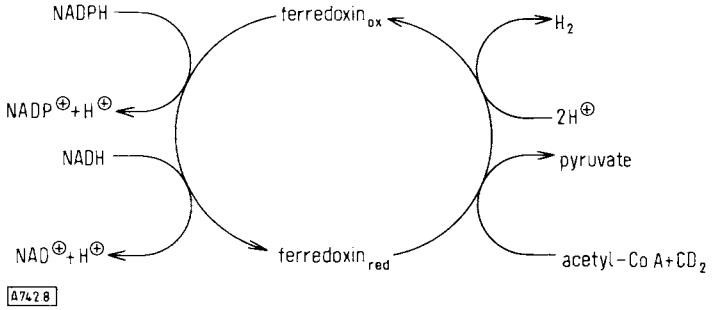


Fig. 8. Ferredoxin-dependent reactions in *C. kluyveri*. The reduction of Fd by NADPH is activated by NAD$^{\oplus}$ and inhibited by NADH, while the reduction of Fd by NADH is activated by acetyl-CoA.

[85] *K. Jungermann, R. K. Thauer*, and *K. Decker*, Europ. J. Biochem. *3*, 351 (1968).

[86] *I. G. Andrew* and *J. G. Morris*, Biochim. biophysica Acta *97*, 176 (1965).

[87] *G. Gottschalk* and *A. A. Chowdhury*, FEBS Letters *2*, 342 (1969).

3.2.2. The Alanine-Glycine Metabolism in *C. sticklandii*. Reduction of Glycine to Acetate and NH_3

Some clostridia can obtain their energy from a redox process in which one mole of an amino acid is dehydrogenated and 2 moles of another are reduced (Fig. 9) [54].

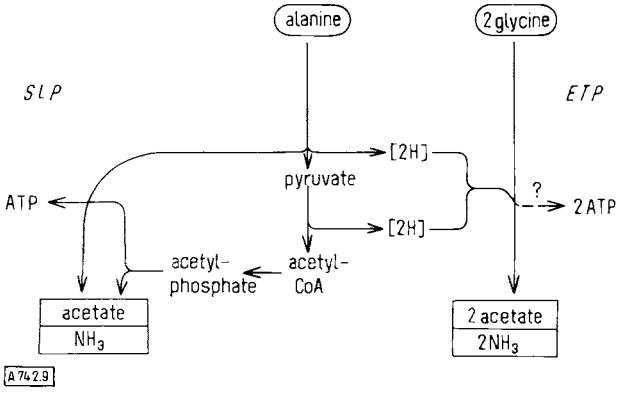


Fig. 9. Scheme of a Stickland reaction (alanine-glycine metabolism of *Clostridium sticklandii*).
SLP = substrate level phosphorylation: *ETP* = electron transport phosphorylation.

The dehydrogenation is associated with a substrate level phosphorylation. In *Clostridium sticklandii* and *Clostridium lentoputrescens*

$$\text{glycine} + \text{NADH} + H^{\oplus} \rightarrow \text{acetate}^{\ominus} + NH_4^{\oplus} + NAD^{\oplus} \quad (\Delta G'_0 = -14.4 \text{ kcal/mole}) \qquad (y)$$

the reducing system [eq. (y)] also appears to be coupled with an ATP* formation [88,89].

[88] *T. C. Stadtman*, Biochem. Z. *331*, 46 (1959).

[89] *T. C. Stadtman*, Arch. Biochem. biophysics *113*, 9 (1966).

The details of this process, which involves several protein fractions and cofactors, are not yet known. Since this phosphorylation is sensitive to uncoupling agents, the presence of electron transport phosphorylation was postulated. If the reductive process were coupled to an electron transport phosphorylation, which should proceed stoichiometrically, the thermodynamic efficiency (η) of the catabolism would be about 65%. Yields as high as this make such a reaction unlikely. Y values have not yet been determined owing to the complicated nutrient requirements of these organisms. It is not yet possible to decide whether electron transport phosphorylation is involved in the reduction of glycine.

3.2.3. The Ethanol-CO_2 Metabolism in *Methanobacillus omelianskii*. Reduction of CO_2 to CH_4

The metabolism of the methane-forming organisms presents some mechanistically and thermodynamically interesting problems. The formation of methane from CO_2 and ethanol is, as a whole, an exergonic process [2 × eq. (45) + eq. (117) = eq. (z)].

$$2\,\text{ethanol} + HCO_3^{\ominus} \rightarrow 2\,\text{acetate}^{\ominus} + H^{\oplus} + CH_4 + H_2O \quad (\Delta G'_0 = -29.3\ \text{kcal/reaction}) \qquad (z)$$

Since the available results [90] indicate that acetate in eq. (45) is not formed *via* acetyl-CoA, the course of the ATP* synthesis in this organism is unknown. Moreover, it has recently been reported that the cultures described as *M. omelianskii* are a symbiotic association of two species of bacteria, one of which has a metabolism according to eq. (45), and the other a metabolism according to eq. (117) [91]. It is thermodynamically impossible, however, for an organism to maintain its energy metabolism by means of the endergonic reaction eq. (45) alone. Certain observations indicate that the organism growing on CO_2 and H_2 also requires acetate for growth [91]. It is not possible at present to give an interpretation of the metabolism of "*M. omelianskii*", and hence of the problem of electron transport phosphorylation.

3.2.4. The Methanol Metabolism in *Methanosarcina barkeri*. Reduction of CH_3OH to CH_4

Methanosarcina barkeri forms methane and CO_2 by a disproportionation of methanol [3 × eq. (104) + eq. (44) = eq. (aa)] [43].

$$4\,CH_3OH \rightarrow 3\,CH_4 + HCO_3^{\ominus} + H^{\oplus} + H_2O \quad (\Delta G'_0 = -75.5\ \text{kcal/reaction}) \qquad (aa)$$

On the basis of an experimental Y_S value of about 3.3, corresponding to $\gamma = 0.3$, one mole of ATP* would be formed per 3–4 moles of methanol consumed; ATP* synthesis could most likely occur in the dehydrogenation of methanol *via* the formyltetrahydrofolate synthetase reaction [eq. (n)]. Since an additional electron transport phosphorylation in the reduction of CH_3OH to CH_4 should give a γ value of 1.0, there is no reason to postulate an electron transport phosphorylation in this fermentation.

[90] *W. J. Brill* and *R. S. Wolfe*, Federat. Proc. *24*, 233 (1964).

[91] *M. P. Bryant, E. A. Wolin, M. J. Wolin*, and *R. S. Wolfe*, Arch. Mikrobiol. *59*, 20 (1967).

3.2.5. The Lactate-Sulfate Metabolism in Desulfovibrio Organisms. Reductions of Sulfate to Sulfide

In these organisms [26,92], the dehydrogenation of lactate (or pyruvate) to acetate is coupled with the reduction of inorganic sulfate [2 × eq. (17) + eq. (125) = eq. (bb) or 4 × eq. (10) + eq. (125) = eq. (cc)].

$$2\,\text{lactate}^{\ominus} + SO_4^{2\ominus} \rightarrow 2\,\text{acetate}^{\ominus} + 2\,HCO_3^{\ominus} + H_2S \quad (\Delta G'_0 = -40.6\ \text{kcal/reaction}) \qquad (bb)$$

or

$$4\,\text{pyruvate}^{\ominus} + SO_4^{2\ominus}\ 4\,H_2O \rightarrow 4\,\text{acetate}^{\ominus} + 4\,HCO_3^{\ominus} + H_2S + 2\,H^{\oplus} \quad (\Delta G'_0 = -85.2\ \text{kcal/reaction}) \qquad (cc)$$

The eight electrons for the reduction of $SO_4^{2\ominus}$ to $S^{2\ominus}$ are provided by the dehydrogenation of lactate (2 moles) or pyruvate (4 moles). The formation of acetate is accompanied by a substrate level phosphorylation, so that 2 ATP*/mole of reduced $SO_4^{2\ominus}$ are formed with lactate as the electron donor, and 4 ATP*/mole of reduced $SO_4^{2\ominus}$ with pyruvate. The reduction of the sulfate is preceded by its activation [eq. (dd)] [14].

$$\text{ATP} + \text{sulfate} \rightarrow \text{adenosine 5'-phosphosulfate} + \text{pyrophosphate} \qquad (dd)$$

Pyrophosphate is presumably hydrolyzed [eq. (l)] also in these bacteria, so that the activation of $SO_4^{2\ominus}$ is associated with a net consumption of 2 ATP*. ATP* synthesized by substrate level phosphorylation would be available for the anabolic requirements of the organism only in the presence of pyruvate, and not of lactate. However, determination of Y_{ATP} with lactate and pyruvate as substrates gave similar values between 9 and 10 [26]. Since *Desulfovibrio* has a cytochrome c_3, which takes up the electrons from the dehydrogenation of pyruvate, and since autotrophic growth has been reported [93], electron transport phosphorylation has been postulated to occur. This hypothesis is supported by reports [94,95] of a phosphorylation coupled to the reduction of sulfate in cell-free extracts of *D. gigas* and its uncoupling by substances such as 2,4-dinitrophenol, which also inhibit oxidative phosphorylation.

Autotrophy, however, has been questioned [96–98]; moreover, all the substrates and products involved in the energy metabolism have not been determined simultaneously. The stoichiometry of eqs. (bb) and (cc)

[92] *J. R. Postgate* and *L. L. Campbell*, Bacteriol. Rev. *30*, 732 (1966); *P. A. Trudinger*, Advances microbial Physiol. *3*, 111 (1969).

[93] *K. R. Butlin, M. E. Adams*, and *M. Thomas*, J. gen. Microbiol. *3*, 46 (1949).

[94] *H. D. Peck*, J. biol. Chem. *235*, 2734 (1960).

[95] *H. D. Peck*, Biochem. biophysic. Res. Commun. *22*, 112 (1966).

[96] *J. R. Postgate*, Z. allg. Mikrobiol., Morphol., Physiol., Genetik Ökol. Mikroorganismen *1*, 53 (1960).

[97] *B. J. Mechalas* and *S. C. Rittenberg*, J. Bacteriol. *80*, 501 (1960).

[98] *Yu. I. Sorokin*, Nature (London) *210*, 551 (1966).

has thus not been experimentally verified. Though the prevailing evidence points to electron transport phosphorylation in *Desulfovibrio*, conclusive proof has not yet been presented.

4. Position of Anaerobes in Phylogeny

Considering important catabolic and anabolic mechanisms an attempt will be made to provide a biochemical basis for the classification of anaerobes and aerobes and for the definition of the principal types of metabolism.

4.1. Molecular Evolution

The first life forms must have arisen at a time when the earth was still surrounded by a reducing atmosphere[2,3]. The nutrients available to these primordial anaerobes were simple abiogenic organic compounds such as amino acids, alcohols, short-chain substituted fatty acids, purine bases, and carbohydrates[99]. These chemoheterotrophic organisms probably obtained their energy by substrate level phosphorylations (fermentations, see below). The ability to utilize the light energy of the sun (photosynthesis, see below) *via* electron transport phosphorylation is believed to have developed later, though still in the anaerobic phase. The first photoautotrophic (still anaerobic) organisms then evolved from these photoheterotrophic organisms.

The change to the oxygen atmosphere of today is generally explained by the biological photolysis of water (of the plant photosynthesis type[*]). The most recent mechanisms of biological energy transformation may therefore be considered to be the chemoheterotrophic and chemoautotrophic redox processes with oxygen as the terminal electron acceptor (respiration, see below), and the aerobic organisms are therefore the most recent organisms.

Remarkable similarity exists between the energy-converting systems in respiration and in photosynthesis; both have particulate electron transporting cytochrome systems, which are coupled to ATP* synthesis. It may therefore be assumed that they did not develop independently, but that one arose from the other. The evolution of the respiratory from the photosynthetic apparatus can easily be pictured since the photosynthetic electron transport effected by cytochrome could in principle have been diverted to oxygen by acquisition of a single autoxidizable enzyme, *i.e.* cytochrome oxidase (Fig. 10). Cytochrome oxidase, *Warburg*'s "Atmungsferment", must therefore be regarded as the specific enzyme of the aerobic energy metabolism.

The enzyme class of oxygenases may be regarded as an even more recent acquisition in the phylogenetic scheme (Fig. 10). They are typical enzymes of aerobic anabolism, but are also involved in catabolism (*e.g.* aromatic compounds) in a few cases[99a].

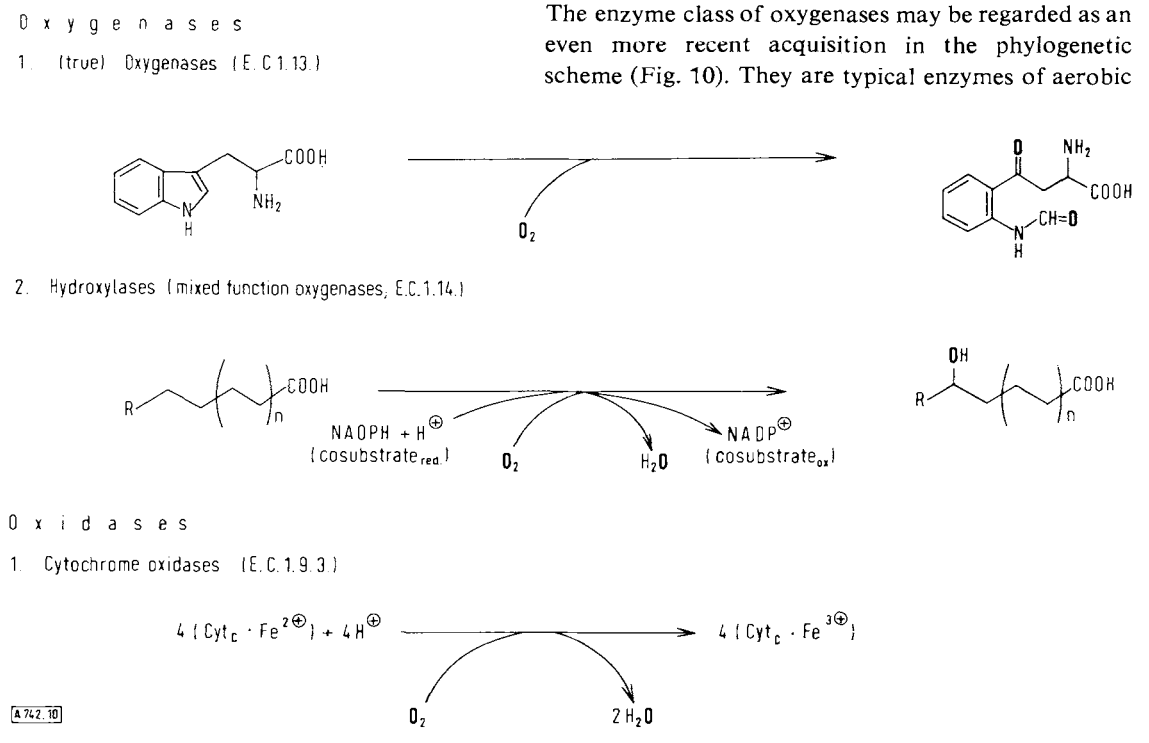


Fig. 10. Reactions of oxygenases, hydroxylases, and oxidases. Oxygenases introduce *both* atoms, and hydroxylases only *one* atom of molecular oxygen into a substrate. Oxidases require molecular oxygen as an electron acceptor; oxygen is *not* introduced into the substrate.

[99] *A. I. Oparin*: Genesis and Evolutionary Development of Life. Academic Press, New York 1968; *S. W. Fox*: The Origins of Prebiological Systems. Academic Press, New York 1965.

[*] Water cannot act as the electron donor in bacterial photosynthesis, and consequently no oxygen is formed.

[99a] *O. Hayaishi, M. Katagiri*, and *S. Rothberg*, J. biol. Chemistry *229*, 905 (1957); *O. Hayaishi*, Annu. Rev. Biochem. *38*, 21 (1969).

4.2. Anaerobes-Aerobes

The usual physiological classification of organisms into anaerobes and facultative and obligate aerobes was based on the ability to grow in the absence and/or in the presence of oxygen [100]. Current knowledge of oxygen-dependent enzyme processes and their molecular evolution now provides a means of substantiating these definitions on the basis of the metabolic chemistry.

Anaerobes are defined as organisms that do not possess cytochrome oxidase and oxygenases. *Facultative aerobes* have an oxygenase-independent metabolism, and obtain their energy both by oxygen-dependent (cytochrome oxidase) and by oxygen-independent (pyridine nucleotide regenerating dehydrogenases or reductases) redox processes. *Obligate aerobes* are organisms that depend in their energy metabolism always upon cytochrome oxidase, and usually in their anabolism also upon oxygenases. This group includes organisms whose anabolism is only indirectly oxygen dependent. These organisms grow only when supplied with substances that are biosynthesized in oxygenase-catalyzed reactions [100a]. Examples of such compounds are polyenoic acids [101], steroids [102, 103], and phycobilins [*] [104], and for most organisms also monoenoic acids and pyridine nucleotides.

According to this definition, brewers yeasts (*e.g. Saccharomyces cerevisiae*) are obligate aerobes, enterobacteria (*e.g. Escherichia coli*) are facultative aerobes, and the lactobacilli (*e.g. Lactobacillus plantarum*) are anaerobes. *Saccharomyces* can grow in the absence of oxygen; under anaerobic conditions, however, it requires the addition of steroids and unsaturated fatty acids [101, 105]. "No life without oxygen" is valid for these organisms, though *Pasteur*'s experiments on anaerobiosis with yeasts had helped to cast doubt on this thesis. *E. coli* has no oxygenases [101], and can be grown in the absence of oxygen. In the presence of oxygen, a cytochrome oxidase dependent metabolism is induced [106], which allows higher growth yields and a shorter generation time; *E. coli* must therefore be regarded as a facultative aerobe. Lactobacilli have neither cytochrome oxidase nor oxygenases [107], and must be regarded as anaerobes; the same is true of the few strains that are capable to some extent of a cytochrome-independent "flavoprotein respiration" catalyzed by constitutive or oxygen-inducible NADH oxidases and NADH peroxidases [108].

The anaerobic lactobacilli and propionibacteria occupy an exceptional position. Some of the lactobacilli form nonheme catalases (pseudocatalases) or, in the presence of exogenous porphyrins, heme catalases [107, 109]. In propionibacteria, in addition to cytochromes and catalases [110], one also finds all the enzymes of the tricarboxylic acid cycle [111], which is responsible for the terminal oxidation of the carbon substrate in aerobes. These properties, which are unusual for anaerobes, suggest that the lactobacilli and the propionibacteria have arisen from facultative aerobes by losses of different extent in the cytochrome system, *i.e.* by reversion to an earlier stage of development [107].

Animals, higher plants, algae, protozoa, and fungi require steroids and polyenoic acids for cell synthesis, and the blue-green algae require polyenoic acids and phycobilins. All eucaryonts and the blue-green algae of the class of procaryonts are therefore obligate aerobes.

Bacteria require neither steroids [112] (but see also [113]) nor polyenoic acids [101] or phycobilins [104], and form pyridine nucleotides and monoenoic acids in oxygenase-independent reactions. Anaerobes and facultative aerobes can therefore occur only among the bacteria. Even here, however, some obligate aerobes are found which synthesize pyridine nucleotides (*Xanthomonas pruni*) [114] and monoenoic acids (*Bacillus megaterium, Micrococcus lysodeikticus, Mycobacterium phlei*, and *Corynebacteria*) [115] only with oxygenases (Table 9).

If lactobacilli and propionibacteria are considered to be revertants, then the clostridia, the methane-forming, and sulfate-reducing bacteria, as well as the purple and green sulfur bacteria, are the true anaerobes. Since autotrophy developed from heterotrophy in evolution, the metabolism of the autotrophic sulfur bacteria is hardly akin to that of the primordial anaerobes. The sulfate-reducing bacteria represent a higher stage of development in view of their cytochrome content. There remain therefore the clostridia and the methane-forming bacteria, whose metabolism most closely resembles that of the primordial anaerobes.

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Table 9. Occurrence of cytochrome oxidases and oxygenases in living organisms.

			Catabolism	Anabolism	
			cytochrome oxidases [a]	oxygenases [b]	
Procaryonts	lower protista	bacteria	−	−	anaerobes
			±	−	falcultative aerobes
			+	±	
		cyanophyta	+	+	
Eucaryonts	higher protista	algae protozoa fungi	+	±	obligate aerobes
	plants		+	+	
	animals		+	+	

[a] Cytochrome oxidases (E.C. 1.9.3.). [b] Oxygenases (E.C. 1.13. and 1.14), *e.g.* tryptophan pyrrolase for NAD(P) synthesis, fatty acid hydroxylase for the synthesis of unsaturated fatty acids, squalene epoxidase for steroid synthesis.

This view is supported by the observation that the ability to metabolize all types of nutrients has been retained only in this group of anaerobes, whereas even the facultative aerobes can utilize only carbohydrates and closely related compounds in the absence of oxygen. This may be regarded as a consequence of a change in the nutrient supply that paralleled the change from a reducing to an oxidizing environment. Whereas a large number of classes of substances were still available to the primordial anaerobes, a large stock of carbohydrates was produced together with the oxygen by photosynthesis. The aerobes that developed were therefore probably selected in the direction of carbohydrate utilization.

The corrin ring can be synthesized by all bacteria, whereas not all can synthesize the porphin ring, and even fewer the phorbin ring. Moreover, the side chains of the pyrrole rings are most completely retained in the corrin system in comparison with the other tetrapyrroles. It may therefore be deduced that the corrin ring system is phylogenetically the earliest (Fig. 11). From this point of view the methane-forming bacteria and the clostridia described in this article are closest to the primordial anaerobes.

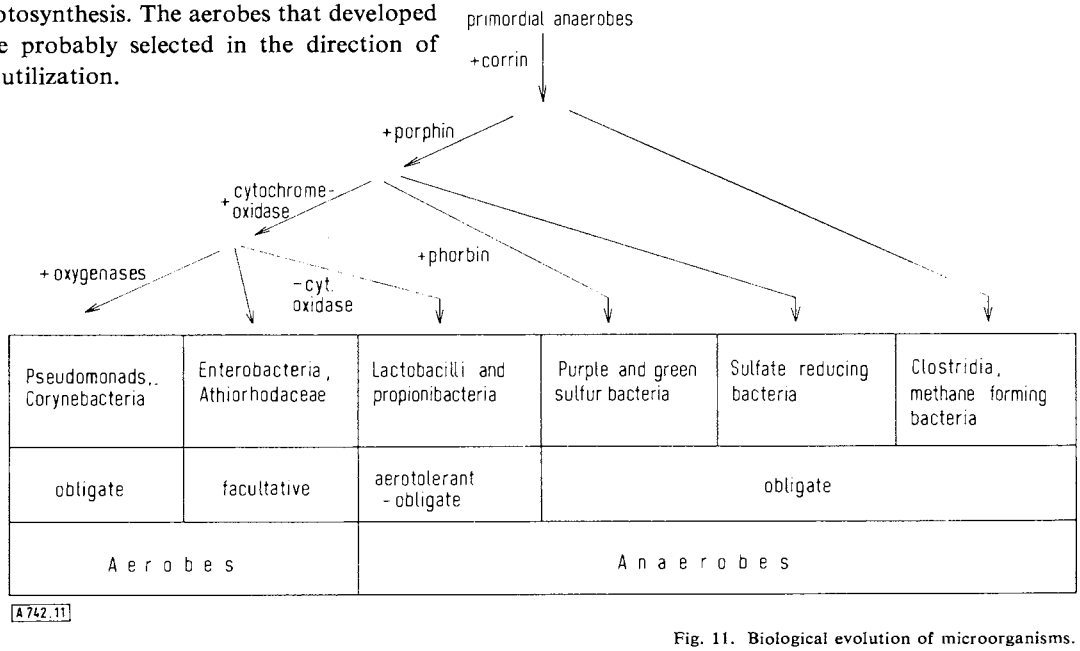


Fig. 11. Biological evolution of microorganisms.

Consideration of the molecular evolution of the tetrapyrrole compounds (Fig. 11) leads to the same result. Corrin, porphin, and phorbin rings are synthesized in the cells from porphobilinogen *via* common intermediates[116]. Since the biosynthesis of the phorbin ring proceeds *via* the porphin system, the porphin ring probably preceded the phorbin ring in the evolution.

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4.3. Fermentation, Photosynthesis, and Respiration

Closely related to the concepts of aerobiosis and anaerobiosis are the terms fermentation and respiration which were mostly derived from physiological observations. These terms are frequently used inconsistently in the literature. Redox processes with organic electron acceptors are usually referred to as fermen-

tations, while those with inorganic electron acceptors (except O_2) are described as anaerobic respiration. Respiration occurs when oxygen acts as the terminal oxidant. Terms such as "fumarate respiration" and "inorganic fermentation" are incompatible with this view.

A self-consistent definition of the basic metabolic types, *i.e.* fermentation, respiration, and photosynthesis, is provided by the relation of electron donor and acceptor systems on the one hand and the ATP* synthesizing pathways on the other (Table 1). In *fermentations*, ATP* is formed by substrate level phosphorylation only, whereas *cell respiration* is a redox process in which ATP* is synthesized mainly by electron transport phosphorylation. Photosynthesis is dominated by light-driven electron transport phosphorylations. *Inorganic fermentation* would thus be a redox process with an inorganic electron acceptor, in which ATP* is formed exclusively by substrate level phosphorylation. *Anaerobic respiration* is an oxygen-free energy metabolism with an ATP* synthesis coupled to electron transport.

A consistent and functionally logical definition is obtained by assigning respiration to electron transport phosphorylation and fermentation to substrate level phosphorylation. The terms organic and inorganic fermentation and aerobic and anaerobic respiration then become unambiguous.

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COMMUNICATIONS

α-Platinum(II) Chloride and Platinum(III) Chloride

By *U. Wiese, H. Schäfer, H. G. v. Schnering, C. Brendel,* and *K. Rinke* [*]

Platinum(II) chloride is usually prepared by the route $H_2PtCl_6 \cdot 6H_2O \rightarrow PtCl_4 \rightarrow PtCl_2$ at about 500 °C in a stream of Cl_2. The resulting "β-$PtCl_2$" has a molecular lattice: Pt_6Cl_{12} molecules contain a regular Pt_6 octahedron, the Cl atoms being arranged in front of its edges [1]. This structural type is encountered, in particular, in niobium-tantalum chemistry.

We have now discovered a new modification, "α-$PtCl_2$", which is formed when Pt_6Cl_{12} is heated in a small ampoule for 1—2 days at 500 °C, or on reaction of the elements in quartz ampoules in a temperature gradient [Pt at 650 °C; α-$PtCl_2$ deposition at 550 °C; $p(Cl_2$, end) ≈ 3 atm].

Like those of the β modification, crystals of α-$PtCl_2$ are almost black and exhibit a reddish luster; when powdered both forms are yellowish brown.

α-$PtCl_2$ is characterized by the following interplanar spacings (Å), the intensities being given in parentheses; Guinier photograph:

6.48 (10); 6.31 (10); 5.43 (5); 3.322 (1); 3.255 (1); 3.242 (1); 3.156 (3); 3.104 (8); 2.885 (3); 2.713 (3); 2.581 (1); 2.544 (3); 2.236 (5); 2.224 (3); 2.106 (3); 1.909 (1); 1.845 (5); 1.781 (3); 1.700 (1); 1.674 (1); 1.656 (5); 1.622 (3); 1.601 (5).

α-$PtCl_2$ is not isotypic with the well known α-$PdCl_2$, which is built up of planar $PdCl_{4/2}$ chains.

Whereas β-$PtCl_2$ dissolves in benzene to form a definite Pt_6Cl_{12}-benzene adduct, α-$PtCl_2$ is insoluble in this solvent. The rate of conversion of β- into α-$PtCl_2$ is so slow that both modifications can be independently studied by thermal analysis (thermobalance, 4 °C/min; 1 atm of argon): quantitative decomposition of α-$PtCl_2$ to the elements is complete at 570 °C, that of β-$PtCl_2$ at 550 °C. In a vacuum (thermobalance, 4 °C/min), extensive volatilization in addition to decomposition is observed only with β-$PtCl_2$. Correspondingly, gaseous platinum chloride is recorded only in the mass spectrum of β-$PtCl_2$. Since the $Pt_6Cl_{12}^+$ ion has the lowest appearance potential, Pt_6Cl_{12} clearly vaporizes.

We have obtained crystals of the known [2] compound platinum(III) chloride (greenish black needles) on chlorination of the metal in a temperature gradient [quartz ampoule; Pt at 600 °C; other end of ampoule at 400 °C; deposition of $PtCl_3$ at intermediate temperatures; $p(Cl_2$, end) = 10 atm].

$PtCl_3$ forms trigonal rhombohedral crystals having a = 21.235 (9), c = 8.550 (10) Å; c/a = 0.403; space group $R\bar{3}$—C_{3i}^2; $d_{X\text{-ray}}$ = 5.39, d_{pyk} = 5.27 g/cm³. The compound has the same structure as the recently described $PtBr_3$ [3]; thus it contains $[Pt_6Cl_{12}]$ and $^1_\infty[PtCl_2^aCl_{4/2}^b]$ units. The average bond lengths are: Pt^{II}—Cl (4×) = 2.32; Pt^{IV}—Cl^a (2×) = 2.37; Pt^{IV}—Cl^b (4×) = 2.29 Å.

Thermal degradation of $PtCl_3$ (thermobalance, 1 atm argon) proceeds quantitatively, *via* a poorly defined β-$PtCl_2$ stage, to the elements. In a vacuum, considerable volatilization of Pt_6Cl_{12} accompanies decomposition, as is also apparent from the mass spectrum.

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Oxidative Addition of the Azide Ion to Olefins. A Simple Route to Diamines [1] [**]

By *H. Schäfer* [*]

Organic anions can be oxidatively added to non-activated double bonds [2]. We have now found that this type of reaction can also be extended to inorganic anions, *e.g.* to the azide ion. In the electrolysis of a 1.2 M solution of sodium azide in glacial acetic acid vigorous evolution of gas is observed at the anode thus indicating formation of azide radicals and their decomposition to nitrogen [3,4]. On addition of olefin to the electrolyte (olefin: glacial acetic acid 1 : 3 v/v) the anodic gas evolution is suppressed and azidoalkanes can be isolated (see Table). The azidoalkanes thus formed were characterized by C, H, N analysis, IR- and NMR spectroscopy, or by reductive elimination of nitrogen with Raney-Ni/hydrogen or $LiAlH_4$ to give amines which were then compared gas chromatographically with authentic substances.

The oxidative addition of the azide ion to olefins affords a one-step synthesis of 1,2- and 1,4-diazidoalkanes, which can be converted into 1,2- and 1,4-diamines respectively by reductive elimination of nitrogen [5].

Olefin	Azidoalkane	Yield (%) [a]	[b]	[c]
Styrene	1,4-Diazido-2,3-diphenylbutane	57		55
α-Methylstyrene	1,4-Diazido-2,3-dimethyl-2,3-diphenylbutane	45		43
Cyclooctene	1,2-Diazidocyclooctane	24		
	Azidocyclooctane			15
	3-Azido-1-cyclooctene			17
1-Octene	1,2-Diazidooctane	17	18	
	1-Azidooctane			3
	1-Azido-2-octene			3
	3-Azido-1-octene			3
Cyclohexene	1,2-Diazidocyclohexane	18		
	3-Azido-1-cyclohexene			5
	Azidocyclohexane			10
1,1-Diphenylethylene	1,2-Diazido-1,1-diphenylethane	15		
	2-Azido-1,1-diphenylethyl acetate	33		

[a] Yield of azide referred to current consumption.
[b] Yield of azide referred to starting amount of olefin.
[c] Yield of amine, referred to current consumption, after reductive elimination of nitrogen.

1,4-Diazido- and 1,4-Diamino-2,3-dimethyl-2,3-diphenylbutane

A solution of sodium azide (12 g) and α-methylstyrene (50 ml, 43 g) in glacial acetic acid is electrolyzed at 40 °C using an anode potential of +1.6 V (against Ag/AgCl) controlled by a potentiostat and a current density of 30 mA/cm^{-2} at platinum electrodes in a cell without diaphragm until consumption of 0.150 Faraday. The solution is then poured into water (200 ml), extracted with ether, and the ethereal phase is washed with dilute sodium hydroxide until neutral and then dried over sodium sulfate. After distilling off the ether and excess α-methylstyrene there remains 21.0 g of crude product. 0.41 g of the diazide can be separated from 0.8 g of the crude product by preparative thin layer chromatography using benzene/petroleum ether (40—60 °C) (1 : 1 v/v) as eluent. 5.6 g of the crude product is hydrogenated in methanol with Raney-Ni/hydrogen to give 2.3 g of the diamine (b.p. 160—165 °C/0.01 torr). The structures are confirmed by C, H, N-analysis, molecular weight, IR-, NMR-, and mass spectra.

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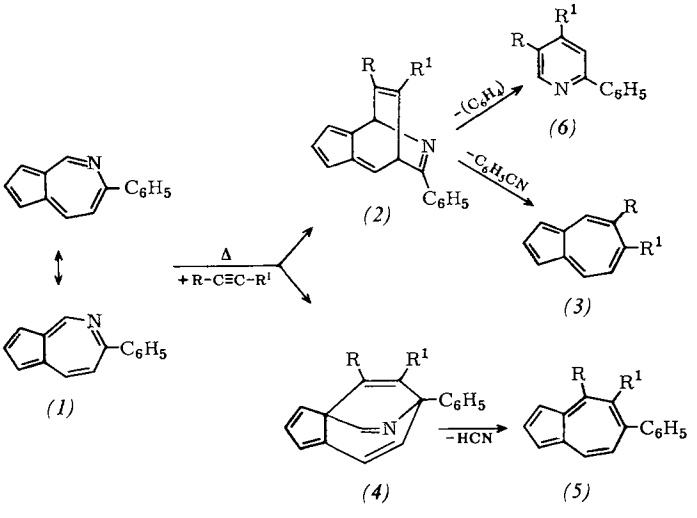
[4] For the coupling of azide radicals with alkyl radicals from the Kolbe electrolysis see *C. M. Wright* and *G. A. Ward*, 127th Meeting of the Electrochem. Soc., San Francisco, May 1965, Abstract No. 141.

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Cycloadditions to the Azulene System

By *K. Hafner*, *J. Häring*, and *W. Jäkel*[*]

Cycloadditions to the azulene system have not hitherto been observed. Instead, azulene reacts, *e.g.*, with maleic anhydride *via* an "addition-substitution route" to give 1-azulenylsuc-



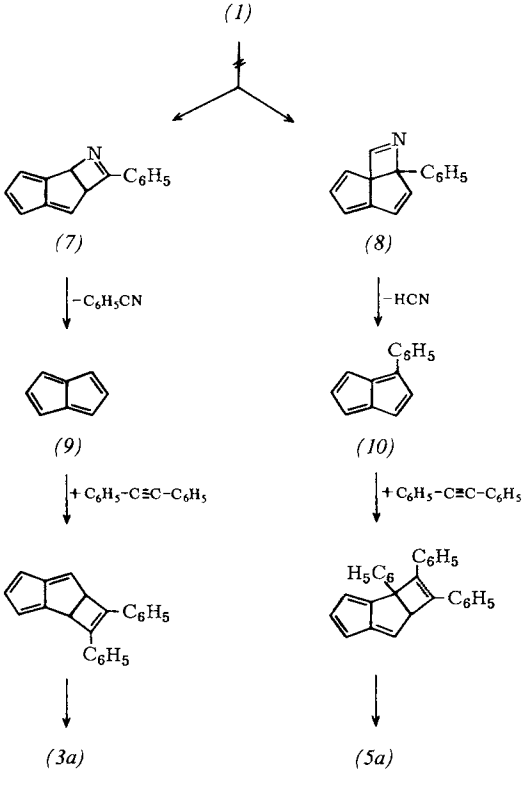
(a), R = R^1 = C_6H_5
(b), R-R^1 = $(CH_2)_6$

Compound	M.p. (°C)	UV λ_{max} (nm) (log ε) (in *n*-hexane)	NMR (τ) [a]
(1)	158—159 blue scales (ligroin)	298 (4.67), 376 (3.79), 561 (2.69), 607 (2.56), 668 (2.07)	0.60 (H-4/s), 1.80 (H-8/d; *J* = 10 Hz), 1.97 (H-1, H-3/m), 2.20 (H-2/t; *J* = 4 Hz), 2.60 (H-7/d; *J* = 10 Hz), 2.40—2.65 (C_6H_5/m) ($CDCl_3$)
(2b)	126 yellow crystals (pet. ether)	231 (4.16), 269 (4.01), 318 (3.51), 404 (2.75)	2.42 (C_6H_5/m), 3.24 (1 H/m), 4.02 (3 H/m), 4.50 (1 H/s), 5.55 (1 H/d; *J* = 8 Hz), 7.34—8.92 (—$(CH_2)_6$—/m) (CCl_4)
(3a)	138—139 blue crystals (ligroin)	248 (4.26), 292 (4.78), 338 (3.75), 352 (3.85), 590 (2.66), 612 (2.65), 643 (2.65), 713 (2.28)	1.49 (H-4/s), 1.70 (H-8/d; *J* = 10 Hz), 2.10 (H-2/t; *J* = 4 Hz), 2.63 (H-1, H-3/d; *J* = 4 Hz), 2.75 (H-7/d; *J* = 10 Hz), 2.89 (2 C_6H_5/s) ($CDCl_3$)
(3b)	56 blue platelets (pet. ether)	240 (4.17), 281 (4.80), 287 (4.77), 301 (3.98), 322 (3.37), 330 (3.51), 333 (3.59), 345 (3.69), 349 (3.79), 361 (3.08), 580 (2.54), 601 (2.52), 632 (2.53), 662 (2.26), 700 (2.23)	1.83 (H-4/s), 1.95 (H-8/d; *J* = 10 Hz), 2.30 (H-2/t; *J* = 4 Hz), 2.87 (H-1, H-3/d; *J* = 4 Hz), 3.04 (H-7/d; *J* = 10 Hz), 6.83—7.17 (—$(CH_2)_2$—/m), 7.93—8.80 (—$(CH_2)_4$—/m) (CCl_4)
(5a)	201—202 blue crystals (ligroin)	245 (4.41), 295 (4.79), 337 (3.74), 353 (4.81), 588 (2.73), 608 (2.71), 642 (2.70), 708 (2.32)	1.59 (H-8/d; *J* = 10 Hz), 2.21 (H-2/t; *J* = 4 Hz) 2.55 (H-1, H-3/m), 2.69 (H-7/d; *J* = 10 Hz) 2.88 (C_6H_5/s), 2.94 (C_6H_5/s), 3.24 (C_6H_5/s) ($CDCl_3$)
(5b)	78 blue platelets (pet. ether)	251 (4.41), 289 (4.75), 293 (4.76), 297 (4.75), 339 (3.63), 349 (3.73), 353 (3.78), 365 (3.29), 582 (2.68), 605 (2.66), 635 (2.64), 703 (2.27)	2.00 (H-8/d; *J* = 10 Hz), 2.31 (H-2/t; *J* = 4 Hz), 2.72 (H-1, H-3/m), 2.75 (C_6H_5/s), 3.09 (H-7/d; *J* = 10 Hz) 6.32—8.97 (—$(CH_2)_6$—/m) (CCl_4)

[a] TMS as internal standard.

cinic anhydride and with tetracyanoethylene to yield 1-tricyanovinylazulene[1].

In contrast, the 5-azaazulene system[2] is able to enter into cycloadditions with alkynes, the heterocycle undergoing simple conversion into previously inaccessible derivatives of carbocyclic azulene. 6-Phenyl-5-azaazulene *(1)*[3] reacts with an excess of tolan at 350 °C to give 30% of 5,6-diphenylazulene *(3a)*[4] and benzonitrile, as well as 5% of 4,5,6-triphenylazulene *(5a)* and hydrocyanic acid. Formation of *(3a)* and *(5a)* would suggest the intermediacy of the 1,4 adducts *(2a)* and *(4a)* and their Alder-Rickert cleavage to the carbocyclic azulene. Disrotatory thermal valence isomerization of *(1)* to *(7)* and *(8)*, which is forbidden by the Woodward-Hoffmann rules[5], and subsequent elimination of benzonitrile or hydrocyanic acid to give the pentalenes *(9)* and *(10)*, respectively, which could also react with tolan to give *(3a)* and *(5a)*[6], was ruled out by experimental findings[3]:



1-Methyl-6-phenyl-5-azaazulene and 4-methyl-6-phenyl-5-azaazulene give different azulenes with tolan. If the reaction sequence *(1)*→*(7)*→*(9)* were to apply, then both azaazulenes would give 1-methylpentalene and thus either the same methyldiphenylazulene or an identical mixture of isomers.

Evidence for 1,4-adduct formation during reaction of *(1)* with acetylenes comes from the reaction of *(1)* with cyclooctyne[7] in the molar ratio 1 : 4 at 170 °C (reaction time: 15 s). From the reaction mixture a 25% yield of the 1,4 adduct *(2b)* can be isolated, whose Alder-Rickert cleavage (250 °C; 30 s) affords 5,6,7,8,9,10-hexahydrocycloocta[*f*]azulene *(3b)* (60%) and a minor amount of 3-phenyl-5,6,7,8,9,-10-hexahydrocycloocta[*c*]pyridine *(6b)*. The strained adduct *(4b)* was also expected but, unlike *(2b)*, decomposes to 6-phenyl-7,8,9,10,11,12-hexahydrocycloocta[*e*]azulene *(5b)* (30%) under the reaction conditions.

The hetero atom in the seven-membered ring of the 5-azaazulene system alters the electron distribution and reduces the π-electron delocalization compared with the azulene system[8]. This effect is probably responsible for the 1,4 addition of the α,β-unsaturated azomethine partial structure in *(1)* to the alkynes. The reaction may proceed *via* a Diels-Alder reaction "with inverse electron demands"[9] or as a two-step cycloaddition. Decomposition of the 1,4 adducts *(2)* and *(4)* to carbocyclic azulene derivatives and pyridine profits from the energy gain involved in formation of the cyclic conjugated systems.

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Metal-Ligand Bonding in Sulfinato Complexes of Transition Metals

By *E. Lindner*, *G. Vitzthum*, *D. Langner*, and *I.-P. Lorenz*[*]

Bis- and tris(sulfinato) complexes are formed in the reaction of sodium sulfinates with soluble compounds of divalent and trivalent transitions metals in water or alcohol:

$$n\ RSO_2Na + MX_n \rightarrow \underset{(1)-(5)}{M(SO_2R)_n} + n\ NaX \qquad (1)$$

(X = halogen, acetate)

M \ R		p-$CH_3C_6H_4$	C_6H_5	CH_3
(n = 2)	Zn	*(1a)*	*(1b)*	*(1c)*
	Cd	*(2a)*	*(2b)*	
	Hg	*(3a)*	*(3b)*	*(3c)*
(n = 3)	Cr	*(4a)*	*(4b)*	*(4c)*
	Fe	*(5a)*	*(5b)*	*(5c)*

The toluene- and benzenesulfinato complexes of zinc, cadmium[1], and mercury[2] *(1a)*–*(3b)* have already been described. We have now succeeded in preparing bis(methanesulfinato)mercury *(3c)* and -zinc *(1c)* as the *S*-type.

Apart from the anhydrous mercury compounds *(3a)* and *(3b)*[3], little has been known about the structure of the complexes *(1a)*–*(2b)* except that the RSO_2^- ligands are linked to M^{2+} *via* oxygen.

We have now found that the type of bonding of the ligands to the metal ion in *(1a)*–*(3b)* is *particularly dependent on the water content* of the compounds.

The benzene- and methanesulfinato complexes *(1b)*, *(2b)*, *(3b)*, and *(3c)* prepared in water at room temperature are

obtained as dehydrated salts after drying over P_4O_{10} in a vacuum at 25 °C for 12 h. Under the same conditions, the *p*-toluenesulfinato complexes *(1a)*–*(3a)* crystallize as 1 : 2 adducts with water; the "crystal water" can be removed from *(1a)*–*(3a)* by drying for a period of 60 h, in the case of *(1a)* at temperatures above 120 °C and in the case of *(2a)* and *(3a)* — contrary to previous reports [1] — at a temperature as low as 25 °C.

If KBr pellets are prepared in a moist atmosphere, the IR spectra of *(1b)*–*(3b)* are surprisingly similar to those of *(1a)* to *(3a)*; all the compounds (except *(3c)*) then contain water and in accordance with the slight difference in frequency between $\nu_s(SO_2)$ and $\nu_{as}(SO_2)$ (cf. Table 1) are to be formulated as distorted octahedrally configurated bis(sulfinato-*O*,*O'*) diaqua complexes. Inter- or intramolecular arrangement of the RSO_2^- groups cannot be differentiated.

The large frequency difference and the shortwave position of $\nu_s(SO_2)$ and $\nu_{as}(SO_2)$ indicate that the anhydrous mercury complexes *(3a)*–*(3c)* are *S*-bonded.

During the conversion of hydrated into the anhydrous cadmium compounds *(2a)* and *(2b)* a reversible re-orientation of the bonding of the RSO_2^- ligands to the Cd^{2+} takes place; the IR spectra of the anhydrous complexes points to a sulfinato-*O* bonding (large frequency difference, longwave $\nu_{as}(SOM)$ bands [3]).

Three SO bands having the irreducible representation $A_2 + 2E$ are found in all cases. Accordingly we assume the complexes *(4a)*–*(5c)* to have an octahedral configuration with D_3 symmetry as is also indicated by the electronic spectrum. The RSO_2^- ligands are linked *via* both oxygen atoms to the central ions (small frequency difference: sulfinato-*O*,*O'* type). The solubilities — *(4c)* and *(5c)* are very readily soluble in ethanol — also indicate that these compounds are monomeric.

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Table 1. SO_2 stretching vibrations (cm^{-1}) of sulfinato complexes of zinc, cadmium, and mercury.

		(a)	*(b)*	*(c)*	Assignment	Bond type
(1)	with H_2O	992 s; 966 sh 943 vs	989 vs; 958 sh 942 vs		$\nu_{as}(SO_2)$; $\nu_s(SO_2)$	Sulfinato-*O O'*
	without H_2O	1050 m, 1020 sh 971 vs, 963 vs	1051 m, 1024 w 1003 m, 985 vs 962 vs	1025 sh, m; 960 s 930 s [4]	$\nu(SO_2)$	Sulfinato-*O*, mainly sulfinato-*O*,*O'*
(2)	without H_2O	1031 s; 924 m 1015 s; 904 m	1030 s; 919 m 1024 s; 903 m		$\nu(SO)$; $\nu_{as}(SOM)$	Sulfinato-*O*
	with H_2O	990 vs; 965 sh 947 vs	988 vs; 965 sh 946 vs		$\nu_{as}(SO_2)$; $\nu_s(SO_2)$	Sulfinato-*O*,*O'*
(3)	with H_2O	1037 vs; 980 s	1022 vs; 980 s			
	without H_2O	1229 m; 1040 vs 1203 vs	1194 vs; 1037 vs	1177 vs, 1061 vs		Sulfinato-*S*

Interpretation of the spectra of anhydrous *(1a)* and *(1b)* is difficult since in addition to the bands of medium intensity (indicative of sulfinato-*O* complex) very intense absorptions also occur, which, on account of their position and frequency-difference, are characteristic of a sulfinato-*O*,*O'* complex: very probably the *O*,*O'* type bond preponderates in this particular case. In contrast to *Carey* and *Clark* [4] we have found that $(CH_3SO_2)_2Zn$ formed by an "SO_2 insertion" reaction, like *(1a)* and *(1b)*, is a sulfinato-*O*,*O'* complex (cf. Table 1). We were able to prepare for the first time the sulfinato-*S* isomer $[H_3C(O_2)S]_2Zn$ ($\nu_{as}(SO_2)$ = 1190 vs, $\nu_s(SO_2)$ = 1060 cm^{-1} s) according to eq. (1).

The green and the yellow tris(*p*-toluene-, benzene-, and methanesulfinato) derivatives, respectively, of chromium *(4a)*–*(4c)* and of iron *(5a)*–*(5c)* are characterized by intense SO stretching vibrations in the region 900–1000 cm^{-1} (cf. Table 2).

Table 2. SO stretching vibrations (cm^{-1}) of tris(sulfinato) complexes of chromium and iron.

	(a)	*(b)*	*(c)*
(4)	972 sh (A_2) 940 vs (E) 927 vs (E)	967 sh (A_2) 945 vs (E) 925 vs (E)	964 sh (A_2) 947 vs (E) 925 vs (E)
(5)	(A_2) masked 952 vs (E) 942 vs (E)	(A_2) masked 948 vs (E) 938 vs (E)	967 s, sh (A_2) 946 vs (E) 919 vs (E)

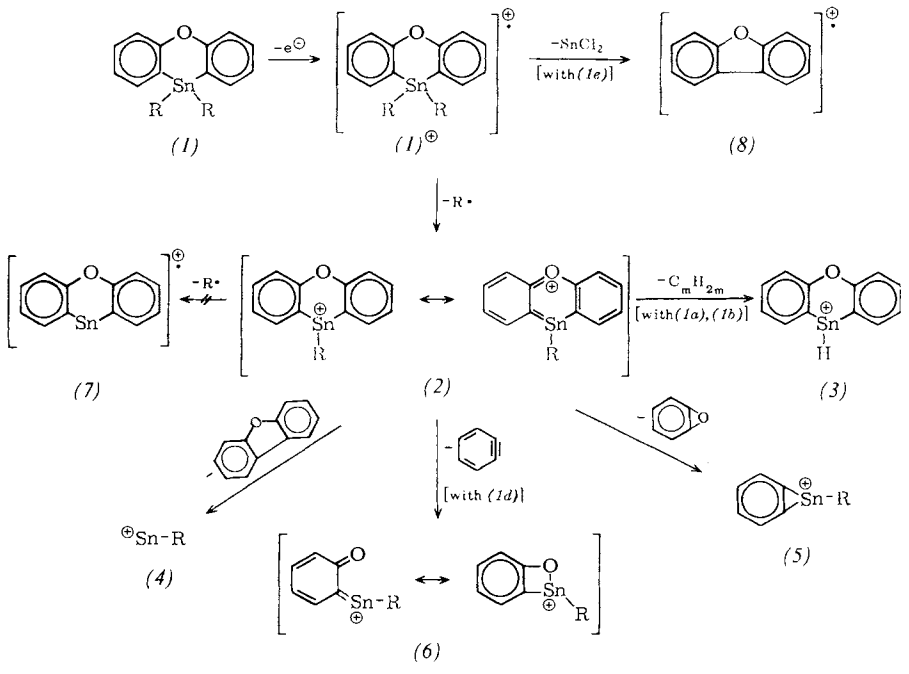
Unusual Cleavage of *Sn,Sn*-Disubstituted Oxastannadihydroanthracene by Electron Impact

By *I. Lengyel* and *M. J. Aaronson* [*]

The two most abundant ions in the mass spectra of 10,10-dialkyl-9-oxo-10-stanna-9,10-dihydroanthracenes *(1)* (R = nC_mH_{2m+1}, $m \geq 2$) are *(2)* and *(3)*, resulting from initial Sn—C_{alkyl} bond cleavage followed by elimination of a neutral alkene from the second 10-alkyl group with concomitant shift of a hydrogen atom to the metal in *(3)* [1] [*e.g.* in compounds *(1a)* and *(1b)*].

In this connection, it was of eminent interest to investigate related compounds constructed in such a way that no easily-transferable hydrogen is available from the substituents in position ten. Suitable models to meet this condition appeared to be the derivatives *(1c)*–*(1e)* [2]. Their mass spectra [3] still exhibit predominant peaks for the ions *(2c)*–*(2e)* but no peaks for *(3c)*–*(3e)*.

Subsequent fragmentation takes a different course, involving competitive expulsion of different neutral particles. The most favored path of further decomposition is ejection of the elements of dibenzofuran, to give ions *(4c)*–*(4e)*, confirmed by the presence of the appropriate metastable peaks for compounds *(1d)* and *(1e)*. Alternatively, elimination of particle C_6H_4O leads to ions *(5c)*–*(5d)*. Finally, for *(1d)*, there is the interesting loss of C_6H_4 (dehydrobenzene), again confirmed by a metastable peak at *m/e* 228.8 (this value applies to the ^{120}Sn isotope [4]), to give *(6)*, *m/e* 289. The elimination of C_6H_4



(a), R = n-C_4H_9; *(b)*, R = C_2H_5; *(c)*, R = CH_3; *(d)*, R = C_6H_5; *(e)*, R = Cl

rom other even-electron ions has been observed in electron-mpact experiments with dialkyl derivatives *(1)*, R = alkyl[5].

One factor that apparently renders the overall energy balance of fragmentation *(2d)* →*(6)* favorable, despite the low stability of the neutral particle expelled, is the resonance-stabilization of the ion *(6d)*.

It is important to note that the ejection of dehydrobenzene — a neutral particle — is still a process of lower energy requirement than ejection of a second phenyl radical [*(2d)* →*(7)*]. It has been pointed out[6] that even-electron to odd-electron decompositions, if not forbidden, are at least rare in organic mass spectrometry. Ion *(7)* is absent in the spectra of all compounds discussed in this paper.

It should be noted that the major decomposition path (as judged by relative peak intensities) of the molecular ion of the dichloro compound *(1e)* is expulsion of neutral $SnCl_2$ rather than $Cl^{\bullet}$, to give metal- and chlorine-free ion *(8)*, *m/e* 168 (the base peak at 12 eV). This observation is consistent with the known[7,8] bond strength differences: the Sn—R bond strength increases in the order Sn-alkyl < Sn-phenyl < Sn—Cl.

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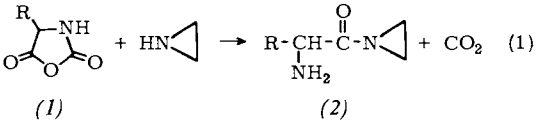
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Diketopiperazines from Leuchs Anhydrides[1][**]

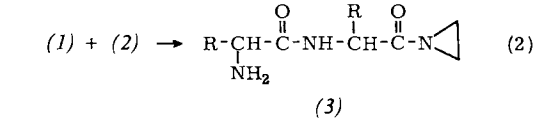
By *P. Rosenmund* and *K. Kaiser*[*]

Leuchs anhydrides (1,3-oxazolidine-2,5-diones) *(1)* prepared from DL-amino acids react instantaneously with aziridines with liberation of CO_2 at room temperature to give pure diketopiperazines (piperazine-2,5-diones) *(4)* in high yield. THF and anhydrous and 95% ethanol are suitable solvents. Highest yields of *(4)* are obtained when the Leuchs anhydride is added in small portions to an excess of aziridine. Diketopiperazines are not formed if amines other than aziridine, *e.g.* triethylamine or diethylamine, are used.

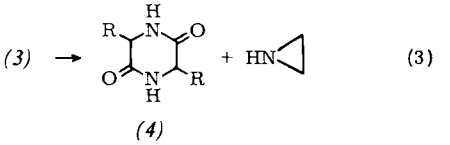
In view of the facts that the reaction is independent of solvent and that aziridines obviously act catalytically we consider that reaction probably proceeds as follows:



(1) *(2)* (1)



(1) + *(2)* → *(3)* (2)



(3) → *(4)* + HN (3)

	R	*(4)*, yield	*(4)*, m.p. (°C)
(a)	$C_6H_5CH_2$	80	297–300
(b)	C_6H_5	75	260
(c)	CH_3	78	270
(d)	$C_6H_5CH_2OCONH(CH_2)_4$	73	205

Because of the relatively low nucleophilicity of aziridine, reaction (1) is slow and consequently the concentration of *(2)* always remains small. Reaction of *(2)* with *(1)* yields the di-

peptide aziridide *(3)* which undergoes rapid cyclization to give *(4)* with simultaneous liberation of aziridine, which thus becomes available for further reaction. This cyclization greatly hinders polymerization which otherwise would readily occur — particularly in the presence of small amounts of base. That reaction (3) proceeds rapidly can be ascribed to the fact that compound *(3)* has the character of an activated carboxylic acid derivative.

We have been able to support this view by the following observations: If *N*-trifluoroacetylphenylalaninaziridide (prepared in 72% yield, m.p. 107—108 °C, by reaction of trifluoroacetylphenylalanine and aziridine by the anhydride method) is treated with 0.2 N NaOH at room temperature in order to remove the trifluoroacetyl residue[2], phenylalanine is formed exclusively; the aziridino residue, therefore, is just as labile as the trifluoroacetyl group. Hydrolysis with semiconcentrated aqueous ammonia affords phenylalaninamide (87%). Moreover, sodium ethoxide in ethanol liberates aziridine from N-trifluoroacetylphenylalaninaziridide.

General method of preparation:

The Leuchs anhydride *(1)* is added in small portions (10 mg) with vigorous stirring at room temperature to a solution of aziridine (0.3 ml) in ethanol (or THF) (3 ml). The mixture is allowed to stand after each addition until evolution of CO_2 is complete and all anhydride has dissolved to give a clear solution; addition of anhydride is discontinued as soon as the solution becomes turbid. After 1—5 min almost analytically pure diketopiperazine *(4)* crystallizes out in 70—80% yield. The mother liquor contains a further 10—15% of *(4)*.

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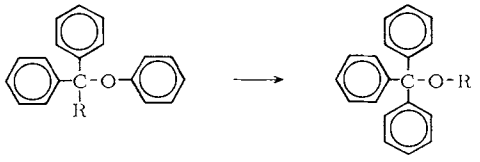
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Ionization and Rearrangement of Diphenylphenoxymethylmagnesium Chloride[**]

By *H. F. Ebel*, *V. Dörr*, and *B. O. Wagner*[*]

In earlier investigations[1] of metalated ethers and their rearrangement (Wittig rearrangement) the change of properties when going from the magnesium and zinc derivatives of diphenylphenoxymethane, *(1a)* and *(1b)* respectively, to the alkali metal derivatives *(1c)* was emphasized. Whereas *(1a)* and *(1b)* are colorless and do not rearrange to the triphenylmethoxides *(2a)* and *(2b)*, the alkali metal compounds *(1c)* are deep red and undergo slow conversion into *(2c)*.



(1) *(2)*

(a), R = MgHal; *(b)*, R = ZnHal;
(c), R = Alkali metal; *(d)*, R = H

Spectral properties and the tendency to rearrange depend on the nature (not specified in the formulas) of the bonds involving the metal atoms; only derivatives *(1)*, in which the C—R bond is ionic, are deeply colored and capable of rearrangement.

We have now found that hexamethylphosphoric acid triamide (HMPT), which has repeatedly been shown to have superior solvation properties for organomagnesium[2,3] and other organometallic compounds[3] and which recently has been called a "super-solvent" in carbanion chemistry[4], changes the properties of *(1a)* profoundly.

On adding a solution of isopropylmagnesium chloride [at least 2 equiv., relative to *(1d)*] in THF to diphenylphenoxymethane *(1d)* at 65 °C, a colorless solution results. If HMPT (30 equiv.) is now added, the mixture starts boiling and gradually assumes a deep red color. After 96 hours there is no *(1d)* present in the hydrolysis product (gas chromatography: 10m SE-30 column, 5% on Chromosorb W, 24 ml N_2/min, 250 °C), and after one crystallization the melting point is that of triphenylmethanol *(2d)* (m.p. 161—161.4 °C). Using only HMPT as solvent, the rearrangement is complete after 30 min at 110 °C (see *Experimental*).

A 0.13 N solution of *(1d)* in ether was refluxed with an excess of isopropylmagnesium chloride in presence of HMPT for several hours, and then diluted with THF in a closed apparatus, the ratio of dilution varying from 1 : 1000 to 1 : 125. The resulting solutions exhibited a well developed absorption band, λ_{max} = 461 nm, which obeyed the Beer-Lambert law. The band differs from the absorption measured earlier[1] for *(1c)* only in a shift to longer wavelengths by 12 nm. We suggest that *(1a)*, Hal = Cl, forms solvent-separated ion pairs in presence of HMPT. Our measurements on magnesium derivatives of diphenylmethane, triphenylmethane, and fluorene led to similar results[5].

Thus we have demonstrated by chemical and spectroscopic means, and using a simple model, that organomagnesium compounds may assume pronounced carbanionoid[6] properties.

Experimental:

HMPT (0.60 mole) is added dropwise under argon to an ethereal solution (100 ml) of isopropylmagnesium chloride (0.097 mole). The ether is then removed by distillation and *(1d)* (0.04 mole) is added at 110 °C to the pale yellow, viscous solution. A clear red solution is formed with evolution of gas (propane). After 30 min the mixture is cooled in an ice bath and treated with twice its volume of 5 N HCl. The colorless crystals of *(2d)* (yield 95% after filtration, washing with water, and drying) are recrystallized from ethanol (yield 83%; m.p. 161—161.5 °C).

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Nucleophilic Imino- and Aminomethylation of Ketones[1] [**]

By *Thomas Kauffmann*, *Edgar Köppelmann*, and *Heike Berg*[*]

Electrophilic aminomethylation (Mannich reaction) is a well known important reaction step in organic synthesis. We have now found that an aminomethyl group can be introduced

into compounds *nucleophilically* by way of diphenylmethyleneaminomethyllithium *(2)*, the $=C(C_6H_5)_2$ group acting as a "synthesis mask". Here, we report on the reactions of *(2)* with ketones.

N-(Diphenylmethylene)methylamine *(1)* is metalated to *(2)* when treated with an equimolar amount of lithium diisopropylamide in THF/ether (10 : 1) at −45 °C (*ca.* 75% *N*-(diphenylmethylene)deuteriomethylamine on addition of D_2O). The solution containing *(2)* reacts with benzophenone at −45 °C to give an adduct that yields the iminomethyl compound 2-(diphenylmethyleneamino)-1,1-diphenylethanol *(3)* (see Table) on hydrolysis with water. At 65 °C the isomeric 2-(diphenylmethylamino)-1,1-diphenylethanol *(5)* is formed (yield 12%, m.p. 186 °C) and not compound *(3)*. Hydrolysis of *(3)* with 2 N HCl (90–100 °C) affords the previously described aminomethyl compound *(4)* (see Table). Analogous reactions can be carried out with all the other ketones mentioned in the Table.

$$(C_6H_5)_2C{=}N{-}CH_3 \xrightarrow{LiN(C_3H_7)_2} (C_6H_5)_2C{=}N{-}CH_2Li$$
(1) *(2)*

$$(2) \xrightarrow[2.\ H_2O]{1.\ O{=}C(C_6H_5)_2} (C_6H_5)_2C{=}N{-}CH_2{-}C(OH)(C_6H_5)_2 \xrightarrow{2N\ HCl}$$
(3)

$H_2N{-}CH_2{-}C(OH)(C_6H_5)_2$ *(4)*

$(C_6H_5)_2CH{-}N{=}CH{-}C(OH)(C_6H_5)_2$ *(5)*

Used	Obtained		Yield [3] (%)
$R{-}C(R^1){=}O$	$R{-}C(R^1)(OH){-}CH_2{-}N{=}C(C_6H_5)_2$	$R{-}C(R^1)(OH){-}CH_2{-}NH_2$	
$R = R^1 = C_6H_5$	m.p. 136–137 °C	m.p. 110 °C (110–111 °C [2])	42 and 76
$R = C_6H_5$, $R^1 = C_6H_4{-}CH_3(p)$	m.p. 105 °C	m.p. 104 °C (108–109 °C [4])	32 and 78
$R + R^1$ = 2,2'-Biphenylylene	m.p. 181 °C	m.p. 140–142 °C	52 and 80
$R = CH_3$, $R^1 = C_6H_5$	b.p. 215–225 °C 10.05 torr	b.p. 150–155 °C/16 torr (97 °C/0.45 torr [5])	32 and 48

Correspondingly, *N*-benzylideneaminobenzylsodium *(6)*, which can be prepared by reaction of *N*-benzylidenebenzylamine with $NaNH_2$ in absolute ether at −35 °C [6], is suitable for imino- and aminobenzylation. Reaction of *(6)* with benzophenone in ether at −35 °C leads to the formation of 2-benzylideneamino-1,1,2-triphenylethanol *(7)* (72% yield), which, on hydrolysis with 2 N HCl (80 °C), affords almost quantitative yields of the previously described aminobenzyl compound *(8)* [7].

$$HC(C_6H_5){=}N{-}CHNa(C_6H_5) \xrightarrow[2.\ H_2O]{1.\ O{=}C(C_6H_5)_2} HC(C_6H_5){=}N{-}CH(C_6H_5){-}C(OH)(C_6H_5)_2 \xrightarrow{2N\ HCl}$$
(6) *(7)*

$H_2N{-}CH(C_6H_5){-}C(OH)(C_6H_5)_2$ *(8)*

If reaction of *(2)* is carried out in pure diethyl ether at 0 °C [addition of benzophenone at −50 °C] instead of in THF/diethyl ether [*(1)* can also be metalated to *(2)* in diethyl ether], *N*-(diphenylmethylene)-2,2-diphenylvinylamine *(9)* is formed (yield 28%, m.p. 183 °C) instead of *(3)*. This reaction (2-azadienation of a carbonyl group) is of interest because 2-azadienes were hitherto relatively difficult to prepare.

$$(2) \xrightarrow[2.\ H_2O]{1.\ O{=}C(C_6H_5)_2/O(C_2H_5)_2} (C_6H_5)_2C{=}N{-}CH{=}C(C_6H_5)_2$$

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] Organolithium and Aluminum Compounds, Part 2. – Part 1: *Th. Kauffmann, L. Bán,* and *D. Kuhlmann*, Angew. Chem. *79*, 243 (1967); Angew. Chem. internat. Edit. *6*, 256 (1967).

[2] *C. Paal* and *E. Weidenkaff*, Ber. dtsch. chem. Ges. *38*, 1688 (1905).

[3] Yields of iminomethyl compound (first figures given) based on ketone, those of amino compound based on iminomethyl compound.

[4] *A. McKenzie, A. K. Mills,* and *J. R. Myles*, Ber. dtsch. chem. Ges. *63*, 904 (1930).

[5] *H. O. House* and *E. J. Grubbs*, J. Amer. chem. Soc. *81*, 4733 (1959).

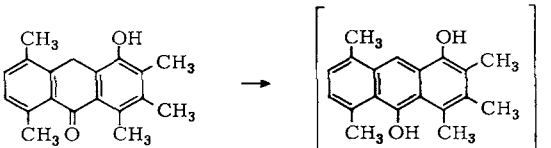
[6] *Th. Kauffmann, G. Beissner, E. Köppelmann, D. Kuhlmann, A. Schott,* and *H. Schrecken*, Angew. Chem. *80*, 117 (1968); Angew. Chem. internat. Edit. *7*, 131 (1968).

[7] *A. McKenzie* and *A. C. Richardson*, J. chem. Soc. (London) *123*, 86 (1923).

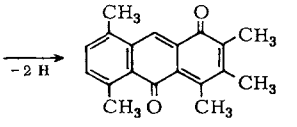
Synthesis of an *ana*-Anthraquinone[1]

By *Peter Boldt* and *Alwin Topp* [*]

We have attempted to prepare 2,3,4,5,8-pentamethyl-1,10-anthraquinone *(3)* and thus, for the first time, a compound containing the long-sought [2] *ana*-anthraquinone system [3] by oxidation of the conjugated hydroquinone *(2)* or its tautomer 4-hydroxy-1,2,3,5,8-pentamethylanthrone *(1)*.

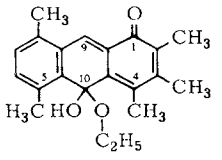


(1) *(2)*

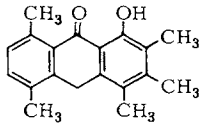


(3)

Compound *(3)* was found to decompose so readily that it could be obtained in pure form only in very dilute solution but not in the solid state. It is formed as a red, amorphous compound in about 50% yield, alongside decomposition products, on dehydrogenation of *(1)* with 2,3-dichloro-5,6-dicyanobenzoquinone at 0 °C[4] in solvents such as anhydrous ether, in which the resulting *(3)* is only moderately soluble. After reaction (about 5 min) the mixture must be immediately cooled to −20 °C. When chromatographed with chloroform (containing 0.3–0.5% ethanol) at −50 °C, the eluate subsequently being concentrated at temperatures below −20 °C, the crude product afforded a red crystalline compound that must be 10-ethoxy-10-hydroxy-2,3,4,5,8-pentamethyl-1(10*H*)-anthracenone *(4)*.



(4)



(5)

This assignment is indicated by the NMR spectrum[5] [2.25, 2.29, 2.49, 2.53, 2.64 (15 H (5 aromatic CH_3)/s); 6.04 (H-9/s); 7.19, 7.27 (H-7/d, H-6/d) ($J_{6,7}$ = 7.8 Hz); 1.0 (3 H (1 aliphatic CH_3/t) (J = 7.0 Hz); 3.0 (2 H (O—CH_2)/m); 7.52 (1 H (OH)/s)], the mass spectrum [essentially only peaks at *m/e* 278, 46 and 45, $M^{\oplus}$ of *(3)*, $M^{\oplus}$ and $[M-1]^{\oplus}$ of ethanol], and the UV and visual spectrum [λ_{max} = 496 nm ($CHCl_3$)]. Moreover, compound *(4)* could be reduced to *(1)*, albeit in only low yield (20%), by zinc or toluhydroquinone.

The presence of a molecular associate of *(3)* and ethanol (1 : 1), as suggested by the mass spectrum, can be ruled out: On repeated chromatography of pure *(4)* with $CHCl_3$/CH_3CD_2OH on silica gel at −50 °C no ethanol exchange was observed. — Since the longest-wave maximum of *(3)*, which was prepared in the absence of water or ethanol, lies at the same position [λ_{max} = 496 nm (ether)] as that of *(4)*, it may be assumed that hemiketal formation has taken place at C-10. Hemiketal formation at C-1 would radically change the chromophore system of *(3)*.

In the solid state and in the absence of moisture and light, compound *(4)* can be stored at 20 °C for several days; in solution, however, it decomposes very rapidly in a second order reaction with respect to *(4)*: $k_2 \approx 50$ l mole^{-1} s^{-1} at 20 °C, $CHCl_3$.

Compound *(1)* could be prepared by Friedel-Crafts reaction of 3,6-dimethylphthalic anhydride with 2,3,4-trimethylphenol, cyclization of the resulting (46% yield) benzoylbenzoic acid with sulfuric acid to 1-hydroxy-2,3,4,5,8-pentamethyl-9,10-anthraquinone (87%), reductive acetylation to 4-acetoxy-1,2,3,5,8-pentamethylanthrone (30%), and hydrolysis (93%).

The position of the carbonyl group in *(1)* was established by comparison of the IR spectrum with that of 1-hydroxy-2,3,4,5,8-pentamethylanthrone *(5)*, which can be obtained from 1-hydroxy-2,3,4,5,8-pentamethyl-9,10-anthraquinone by reduction with tin/hydrochloric acid [*(1)*, OH: sharp, strong band 3350, CO 1635 cm^{-1}; *(5)*, OH: broad, very weak band 3420, CO 1614 cm^{-1}, in KBr]. The structures of all intermediates are in accord with the results of elemental analyses and with the NMR spectra.

As shown by the firm bonding of the ethanol in the hemiketal *(4)*, the slight change in the absorption maximum on hemiketal formation [*(3)* → *(4)*], and the ease with which *(3)* and *(4)* decompose, compound *(3)* is best described as a substituted *o*-benzoquinone methide.

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[1] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the State of Niedersachsen.

[2] See *H. Muxfeldt* and *V. Koppe*, Chem. Ber. *91*, 838 (1958), and literature cited there.

[3] *K. Zahn*, Ber. dtsch. chem. Ges. *67*, 2063 (1934), described 1,10-anthraquinone as "*ana*-anthraquinone".

[4] Below 0 °C dehydrogenation proceeds too slowly, possibly owing to the reaction *(1)* → *(2)*.

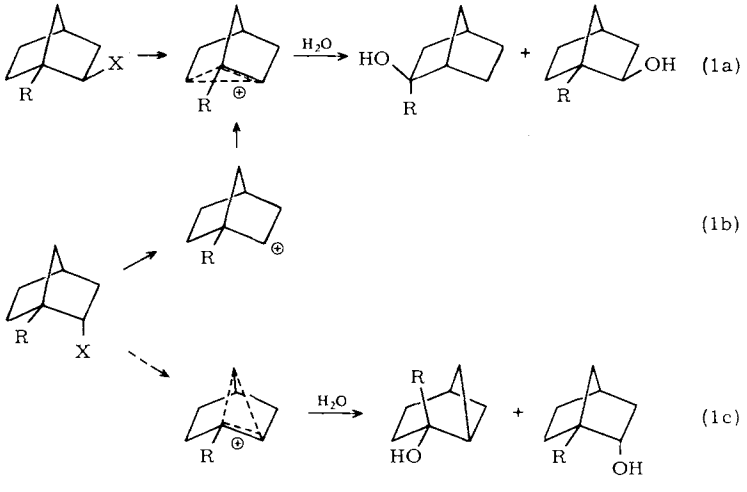
[5] δ-values, measured in deuteriochloroform at −25 °C, TMS internal standard. The fact that the aliphatic CH_3 and OCH_2 groups are adjacent was established by double resonance, the assignment of the OH band by deuteration

Rearrangement of Norbornanes to Norpinanes

By *Wolfgang Kirmse*, *Günter Arend*, and *Rainer Siegfried*[*]

Wagner-Meerwein rearrangements of *exo*-norbornyl derivatives proceed *via* routes involving the C-1—C-6 bond [eq. (1a)][1]. In contrast, reactions of *endo*-norbornyl derivatives involving the C-1—C-7 bond [eq. (1c)] are hardly known[2,3] because of the increased ring strain of the bicyclo[3.1.1]-heptane skeleton (or the bridged ions leading to this system). As a rule *endo*-norbornyl derivatives solvolyze to the same products as the *exo*-isomers, although a classical norbornyl cation must be invoked as intermediate [eq. (1b)].

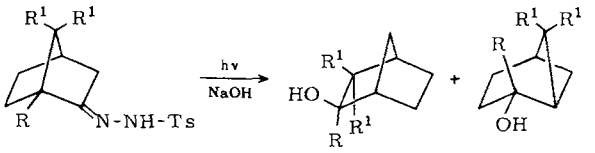
We have found that the reaction can follow the route shown in eq. (1c) when the leaving group is X is $-N_2^+$ and R is an electron-donating substituent. On irradiation of 1-substituted norcamphor- and apocamphor-tosylhydrazones *(1a)*—*(1c)*



(1a)

(1b)

(1c)

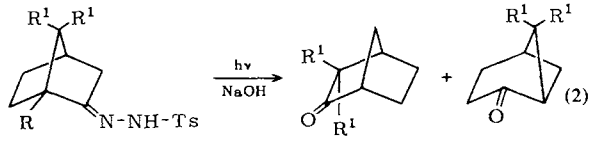


(1a)-(1c) (2) (3) (4)

(1a)–(1c)	(2)	(3)	(4)
(a), R^1 = H, R = CH_3	79.5 [4]	7.5	*exo* 1.6; *endo* 5.9
(b), R^1 = H, R = C_6H_5	69.3	1.9	*exo* 0.3; *endo* 0.2
(c), R^1 = CH_3, R = CH_3	31.4	3.1	*exo* 0.9; *endo* 0.4

in alkaline solution we observed rearrangement to bicyclo-[3.1.1]heptane derivatives *(3)*.

(1a)–(1c) were found to yield not only *(2)–(4)* but also olefins derived from the cationic intermediates of the rearrangement by elimination of a proton. Compound *(1c)* also afforded ring-cleavage products (limonene, terpinolene, α-terpineol). The reaction proceeds more cleanly with oxygen and nitrogen functions on C-1; the ketones *(5)* and *(6)* are then obtained as end products [eq. (2)]. Moreover, compounds bearing substituents with nonbonding electron pairs give higher yields of bicyclo[3.1.1]heptane derivatives than do *(1a)–(1c)*. This substituent effect increases in the order HO < NH—COR < NH_2. Replacement of H on C-7 by methyl also favors formation of bicyclo[3.1.1]heptane derivatives [cf. *(1f)* and *(1k)*, *(1g)* and *(1m)*].

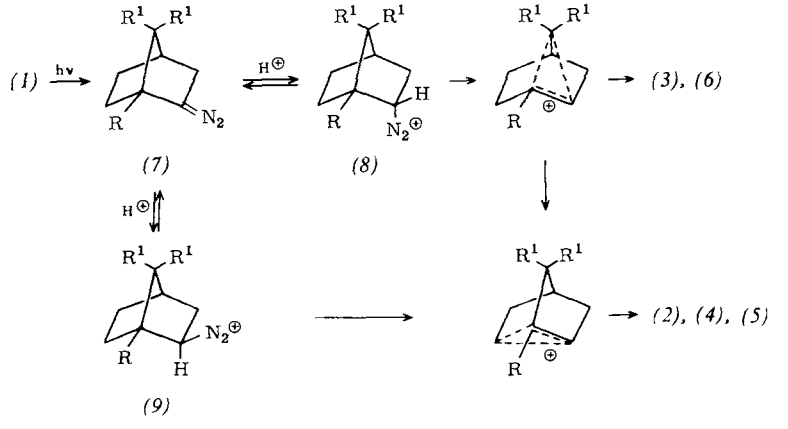


(1d)-(1m) (5) (6)

(1d)–(1m)	(5)	(6)
(d), R^1 = H, R = OCH_3	94 [5]	6
(e), R^1 = H, R = OH	89	11
(f), R^1 = H, R = NH—CO_2CH_3	88	12 [6]
(g), R^1 = H, R = NH_2	74	26
(h), R^1 = CH_3, R = $OCOCH_3$	92	8
(i), R^1 = CH_3, R = OH	86	14
(k), R^1 = CH_3, R = NH—CO_2CH_3	60	40 [6]
(l), R^1 = CH_3, R = NH—$COCH_3$	15	85 [6]
(m), R^1 = CH_3, R = NH_2	3	90

Wilt and *Wagner*[7] obtained only norcamphor *(5)*, R^1 = H, on solvolysis of 1-amino- and 1-acetoxy-2-*exo*-bromonorbornane.

We explain our results as being due to predominating *exo*-protonation of the diazo compound *(7)* initially formed from *(1)*. In the *endo*-diazonium ion *(8)* the steric situation is favorable for decomposition to *(3)* or *(6)* with anchimeric participation of the C-1—C-7 bond. If this process receives insufficient support from electron-donating substituents on C-1 and C-7, the more stable product *(2)*, *(4)*, or *(5)* is formed *via* the isomeric diazonium ion *(9)*.



(9)

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[1] *J. A. Berson* in *P. de Mayo*: Molecular Rearrangements. Interscience, New York 1963, Vol. 1, p. 111; *D. Bethell* and *V. Gold*: Carbonium Ions. Academic Press, London 1967, p. 223.

[2] *P. Yates* and *R. J. Crawford*, J. Amer. chem. Soc. *88*, 1561 (1966).

[3] *C. J. Collins*, *V. F. Raaen*, *B. M. Benjamin*, and *I. T. Glover*, J. Amer. chem. Soc. *89*, 3940 (1967).

[4] The figures given are relative yields that take into consideration the olefins formed at the same time (olefins = 100 − sum of alcohols); overall yield determined by gas chromatography as 80–95%.

[5] The figures given are relative yields; overall yields determined by gas chromatography as 50–90%.

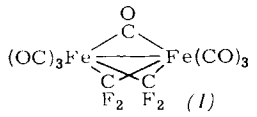
[6] In the case of this compound the amount of *(6)* increases with increasing NaOH concentration while the overall yield decreases. The values given are for 0.2 N NaOH.

[7] *J. W. Wilt* and *W. J. Wagner*, J. Amer. chem. Soc. *90*, 6135 (1968).

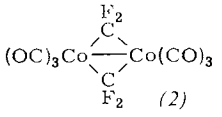
μ-Carbonyldi-μ-difluoromethylenebis(tricarbonyliron)(Fe–Fe) and Di-μ-difluoromethylenebis(tricarbonylcobalt)(Co–Co)

By *Fritz Seel* and *Gerd-Volker Röschenthaler*[*]

We have been able to prove that the CO bridges in polynuclear carbonylmetal complexes can be replaced by CF_2 groups. Irradiation of a mixture of pentacarbonyliron and dibromodifluoromethane vapors with a high-pressure mercury vapor lamp[1] leads to the formation of μ-carbonyldi-μ-difluoromethylenebis(tricarbonyliron) (Fe–Fe) *(1)* along with $Fe(CO)_4Br_2$ and $FeBr_2$. Irradiation of a solution of tricarbonylnitrosylcobalt in CF_2Br_2 affords di-μ-fluoromethylenebis(tricarbonylcobalt) (Co—Co) *(2)*, $Co(NO)_2Br$, and $CoBr_2$.



(1)



(2)

Detailed information about the composition and structure of compounds *(1)* and *(2)*, which readily sublime at room temperature, was provided by their 70 eV mass spectra. The signals of highest intensity are due to the fragments $M(CF_2)_2M^+$ (M = Fe, Co); other signals occurring are those due to the molecular ions and the dissociation products resulting from CO cleavage as well as those of the fission fragments of $M(CF_2)_2^+$. The IR spectra of the complexes (see Table) are also in accord with the proposed structures; the spectra show that compound *(1)* contains a bridging CO group whereas compound *(2)* does not. The compounds are diamagnetic and therefore must contain metal-metal bonds. *(1)* and *(2)* are readily soluble in organic solvents such as ether, petroleum ether, benzene, or methanol and crystallize therefrom in the form of yellow needles. Just as $Fe_2(CO)_9$ is more stable than $Co_2(CO)_8$, compound *(1)* is more stable than *(2)* in air; however, it melts at 104 °C with decomposition. *(2)* sublimes at 45 °C under atmospheric pressure.

If a *solution* of $Fe(CO)_5$ in CF_2Br_2 is subjected to irradiation, orange-yellow, volatile tetracarbonylbis(bromodifluoromethyl)iron $(CF_2Br)_2Fe(CO)_4$ *(3)* is formed. This compound, which is probably a precursor of *(1)*, was also characterized by its IR (cf. Table) and mass spectra. Since *(3)* exhibits more than one IR-active CO absorption band it must be present in the *cis*-form. The signals of the molecular ion and fragment ions in the mass spectrum of *(3)* exhibit triplet and doublet structure as a result of the isotopy of bromine.

Table. CO bands (cm^{-1}) of the IR spectra of *(1)*, *(2)* and *(3)* in *n*-hexane solution, of $Fe_2(CO)_9$ in the solid state, of $Co_2(CO)_8$ (bridge form) in *n*-hexane, and of *cis*-$Fe(CO)_4Br_2$ in chloroform.

$Fe_2(CF_2)_2(CO)_7$ *(1)*	$Fe_2(CO)_9$ [2]
2091 vs 1894 s	2082 s 1829 vs
2064 s	2019 vs
2056 s	
$Co_2(CF_2)_2(CO)_6$ *(2)*	$Co_2(CO)_8$[3]
2128 w	2112 vw 1866 m
2095 s	2071 vs 1857 s
2086 m	2044 vs 1832 vw
2070 vs	2031 s
2041 m	2001 w
$Fe(CO)_4(CF_2Br)_2$ *(3)*	*cis*-$Fe(CO)_4Br_2$[4]
2131 w	2155 w
2100 vs	2112 s
	2109 s
2065 s	2082 s

Experimental:

For the preparation of *(1)* equimolar amounts of $Fe(CO)_5$ and CF_2Br_2 are introduced into an evacuated quartz glass reaction flask at 0 °C ($p \approx 80$ torr) and the resultant gas mixture is irradiated; for the preparation of *(2)* and *(3)*, 0.03 M solutions of $Co(CO)_3NO$ and $Fe(CO)_5$ in CF_2Br_2 resp. are subjected to irradiation.

Reaction is complete in about 3 hours, when dark colored reaction products are deposited on the walls of the reaction vessel. Termination of the gas reaction can be recognized by a cessation of the pressure increase that accompanies evolution of carbon monoxide and tetrafluoroethylene. After pumping off the gases and excess starting materials compound *(1)* can be sublimed into a cold-trap (liquid nitrogen) and recrystallized from petroleum ether. The suspensions containing *(2)* and *(3)* must be filtered under nitrogen before evaporation in vacuum. The pure compounds can be sublimed onto a cold finger (Dry ice) in high vacuum. As is frequently the case in photochemical reactions, the yields are low: 15 to 20 mg from a 100 ml volume of gas (or solution).

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[1] Type TQ 81, Quarzlampen GmbH Hanau.

[2] *F. A. Cotton, A. D. Liehr*, and *G. Wilkinson*, J. inorg. nuclear Chem. *1*, 175 (1955).

[3] *G. Bor*, Spectrochim. Acta *19*, 1209, 2065 (1963).

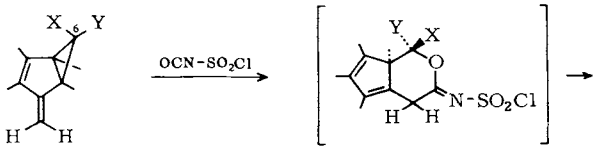
[4] *R. C. Taylor* and *W. D. Horrocks*, Inorg. Chem. *3*, 584 (1964).

Cycloaddition to Homofulvenes

By *Rainer Askani*[*]

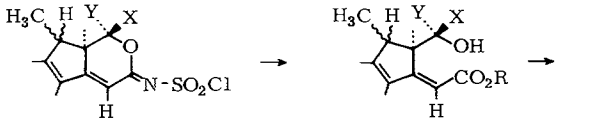
Whereas [6 + 2]-cycloadditions with fulvenes as 6π-electron components are still unknown, the homofulvene derivatives *exo*- and *endo* - 1,2,3,5,6 - pentamethyl - 4 - methylenebicyclo-[3.1.0]hex-2-ene *(1a)* and *(1b)*[1] have been found to undergo homo-[6 + 2]-cycloaddition with *N*-chlorosulfonyl isocyanate to give the adducts *(3a)* and *(3b)*, respectively, the reaction involving inversion at C-6. This finding is in accord with the requirements for a symmetry-allowed concerted reaction of the kind $[(\sigma 2_a + \pi 4_s) + \pi 2_s]$, while a corresponding reaction of fulvenes, being a $[\pi 6_s + \pi 2_s]$ process, is symmetry-forbidden[2]. A further possibility in the case of *N*-chlorosulfonyl isocyanate, *i.e.* that the reaction proceeds stepwise, would require stereospecific opening of the three-membered ring since no products exhibiting retention could be detected alongside those that had undergone inversion at C-6.

Reaction of *(1a)* and *(1b)* with *N*-chlorosulfonyl isocyanate is assumed to give initially *(2a)* and *(2b)*, respectively, which are converted into the conjugated isomers *(3a)* and *(3b)* by an allylic hydrogen shift under the reaction conditions[**]. Since only one product can be isolated in each case, this shift must be stereospecific; however, the available spectral data provide no definite information about the steric course. The conversion of both *(3a)* and *(3b)*, *via* the acids *(4a)* and *(4b)* and the esters *(5a)* and *(5b)*, into the same ketone *(6)* shows



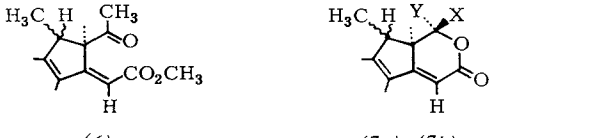
(1a), X = H, Y = CH_3
(1b), X = CH_3, Y = H [a]

(2a), *(2b)*



(3a), *(3b)*

(4a), *(4b)*, R = H
(5a), *(5b)*, R = CH_3



(6)

(7a), *(7b)*

[a] This assignment is retained in the subsequent formulas; the lines radiating from the rings signify methyl groups.

Cpd. [a] m.p. (°C)	NMR [b]	IR (cm^{-1})	UV (nm) (ε)
(3a) 123–124	4.10 (s) =C–H, 5.60 (q, J = 6.5 Hz) O–C–H, 7.44 (q, J = 7.0 Hz) C–H, 8.02 (m) 8.13 (m), 8.44 (d, J = 6.5 Hz), 8.83 (d, J = 7.0 Hz), 9.05 (s) CH_3 [1:1:1:3:3:3:3:3 ($CDCl_3$)]	νC=C 1620 (m) 1590 (s) νC=N 1500 (s) νSO_2 1350 (s) 1170 (s) (KBr)	328 (28300) (dioxane)
(3b) 100–101	4.25 (s) =C–H, 5.00 (q, J = 6.5 Hz) O–C–H, 7.26 (q, J = 7.0 Hz) C–H, 8.05 (m), 8.12 (m), 8.64 (d, J = 6.5 Hz), 8.82 (s), 8.85 (d, J = 7.0 Hz) CH_3 [1:1:1:3:3:3:3:3 ($CDCl_3$)]	νC=C 1620 (m) 1590 (s) νC=N 1500 (s) νSO_2 1350 (s) 1170 (s) (KBr)	331 (28200) (dioxane)
(4a) 164–165	4.13 (s) =C–H, 4.66 (q, J = 6.5 Hz) O–C–H, 6.90 (q, J = 7.0 Hz) C–H, 8.23 (m), 8.27 (s), 8.37 (m), 8.87 (d, J = 6.5 Hz), 8.89 (d, J = 7.0 Hz) CH_3 [1:1:1:3:3:3:3:3 (pyridine)]	νC=O 1680 (s) νC=C 1640 (m) 1590 (s) (KBr)	283 (20000) (CH_3OH)
(4b) 160–161	3.93 (s) =C–H, 4.76 (q, J = 6.5 Hz) O–C–H 6.94 (q, J = 7.0 Hz) C–H 8.27 (m), 8.39 (m), 8.43 (s), 8.69 (d, J = 6.5 Hz), 9.00 (d, J = 7.0 Hz) CH_3 [1:1:1:3:3:3:3:3 (pyridine)]	νC=O 1680 (s) νC=C 1640 (m) 1590 (s) (KBr)	285 (19500) (CH_3OH)
(5a) 86–87	4.62 (s) =C–H, 5.30 (q, J = 6.5 Hz) O–C–H, 6.40 (s) OCH_3, 7.23 (q, J = 7.0 Hz) C–H, 8.15 (m), 8.35 (m), 8.68 (s), 8.97 (d, J = 7.0 Hz), 9.18 (d, J = 6.5 Hz) CH_3 [1:1:3:1:3:3:3:3:3 (CCl_4)]	νC=O 1700 (s) νC=C 1640 (m) 1590 (s) (CCl_4)	283 (23800) (ether)
(5b) oil	4.47 (s) =C–H, 5.53 (q, J = 6.5 Hz) O–C–H, 6.35 (s) OCH_3, 7.24 (q, J = 7.0 Hz) C–H, 8.17 (m), 8.33 (m), 8.84 (s), 8.96 (d, J = 6.5 Hz), 8.97 (d, J = 7.0 Hz) CH_3 [1:1:3:1:3:3:3:3:3 (CCl_4)]	νC=O 1700 (s) νC=C 1640 (m) 1590 (s) (CCl_4)	285 (23600) (ether)
(6) 87–88	4.25 (s) =C–H, 6.20 (s) OCH_3, 7.21 (q, J = 7.0 Hz) C–H, 7.92 (s) $COCH_3$, 8.05 (m), 8.17 (m), 8.72 (s), 8.92 (d, J = 7.0 Hz) CH_3 [1:3:1:3:3:3:3:3 ($CDCl_3$)]	νC=O 1700 (s) νC=C 1640 (m) 1590 (s) (KBr)	283 (22200) (dioxane)
(7a) 177–178	4.50 (s) =C–H, 5.79 (q, J = 6.5 Hz) O–C–H, 7.62 (q, J = 7.0 Hz) C–H, 8.15 (m), 8.22 (m), 8.65 (d, J = 6.5 Hz), 8.92 (d, J = 7.0 Hz), 9.08 (s) CH_3 [1:1:1:3:3:3:3:3 ($CDCl_3$)]	νC=O 1680 (s) νC=C 1640 (m) 1600 (s) (KBr)	278 (20200) (dioxane)
(7b) 124–125	4.50 (s) =C–H, 5.37 (q, J = 6.5 Hz) O–C–H, 7.34 (q, J = 7.0 Hz) C–H, 8.15 (m), 8.23 (m), 8.74 (d, J = 6.5 Hz), 8.81 (s), 8.93 (d, J = 7.0 Hz) CH_3 [1:1:1:3:3:3:3:3 ($CDCl_3$)]	νC=O 1680 (s) νC=C 1640 (m) 1610 (s) (KBr)	282 (18400) (dioxane)

[a] Satisfactory analytical results were obtained for all compounds.
[b] TMS as internal standard, τ scale.

that the adducts *(3a)* and *(3b)* differ only in the configuration of the carbon atom bound to the oxygen[3]. The ^1H—NMR signals of the group X—C—Y in *(3a)* and *(3b)* and of the lactones *(7a)* and *(7b)* accessible from *(4a)* and *(4b)*, respectively, (benzene, *p*-toluenesulfonic acid, water separator) suggest that inversion at C-6 takes place during the addition to *(1)*.

Methyl 2-(2-acetyl-2,3,4,5-tetramethyl-4-cyclopenten-1-ylidene)acetate (6)

A solution of *N*-chlorosulfonyl isocyanate (2.0 g) in ether (30 ml) is added dropwise to a solution of *(1a)* or *(1b)* (2.0 g) in ether (50 ml), to which a small amount of anhydrous potassium carbonate has been added, at −60 °C. The reaction mixture is kept at −60 °C for another hour, permitted to warm up to room temperature overnight, and then filtered. The filtrate is evaporated down to a volume of about 10 ml and placed in a refrigerator; pale yellow crystals of *(3a)* (2.2 g, 59 %) or *(3b)* (1.2 g, 32 %) are precipitated.

A solution of *(3a)* or *(3b)* (1.5 g) in dioxane (40 ml) is permitted to react for 24 h, with stirring, at 60 °C with a solution of potassium hydroxide (4 g) in water (30 ml). The aqueous phase remaining when the dioxane is distilled off is extracted with ether and acidified with hydrochloric acid. *(4a)* or *(4b)* (0.8—0.9 g, 70—80 %) is obtained.

A solution of 1.0 g of the ester *(5a)* or *(5b)*, obtained in 85 to 90 % yield from *(4a)* or *(4b)* on reaction with diazomethane, in acetone (5 ml) is treated with a solution of chromium trioxide (1.0 g) in water (5 ml) and conc. sulfuric acid (1 ml). After 10 min, water (100 ml) is added to the reaction mixture and the product *(6)* (0.9 g, 90 %) is extracted with ether.

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[**] *Note added in proof* (January 31, 1970): If acetylenedicarboxylic esters, azodicarboxylic esters, maleic anhydride, or tetracyanoethylene is used as reactant instead of *N*-chlorosulfonyl isocyanate the adducts corresponding to *(2)* are isolated.

[3] According to the NMR spectra the configuration of the second H–C–CH_3 is identical in *(3a)* and *(3b)*; the same also applies to *(5a)* and *(5b)*.

Catalytic Cleavage of Aldehydes to Olefins, Carbon Monoxide, and Hydrogen

By *Jürgen Falbe*, *Hans Tummes*, and *Heinz-Dieter Hahn*[*]

The hydroformylation of olefins (oxo synthesis) according to *O. Roelen*[1] usually affords isomeric mixtures of aldehydes. All attempts to improve the selectivity in favor of straight-chain products have hitherto met with only limited success. Thus in the present-day industrial (10^6 t/a) hydroformylation of propene to butyraldehydes most processes produce at least one part of isobutyraldehyde for every four parts of *n*-butyraldehyde[2,3]. Only a small proportion of the large amount of isobutyraldehyde produced finds any application in the chemical industry, the rest being burnt for heating purposes.

Our experiments designed to alleviate this unsatisfactory state of affairs have now led to a highly selective cleavage of the isobutyraldehyde into the reactants of the oxo synthesis, propene, carbon monoxide, and hydrogen[4]:

$$\begin{array}{l} CH_3\text{-}CH\text{-}CHO \\ \quad\quad | \\ \quad CH_3 \end{array} \xrightarrow{\text{catalyst}} CH_3\text{-}CH{=}CH_2 + CO + H_2$$

The reaction takes place at 250–350 °C on a fixed-bed catalyst containing a metal of the platinum group in the gas phase at conversions of 80–100 %[4]. Only a small amount of the propene is hydrogenated to propane.

Experiments in a continuously operated pilot plant showed the catalysts to have adequate lifetimes; moreover, they can be regenerated a considerable number of times. Deposits of carbon or other decomposition products on the catalyst can be removed in the reactor by combustion in air.

By returning the above cleavage products to the oxo synthesis it is therefore possible to convert propene almost completely into the desired *n*-butyraldehyde.

The cleavage reaction can also be carried out with other aldehydes (see Table). Benzaldehyde yields the decarbonylation product benzene.

Examples (T = 280–300 °C; residence time [a] 3–4s).

Aldehyde	Conversion (%)	Yield in moles/100 moles of reacted aldehyde (selectivity)		
		Olefin	CO	H_2
Isobutyraldehyde	82	93 (propene)	100	84
n-Butyraldehyde	76	87 (propene)	100	83
3-Methylbutanal	97	83 (isobutene)	97	81
2-Ethylhexanal	85	89 [b] (heptene)	98	82
Benzaldehyde	67	100 (benzene)	100	–

[a] For the aldehyde.
[b] Mixture of positional and configurational isomers of heptene.

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Dichlorocarbene from Trichloromethyllithium[**]

By *Gert Köbrich*, *Horst Büttner*, and *Ernst Wagner*[*]

Despite numerous investigations[1–9] the question as to whether free dichlorocarbene is involved in the electrophilic reactions of trichloromethyllithium (TML) still remains unanswered. The thermolytic behavior of TML – compared with that of other carbenoids[8] – indicates a highly electrophilic species (thermally less stable than dichloromethyllithium[7,9], CCl_2 insertion into the α-CH bond of the solvent THF[7], high yields of cyclopropanes with olefins[1,3,4,7,9]), which could *a priori* be TML itself, a carbene complex having an ionized CCl bond, or free dichlorocarbene. Competition reactions, such as are used for the detection of unstable intermediates, suggest themselves as a possible means of distinguishing between these alternatives, particularly since numerical values are already available[13] for dichlorocarbene transfers to olefin mixtures from other substrates (chloroform/K *tert*-butoxide[10], Na trichloroacetate[11], phenyl trihalogenomethylmercury[12]).

Table 1. Dichlorocyclopropanes from trichloromethyllithium (competition experiments using 5 olefin + 5 cyclohexene + 1 TML; two experiments in each case).

$$\begin{array}{l} Li{-}CCl_3 \rightarrow LiCl + :CCl_2 \\ (-110\,^\circ C) \qquad (-73\,^\circ C) \end{array} \quad \begin{array}{l} \xrightarrow[k_a]{\text{olefin}} \text{dichlorocyclopropane ("A")} \\ \xrightarrow[k_b]{\text{cyclohexene}} \text{dichloronorcarane ("B")} \end{array}$$

Olefin	Product yields (%) (w.r.t. Li–CCl_3)				k_a/k_b	k_a/k_b – Comparative values from other substrates					
	A	B	A + B	$Cl^\ominus$		$C_6H_5HgCCl_2Br$ (80 °C) [13a]	CCl_3CO_2Na (80 °C) [13a]	$C_6H_5HgCCl_3$ (NaI, 80 °C) [13b]	$C_6H_5HgCCl_2Br$ (NaI, –15 °C) [13b]	$CHCl_3/KOC(CH_3)_3$ (–15 °C) [13b]	[13c]
2,3-Dimethyl-2-pentene	85.6 82.8	3.7 3.5	89.3 86.3	 97	23.1 23.8	22.5	24.8	23.2	22.7		
2-Ethyl-1-hexene	67.9 53.7	21.6 17.0	89.5 70.7	93 87	3.14 3.15	2.31		2.30			
cis-2-Pentene	44.8 44.0	33.7 32.8	78.5 76.8	97 97	1.33 1.34				1.44	1.52	1.62
trans-2-Pentene	40.4 40.3	51.0 50.6	91.4 90.9	102 99	0.79 0.79				0.834	0.86	2.14 (?)
trans-3-Heptene	24.0 18.4	59.8 46.7	83.8 65.1	91 84	0.40 0.39	0.52	0.52	0.537	0.435	0.435	
1-Heptene	9.6 8.6	77.5 70.2	87.1 78.8	95 95	0.12 0.12	0.24	0.22	0.218	0.11		

We have investigated the decomposition of TML (−73 °C in THF) in the presence of six different mixtures of cyclohexene and a second olefin. The resulting compounds, dichloronorcarane ("B") and dichlorocyclopropane ("A"), were identified by comparison with authentic samples and analyzed by gas chromatography; the decomposition of TML was determined by $Cl^{\ominus}$ titration[4,7] (Table 1). Despite the fact that total yields in duplicate experiments often differ, the yield ratios corresponding to the rate ratios k_a/k_b are very accurately reproducible. The good agreement of our ratios with those in the literature (Table 1) leaves no doubt of a common intermediate in all cyclopropanations: dichlorocarbene. The small deviations can be ascribed to different excess energies[14] and to solvation effects. The carbene transfers from TML show no increased selectivity, as would be feasible for a "moderated" carbene (also on account of the mild conditions) and recognizable by a more pronounced tendency for the ratios to deviate from unity.

The ratios given in Table 1 reflect, above all, the electrophilicity of the intermediate. Competition experiments carried out according to *Moss* with vinylalkanes[15] reveal the steric factors involved in dichlorocarbene transfer. The rate ratio for 1-butene + 3-methyl-1-butene in the system chloroform/K *tert*-butoxide is 2.34[15]; in the case of TML we have obtained a value of 2.44 (total yield 34%). The good agreement of these data supports the conclusion that free dichlorocarbene is a common intermediate.

We have also reinvestigated the question of whether olefins accelerate the decomposition of TML. This investigation presented, as previously[3,4,5,7], a number of experimental difficulties since TML is quantitatively obtainable in a stable form only at −110 °C (in THF)[2,4,7] but is very sparingly soluble at this temperature and only slowly dissolves when warmed to the decomposition temperature (−73 °C); unavoidable variations in amount and quality of the solid phase lead to considerable deviations in the results (cf. the absolute yields of cyclopropanes, Table 1). The values given in Table 2 are average values obtained from four to eight independent experiments [constant solvent polarity ensured by keeping the total number of moles (cyclohexene + methylcyclohexane) the same] and serve much better than previous results[3,4,5,7] to illustrate beyond doubt the strong acceleration of TML decomposition by cyclohexene. These results — which are *per se* also consistent with a direct reaction between TML and the olefin — together with the previously mentioned results, are proof of the carbene transfer to cyclohexene as the rate-determining reaction step.

Table 2. Acceleration of Li—CCl_3 decomposition by cyclohexene (90 min at −73 °C).

20 mmoles of Li—CCl_3 +	Decomposition (LiCl)	Dichloronorcarane	No. of experiments
200 mmoles methylcyclohexane	36%	—	8
50 mmoles cyclohexene + 150 mmoles methylcyclohexane	86%	56%	6
190 mmoles cyclohexene + 10 mmoles methylcyclohexane	91%	72%	4

As indicated by the LiCl determination there is no enrichment of dichlorocarbene in the solution. It follows that at −73 °C a fast equilibrium is set up between TML, dichlorocarbene, and lithium chloride, from which dichlorocarbene is trapped in slower but irreversible consecutive reactions (the little known thermolysis reactions[7] and the addition to olefins to give cyclopropane).

$$LiCCl_3 \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} LiCl + :CCl_2 \xrightarrow{\text{slow}} \begin{cases} \rightarrow \text{cyclopropane} \\ \rightarrow \text{"normal" products of thermolysis} \end{cases}$$

Carbenoid/carbene equilibria are *mutatis mutandis* also known for the trichloromethyl anion in aqueous medium[16] and for tris(phenylthio)methyllithium[17,18].

Procedure:

Trichloromethyllithium, prepared by treating a solution of chloroform (2.40 g, 20.0 mmoles) in THF (70 ml), ether (5 ml), and petroleum ether (5 ml) with *n*-butyllithium (1.0—1.5 M in petroleum ether) at −115 to −110 °C[7] (dropwise addition over 40 minutes followed by 10 minutes' stirring) was allowed to warm to −100 °C within 15 minutes and 100 mmoles of each olefin was then added dropwise over a period of 10 minutes. The mixture was stirred for about 35 minutes and allowed to warm to −73 °C (± 2 °C) (internal temperature). After 90 minutes at this temperature the reaction flask was transferred to another cooled bath (−117 °C) and the reaction mixture was treated with a solution of methanol (1.0 g) and glacial acetic acid (2.0 g) in ether (5 ml). The usual working-up procedure was followed by potentiometric $Cl^{\ominus}$ titration of aliquots of the aqueous layer. The dichlorocyclopropanes present in the organic residue remaining after removal of the solvent by fractional distillation were then determined gas-chomatographically by comparison with authentic samples[10] and the aid of calibration curves using alkanes as internal standards (4 m columns, C-wax, SE30 or APL).

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The Problem of an Intermolecular Charge-Transfer Triplet Excited State

By *Günther Briegleb* and *Dieter Wolf*[*]

Iwata, Tanaka, and *Nagakura*[1] have observed a structureless, long-wave (lw), long-lived (ll) emission band on excitation in the charge-transfer (CT) absorption band of relatively weak electron donor-acceptor (EDA) complexes of the electron acceptors (A) 1,2,4,5-tetracyanobenzene *(1)*, tetrachlorophthalic anhydride *(2)*, and pyromellitic dianhydride *(3)* with the electron donors (D) mesitylene *(6)*, durene *(7)*, hexamethylbenzene *(8)*, and phenanthrene *(9)*, *etc.*, in solution in diethyl ether-isopentane glass at $T = 77\,^{\circ}K$; they interpret this emission as CT phosphorescence of a complex triplet excited state $|\overset{\uparrow}{D}\overset{\uparrow}{A}^{-}|^{*}_{T}$. This would be the first detection of a CT triplet excited state, a finding of considerable theoretical interest[3] and of great significance, *e.g.* for the interpretation of photochemical processes, the photoconductivity of organic compounds, *etc.*

In this communication we report on the results of studies on complexes of *(1)* with the donors toluene *(4)*, *p*-xylene *(5)*, *(6)*, *(7)*, and *(8)* which lead us to a different interpretation of the green lw,ll emission under discussion.

a) 1,2,4,5-Tetracyanobenzene (1). After excitation in the 31600 cm^{-1} peak of the long-wave $S_0 \rightarrow S_1$ absorption band of *(1)* in solution in dipropyl ether glass at $T = 100\,^{\circ}K$ for a few minutes a gradual change may be observed in the primarily emitted, structured, blue phosphorescence of *(1)* (Fig. 1: 3a; 0,0 band: 22600 cm^{-1}, mean lifetime $\tau_0 = 2.7$ s): the maximum is shifted towards longer wavelengths and the mean lifetime is shortened. A plot of the difference between the phosphorescence spectra measured at different times results in a lw,ll emission band $\tilde{\nu}^{llEm} = 19600\ cm^{-1}$ in the green region of the spectrum (Table 1: 5). At the same time, irradiation in the region of the 31600 cm^{-1} absorption of *(1)* produces a new absorption spectrum with two characteristic absorption regions at ≈ 22000 and $\approx 26000\ cm^{-1}$ (Fig. 1: 2), due to a new molecular species hereafter designated as X[4,10]. It can be shown that X is formed *via* the triplet excited state of *(1)*[10]. The formation of X can be detected not only in glass solutions but also in crystals at $T = 77\,^{\circ}K$.

Irradiation in the long-wave absorption peak of X, $\tilde{\nu}_X^{Abs} \approx 21000\ cm^{-1}$, gives rise to a fluorescence $\tilde{\nu}_X^F$ (Table 1: 4) in the green spectral range having a maximum corresponding to that of the lw,ll emission band $\tilde{\nu}^{llEm}$ (Table 1: 5). We therefore interpret the green lw,ll emission band as delayed fluorescence $\tilde{\nu}_X^{llEm}$ of X as a result of energy transfer from triplet excited *(1)* to X in a frequency range in which the phosphorescence band of *(1)* and the long-wave absorption band of X (Table 1: 3) are superposed.

b) EDA complexes with A = (1); high donor concentration: $q = c_D/c_A = 2.8 \times 10^2$—$10^4$, $c_{(1)} \approx 1 \cdot 10^{-4}$ M (Table 1: 7).

Excitation of complexes of *(1)* with *(4)*, *(5)*, *(6)*, *(7)*, or *(8)* in dipropyl ether at $T = 100\,^{\circ}K$ within the CT absorption band $\tilde{\nu}_{CT}^{Abs}$ (Table 1: 2) produces the normal CT fluorescence. In addition, a green, structureless, lw,ll emission band $\tilde{\nu}^{llEm}$ very similar to the long-wave, long-lived emission of uncomplexed *(1)* may be observed (Table 1: 5 and Fig. 1: 5). As in the case of *(1)*, a new absorption band also appears which is characteristic of a molecular species X′. In this case, X′ is an aggregation of X with D, *i.e.* X′ ≡ X · D.

Accordingly, a shift towards longer wavelengths exhibited by both $\tilde{\nu}_X^F$ and $\tilde{\nu}^{llEm}$ and by the long wave absorption peak of X′ may be observed in the order (λ): *(7)* · *(1)* > *(6)* · *(1)* > *(5)* · *(1)* > *(4)* · *(1)*. This order runs parallel to decreasing donor strength or increasing ionization potential. X′ is formed *via* triplet excited *(1)*, which is excited *via* the singlet excited CT complex[9].

On excitation in the longest-wave peak of the X′ absorption band $\tilde{\nu}_{X'}^{Abs}$ (Table 1: 3) the fluorescence $\tilde{\nu}_{X'}^F$ of X′ (Table 1: 4 and Fig. 1: 4) occurs at a frequency corresponding to the lw,ll emission $\tilde{\nu}^{llEm}$ (Table 1: 5; Fig. 1: 5); as in the case of *(1)*, we therefore regard $\tilde{\nu}^{llEm}$ as delayed fluorescence of X′ due to energy transfer from triplet-excited *(1)* to X′[6].

Table 1. Band maxima of the absorption and emission spectra of 1,2,4,5-tetracyanobenzene *(1)* and the EDA complexes $|D \cdot (1)|$ (cf. Fig. 1).

	$\tilde{\nu}_{CT}^{Abs}$ ($10^3\ cm^{-1}$)	$\tilde{\nu}_X^{Abs}$ ($10^3\ cm^{-1}$)	$\tilde{\nu}_X^F$ ($10^3\ cm^{-1}$)	$\tilde{\nu}^{llEm}$ ($10^3\ cm^{-1}$)		$q = c_D/c_A$ [$c_{(1)} = 1 \times 10^{-4}$ M]
1	2	3	4	5	6	7
(1)	—	21.6	19.6	19.6	—	—
D = Toluene *(4)*	[a]	21.7	19.7	19.8	—	1×10^4
p-Xylene *(5)*	28—30 [b]	21.6	19.3	19.5	—	3.5×10^3
Mesitylene *(6)*	28.3 [c]	21.4	18.9	18.9	19.8 [f]	3.7×10^3
Durene *(7)*	25 [d]	21.2	18.7	18.8	19.5 [f]	2.9×10^2
Hexamethylbenzene *(8)*	24.6 [e]	21.3	19.1	18.3	18.3 [f]	1.1×10^{-1}
		21.1	19.0	17.8	—	1.1×10^2

[a] In the case of the complex $|(4) \cdot (1)|$ irradiation was carried out in the long-wave flank of the CT band (at 28500 cm^{-1}) since the maximum lies in the region of the 31600 cm^{-1} peak of *(1)*. [b] No separable maximum. [c] In the crystal [2]. [d] In CH_2Cl_2, $T = 293\,^{\circ}K$ [2]. [e] In dipropyl ether at $T = 293$ and $100\,^{\circ}K$. [f] $\tilde{\nu}^{llEm}$ band maxima measured by *Iwata*, *Tanaka*, and *Nagakura* [1, 5b] and interpreted as CT phosphorescence (in diethyl ether/isopentane (1 : 1), $T = 77\,^{\circ}K$).

The intensity decay of the long-lived emission is initially non-exponential ($\tau < 2.7$ s); but after about 5 s the intensity decreases exponentially with $\tau_0 = 2.7$ s.

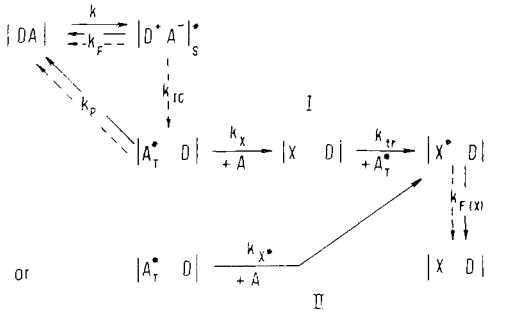
c) EDA complexes with A = (1); low donor concentration: $q = c_D/c_A = 4$—77, $c_{(1)} = 1.1 \times 10^{-4}$ M.

On low-intensity excitation at low D concentration and low constant concentration of *(1)* formation of X is suppressed to such an extent that all the complexes of *(1)* with *(4)*, *(5)*, *(6)*, or *(7)* yield primarily the structured phosphorescence of *(1)*[7] (Fig. 1: 3). The fine-structure bands of this phosphorescence, which is excited *via* the CT singlet $|\dot{D}^{+}\dot{A}^{-}|^{*}_{S}$, are inevitably broadened by superposition[8] with the delayed fluorescence of X′. Consequently the intensity maximum shows a shift towards longer wavelengths.

d) The following reaction scheme (p. 172) is in accord with all observed phenomena, including the results of kinetic investigations[10].

No decision could be made in favor of either I or II, but it was possible to rule out other conceivable reaction mechanisms.

As is demonstrated by the occurrence of the phosphorescence spectrum of *(1)* on irradiation in the CT band at low



donor concentration under conditions which give rise to only low concentrations of X, the relation $E|\dot{D}+\dot{A}^-|_S^* > E|DA_T^*|$ applies to the complexes of *(1)* with *(4)*, *(5)*, *(6)*, or *(7)*. Consequently, in this case the species X′ which can only be formed *via* the triplet excited state of *(1)* may be observed after irradiation in the complex CT band [9].

e) Hexamethylbenzene-tetracyanobenzene. Irradiation in the CT band (24600 cm^{-1}) of the complex $|(8)\cdot(1)|$ at 100 °K does not give rise to the structured phosphorescence of *(1)*, even at low acceptor and donor concentrations; however, the delayed fluorescence of X′, $\tilde{\nu}_{X'}^{IIEm}$ (Table 1: 5) is observed in the green region of the spectrum. It is shifted towards relatively long wavelengths because of superposition by the phosphorescence of a mixed excimer $|(8)\cdot(1)_T^*|$ of a triplet excited $(1)_T^*$ and *(8)* which lies in the red region of the spectrum. The decrease in the $\tilde{\nu}_{X'}^{IIEm}$ intensity is not exponential (τ = 0.4 to 1.1 s). At increasing concentration of *(8)*, and accordingly increasing excimer concentration, the maximum $\tilde{\nu}_{X'}^{IIEm}$ shifts towards longer wavelengths. At higher temperatures (T = 112 °K), when the dipropyl ether glass starts to become viscous, the concentration of X, which may be enriched only in the glass (or crystal) matrix, is reduced to such an extent that only the red excimer-phosphorescence band ($\tilde{\nu}_{max}^{PE}$ = 16.5 × 10^3 cm^{-1}; Fig. 1: 6) may still be observed.

f) The results of our studies show that the II,Iw emission bands which have been discussed in connection with the question of a CT triplet excited state [1] have to be interpreted as delayed fluorescence of a molecular species X [4, 10]. In the case of the EDA complex $|(8)\cdot(1)|$, an additional mixed excimer phosphorescence of $|(8)\cdot(1)_T^*|$ is observed at longer wavelengths.

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[1] *S. Iwata, J. Tanaka*, and *S. Nagakura*, J. chem. Physics *47*, 2203 (1967); see also [5b]!

[2] *S. Iwata, J. Tanaka*, and *S. Nagakura*, J. Amer. chem. Soc. *88*, 894 (1966).

[3] *S. P. McGlynn* and *J. D. Boggus*, J. Amer. chem. Soc. *80*, 5096 (1958); *R. S. Mulliken*, Proceedings R. H. Welch Foundation Conference on Chemical Research XI. Radiation and Structure of Matter, 1967, p. 109; *G. D. Short*, Chem. Commun. *1968*, 1500.

[4] X seems to be a radical ion pair $|\dot{A}^+\dot{A}^-|$ formed by electron transfer $A_T^* + A \rightarrow |\dot{A}^+\dot{A}^-| \rightleftarrows \dot{A}^+ + \dot{A}^-$ due to the increase in the electron affinity of *(1)* by an amount equal to the triplet excitation energy. The concentration of X may be increased to such an extent that it becomes detectable by absorption spectroscopy in a glass matrix or a crystal lattice both at 100 °K and at 77 °K: incorporation of the radical ions into the glass matrix hinders the reverse process $\dot{A}^+ + \dot{A}^- \rightarrow A + A$ so long as the matrix does not become viscous or fluid. Then the absorption spectrum of X disappears, but small concentrations of X [10] still remain detectable only by its green fluorescence. *Hayashi, Iwata*, and *Nagakura* [5] deduce the presence of $(1)^-$ from the ESR spectra of irradiated solid solutions of *(1)* and of complexes of *(1)* with *(4)*, *(5)*, *(6)*, *(7)*, or *(8)* in ethanol, as well as of *(1)* in *(6)*, *(4)*, or in *(4)*-ether at T = 77 °K. The interpretation of the Δm = 2-triplet ESR resonance at 1440–1610 gauss as an ESR signal of a CT triplet excited state should be reconsidered.

[5] a) *H. Hayashi* and *S. Nagakura*, Molecular Physics *13*, 489 (1967); b) *H. Hayashi, S. Iwata*, and *S. Nagakura*, J. chem. Physics *50*, 993 (1969).

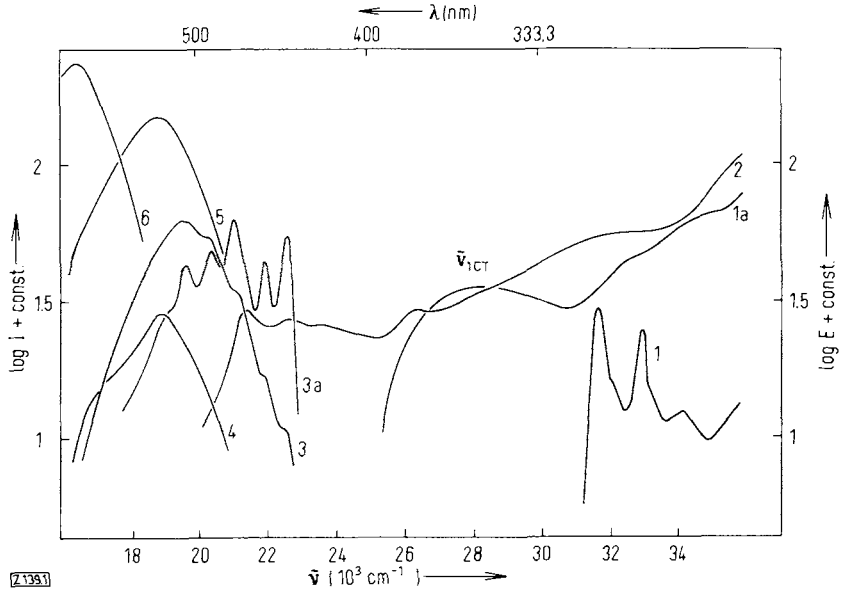


Fig. 1. Absorption and emission spectra of 1,2,4,5-tetracyanobenzene *(1)* and of EDA complexes $|D\cdot(1)|$ (cf. Table 1 and text).
1: Absorption spectrum of *(1)* (c = 1.1 × 10^{-4} M). 1a: Absorption spectrum of *(1)* with *(6)*. $\tilde{\nu}_{1CT}$: First charge-transfer absorption band; a second CT band lies in the absorption region of *(1)*. 2: Absorption spectrum of X′. 3a: Phosphorescence spectrum of *(1)* (c = 1.1 × 10^{-4} M). 3 and 5: Emission spectra of *(1)* with *(6)* in dipropyl ether glass at T = 100 °K. 3: $c(1)$ = 1.1 × 10^{-4}, $c(6)$ = 8.5 × 10^{-3} M; 5: $c(1)$ = 1.37 × 10^{-4}, $c(6)$ = 5.1 × 10^{-1} M. 4: Fluorescence spectrum of X. 6: Mixed excimer phosphorescence of $(1)_T^*$ with *(8)* ($c(1)$ = 1.1 × 10^{-4} $c(8)$ = 6.2 × 10^{-4} M; T = 112 °K).

[6] *Iwata, Tanaka*, and *Nagakura* [1] observed the green lw,ll emission which they interpret as CT triplet phosphorescence only in complexes with D = *(6)*, *(7)*, or *(8)*, but not for complexes with D = *(4)* or *(5)*. In contrast, we find the green, structureless lw,ll emission band also for the complexes with *(4)* and *(5)* but at high D concentrations.

[7] *Iwata, Tanaka*, and *Nagakura* [1] found the structured phosphorescence of *(1)* on excitation in the CT band only with complexes of *(1)* with benzene and with *(4)* and *(5)* and in accordance with their interpretation they assumed CT phosphorescence to make only a very slight contribution.

[8] This superposition effect is considerably stronger at medium and high D concentration; the fine structure disappears and the shifts of the maxima of the lw,ll emission increase with the donor concentration.

[9] In cases where $E|\dot{D}^{+}\dot{A}^{-}|_{S}^{*} < E|DA_{T}^{*}|$ formation of X' could not be detected (*e.g.* when A = *(1)*, D = tetramethyl-*p*-phenylenediamine).

[10] Further details, also regarding complexes with A = *(2)* or *(3)*, see *G. Briegleb* and *D. Wolf*, to be published.

Plant Bioregulators in the Metathoracic Glands of Myrmicine Ants[**]

By *Hermann Schildknecht* and *Knut Koob*[*]

Atta sexdens, the leaf-cutting ant, is a highly developed evolutionary form of the colony-building ants. Its behavior has been the subject of many investigations — the chemistry of its glands, on the other hand, has been studied in part only[1], despite the fact that both these topics are closely interrelated. We were surprised to learn that the metathoracic glands contain phenylacetic acid[2] and even more surprised by the results of a recent analysis of the contents of these glands that are very sparingly soluble in water.

Pure secretion from 60 glands could be separated by thin-layer chromatography on silica gel GF (Merck) in petroleum ether/ether/acetic acid (67 : 30 : 3) into two fluorescence-quenching zones, that nearer the front (R_f = 0.5) being due to phenylacetic acid and the other (R_f = 0.3) to an unknown substance. Since this unknown substance rapidly decomposed with discoloration from pink to brown we isolated it from a metathoracic extract obtained from a 40 g quantity of ants by column chromatography on Sephadex (LH20). According to its UV spectrum and its reaction with van Urk's reagent[3] the unknown substance had to be an indole derivative. Polarity of the molecule suggested the presence of a carboxyl group; since the acid itself readily decomposed, the methyl ester was isolated, purified, and identified.

Of the many substances used for comparison with the gel-chromatographically isolated unknown component only 3-indolylacetic acid had the same R_f value and exhibited the same color reaction and UV absorption. Furthermore, we were able to identify the corresponding fraction, obtained by column chromatography in the esterified secretion as methyl 3-indolylacetate, mass spectrometrically. Quantitative UV spectrometry showed that each gland contained 10^{-7} to 5×10^{-7} g or 5.7×10^{-10} to 2.8×10^{-9} mole of 3-indolylacetic acid; this corresponds to a 1–6% solution of 3-indolylacetic acid in the glands.

We have also detected 3-indolylacetic acid in the ant *Myrmica laevinodis*. This finding is very interesting because the myrmicine ants gather their food for winter[4] as did primitive men earlier. The leaf-cutting ants go one step further — they cultivate fungi[5]. The "collectors and growers", therefore, very probably learned much earlier than man to breed growing things and then store them as food. The heteroauxin 3-indolylacetic acid not only influences growth but also hinders seed germination[6]. We now wish to ascertain whether the phenylacetic acid and 3-indolylacetic acid act synergistically[7].

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[**] This work was supported by the Deutsche Forschungsgemeinschaft. We thank Prof. Dr. *K. Gösswald*, Würzburg, for the supply of leaf-cutting ants.

[1] *A. Butenandt, B. Linzen*, and *M. Lindauer*, Arch. Anat. microsc. Morph. exp. *48*, 13 (1959).

[2] *U. Maschwitz, K. Koob*, and *H. Schildknecht*, Insect Physiol. *16*, 387 (1970).

[3] *E. Stahl* and *H. Kaldeney*, Hoppe-Seylers Z. physiol. Chem. *323*, 182 (1961).

[4] Proverbs *6*, vv., 6–8.

[5] *H. Markl* in: Grzimeks Tierleben, Enzyklopädie des Tierreiches. Kindler Verlag, Zürich 1969, Vol. II, p. 503.

[6] *W. Sexton*: Chemische Konstitution und biologische Wirkung. Verlag Chemie, Weinheim 1958, p. 364.

[7] Cf. [6], p. 379.

CONFERENCE REPORTS

Structural Chemistry of Refractory Metallic Compounds

By *H. Nowotny*[*]

The compounds having the highest melting points known so far, HfC and TaC, belong to the structurally simple transition metal (T) monocarbides. Although many of these compounds are nonstoichiometric, due to a carbon deficiency, the vacancies (and the carbon atoms) nevertheless exhibit some degree of order[1]. This order is even more pronounced in the subcarbides T_2C, which were previously generally regarded as hexagonally close-packed metal host lattices having a random distribution of carbon atoms. In fact a series of ordered structures is now known, *e.g.* the anti-CdI_2, ζ-Fe_2N, or ξ-Nb_2C types, which all exhibit an unequal T—C—T and T-vacancy-T distance. This emphasizes the significance of the octahedral structural unit $[T_6C]$. It is remarkable that similar structural principles are encountered in transition metal carbide hydrides. Thus, Zr_2CH can be regarded as an interstitial compound of hydrogen with a Zr_2C host lattice (anti-CdI_2 type).

A large number of carbides, which are formed, *e.g.*, by the action of a further transition metal or of a meta-metal on TC or T_2C, yield a uniform class, in which the octahedral unit dominates; inclusion of other small nonmetal atoms and the trigonal-prismatic structural unit extends this class considerably. This classification naturally also permits inclusion of long-known complex carbides and related compounds such as the η_1-carbides in high-speed tool steels and the η_1-oxide in ferrotitanium. Linkage of the $[T_6X]$ octahedra *via* corners leads to the perovskite carbides, *e.g.* Ti_3AlC, or to the filled U_3Si type, *e.g.* Cr_3AsN, or to the filled β-Mn type, *e.g.* Mo_3Al_2C, *etc.* Linkage of the $[T_6X]$ octahedra *via* edges produces the H phase, *e.g.* Cr_2AlC, or the Ti_3SiC_2 type, *etc.* Common features become apparent regarding the components and the composition in agreement with the structural units: *e.g.* the H phase V_2PC can be considered as the sum of the two kinds of building units [VC]-octahedra + [VP]-trigonal-prisms, which are already present in the binary compounds; similarly, Mo_2BC is built up from the structural elements occurring in the cubic form MoC_{1-x} and MoB.

There are good reasons for assuming that the metallic host lattice is mainly responsible for the high stability of carbides,

complex carbides, and their analogs; electron transfer to the host lattice strengthens the T—T bonds. Band calculations on the basis of OPW and APW methods, and ESCA measurements suggest strong T—X bonds.

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[1] See *H. Nowotny* and *F. Benesovsky*, Planseeber. Pulvermetallurgie *16*, 204 (1968).

Solid State Reactions with and without Gas Phase at High Temperatures with Special Consideration of High-Frequency Plasma

By *Hk. Müller-Buschbaum* [*]

In recent years high-frequency plasma torches have found increasing use besides the usual laboratory heat supplies suitable for solid-state reactions. The high frequency energy is transferred to plasmas inductively or *via* a peak discharge at very high frequencies. Principally, there are two types of plasma torch.

1. High-pressure plasma torch (pressure range: 760 torr)
2. Low-pressure plasma torch (pressure range: 10^{-3} to 10^{-1} torr)

The use of torches opened at one end (high-pressure plasma torches) for the production of large single crystals by a modified Verneuil process has been described by several authors. The main advantage of such torches is that a defined gaseous atmosphere can be set up at a low plasma speed. However, they have disadvantages; for example, the uncontrollable stay period of the sample in the hot zone at unknown reaction temperatures, and a separation of the starting material components by mechanical and electromagnetic forces. A low-pressure plasma inside a closed system developed by our group makes the heating of small amounts of a substance possible and is particularly suitable for the preparation of small single crystals. Compared with high pressure plasma torches there is one disadvantage of this closed type of torch, *i.e.* the reduced pressure in the plasma which results in poorer reactions as far as thermally moderately decomposing or volatilizing substances are concerned. In a reaction between plasma and solid effects occur that are due to ionization of the gases: highly positively charged atoms of heavy gases (at extremely high temperatures) no longer exhibit the chemical characteristics of the corresponding molecular or atomic gas. This is also the case for ionized hydrogen, which does not have reducing properties. True "Plasma chemistry" (in the plasma state only!) therefore appears to be a difficult and questionable experimental field.

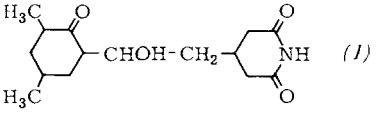
Lecture at Kiel, October 16, 1969 [VB 221 IE]
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Internal and External Contributions to the Biogenesis of Mitochondrial Proteins

By *W. Sebald* (lecturer), *W. Neupert*, and *G. D. Birkmayer* [*]

The biogenesis of mitochondria involves cooperation of the extramitochondrial protein synthesis with the protein-synthesis system localized within the mitochondria. The capacity of this system for protein synthesis is illustrated *inter alia* by the finding that growing peptide chains can be detected on the mitochondrial ribosomes after incubation of isolated mitochondria with ^{14}C-amino acids. The ^{14}C-amino acids that are incorporated *in vitro* are also found in the inner mitochondrial membrane. After separation of the membrane proteins by gel electrophoresis, four to five of the protein bands contain tracer. The highest content of tracer is found in the fourth band from the starting point; this band contains 4% of the total membrane protein and it is found to migrate at about the same rate in the gel electrophoresis of mitochondrial membranes of rat liver, locust flight muscles, and *Neurospora crassa*. In the corresponding band of cytoplasmic *mi*-1-mutants of *Neurospora crassa*, in which only traces of cytochrome aa_3 and b are spectrally detectable, less protein and no radioactivity are found.



(1)

The *in vitro* results can be confirmed *in vivo* by an independent method. If the hyphae of *Neurospora crassa* are preincubated in 3-[2-(3,5-dimethyl-2-oxocyclohexyl)-2-hydroxyethyl]glutarimide [cycloheximide *(1)*] (0.1 mg/ml), incorporation of ^{14}C-amino acids into the extramitochondrial and soluble mitrochondrial proteins is inhibited to an extent of more than 99%. About 15% of the membrane proteins are formed by cycloheximide-resistant mitochondrial protein synthesis. These membranes, when labeled *in vivo*, exhibit the same distribution of radioactivity after gel electrophoresis as do those that are labeled *in vitro*.

Incorporation of ^{14}C-amino acids into the proteins of gradient-purified mitochondrial ribosomes *in vivo* is completely inhibited by *(1)*. Consequently this part of the mitochondrial protein synthesis apparatus is afforded by the extramitochondrial system. On isolation of enzymically active, spectrally pure cytochrome oxidase from mitochondria labeled *in vivo* in the presence of *(1)* by treatment with Triton X-100 followed by fractional ammonium sulfate precipitation and chromatography on DEAE cellulose, the specific activity decreases substantially compared to that of the total membrane proteins. In the chromatographic separation on DEAE cellulose, the protein from band 4, and consequently the activity, accumulates in one fraction which does not contain cytochrome oxidase. This protein can be further purified on CM cellulose, the specific activity being increased to an amount 10 times greater than that of the membranes. It thus serves as a possible means of integrating cytochrome oxidase into the inner mitochondrial membrane (*i.e.* as an "integrator protein").

Lecture at Göttingen on November 21, 1969 [VB 223 IE]
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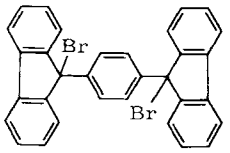
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Color by the Action of Mechanical Forces on Organic Molecules

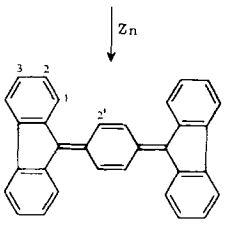
By *Hans Weidinger* and *Reinhard Steinmetz* (lecturer) [*]

Dehalogenation of 1,4-bis(9-bromo-9-fluorenyl)benzene *(1)* leads to the formation of the saturated solvent-containing oligomer *(3)* and not the expected quinonoid *p*-xylylene *(2)* [1]. Osmometric molecular weight determinations in benzene at 37 °C, in tetrahydrofuran at 45 °C, and in pyridine at 60 °C, yield values of about 1600 (n = 4) for the molecular weight of *(3)*.

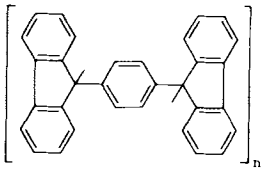
A slight amount of cleavage and blue-violet coloration takes place when compound *(3)* is subjected to heat or mechanical pressure, both in the solid state and in solution. Although the monomeric fragments occur mainly as quinonoid *p*-



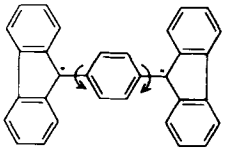
(1)



(2)

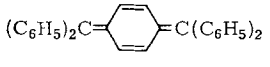


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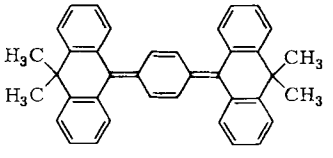


(4)

xylylene *(2)* in solution, the paramagnetism of the blue-violet crystals indicates the presence of radicals (and possibly twisted biradicals *(4)*). By suitable substitution of the dibromide *(1)*, it can be shown that the difference in behavior of the Thiele hydrocarbon *(5)* from that of the *p*-xylylene *(2)* is due to interaction of the mutual hindrance of the H atoms on C-1 and C-2′ with the aromatization tendency of the quinonoid system.

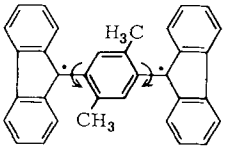


(5)

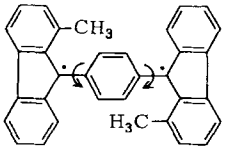


(6)

Thus the properties of the *p*-xylylene system *(2)* remain essentially unchanged by substitution at C-2 and C-3, whereas radicals very sensitive to oxygen are obtained, *e.g.* *(7)* and *(8)*, when methyl groups are introduced in positions 1 or 2′.



(7)



(8)

In hydrocarbon *(6)*, on the other hand, the mutual hindrance of the H atoms in positions 1 and 2′ is removed as a result of the angular structure. Hence compound *(6)*, like the Thiele hydrocarbon *(5)*, is stable as the *p*-xylylene and in contrast to *(2)* shows no tendency to oligomerize.

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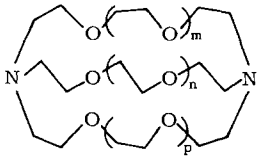
Cryptates, a New Class of Cation Complexes

By *J. M. Lehn*[*]

Formation of complexes between cations of alkali metals or alkaline earth metals and organic ligands is of importance in:

1. The activation of inorganic anions in organic solvents;
2. The transport of cations.

We have synthesized diazapolyoxa macrobicyclic compounds of the following type[1]:



(1), m = n = p = 1
(2), m = n = 1; p = 2
(3), m = 1; n = p = 2
(4), m = n = p = 2

The substances react with a variety of cations to form stable complexes which may be regarded as inclusion compounds. Since the cation is "hidden" in the center of the molecule, the name "cryptates" is proposed for these compounds.

The stability constants of complexes of *(1)* with alkali metals and alkaline earth metals decrease in the following order: $Ba^{2+} > Sr^{2+} > K^{+} > Ca^{2+} > Rb^{+} > Na^{+} > Li^{+} > Cs^{+}$ (in water). Both the bicyclic compounds and the complexes can occur in several conformations.

Compound *(1)* can be used as a means for dissolving inorganic salts in organic solutions, *e.g.* KSCN, KF, and $Ba(SCN)_2$ can be dissolved in chloroform.

In a few cases the rate of cation exchange (in D_2O) could be measured by NMR spectroscopy. At 30 °C alkali metal cations exchange much more rapidly than alkaline earth metals.

If potassium hydroxide is dissolved in tetrahydrofuran together with *(1)*, the hydroxide ion becomes a very strong base which, among other things, cleaves a proton from the methylene group in fluorene.

Lecture at Karlsruhe, December 11, 1969 [VB 225 IE]
German version: Angew. Chem. *82*, 184 (1970)

[*] Prof. Dr. J. M. Lehn
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Strasbourg, 1 rue Blaise Pascal (France)

[1] *B. Dietrich, J. M. Lehn*, and *J. P. Sauvage*, Tetrahedron Letters *1969*, 2885, 2889.

Radioactive Drugs

By *Martin Wenzel*[*]

Radioactive drugs, *e.g.* compounds containing ^{131}I or ^{32}P, are widely used in nuclear medicine as radiopharmaceuticals for localization of different organs and functional diagnosis. Moreover, the term "radioactive drugs" can also refer to drugs that are, in themselves, not radioactive but have been labeled with radioisotopes. Such labeled compounds are used in the elucidation of questions involving the resorption, distribution, and excretion, as well as for the study of the metabolism, of these drugs in the organism.

The development and testing of new drugs by the pharmaceutical industry would nowadays be almost unthinkable without using radioisotopes. In contrast, these methods have found almost no application in pharmaceutical education at universities.

Radioactive drugs can be synthesized by the standard methods of preparative chemistry. Since only the weak β-emitters ^{14}C and ^{3}H are generally used for labeling, the experimental operator has to take precautions against incorporation, and consequent internal irradiation, but not against external irradiation.

Control of the radiochemical purity is important, and this is best accomplished by chromatographic methods. Radioactive drugs can be located in organs and in cell organelles by autoradiography. Metabolic routes can be established by chromatographic separation of radioactive excretion products.

It is even possible, after injection of "metabolically labile" substances labeled with tritium, to recognize specific reactions *in vivo* in the overall organism when the tritiated water content of the respiratory water is determined; this technique is illustrated by studies on the *in vivo* oxidation of testosterone[1] and estradiol.

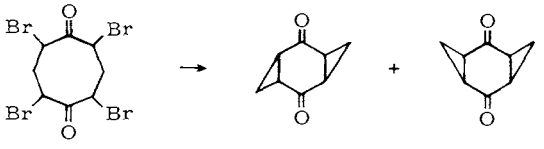
Lecture at Berlin on November 6, 1969 [VB 226 IE]
German version: Angew. Chem. *82*, 184 (1970)

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[1] *M. Wenzel*, Angew. Chem. *80*, 191 (1968); Angew. Chem. internat. Edit. *7*, 211 (1968).

SELECTED ABSTRACTS

Bishomoquinone, tricyclo[5.1.0.0^{3,5}]octane-2,6-dione, has been synthesized in the *anti- (2a)* and *syn* form *(2b)* by *A. Yogev, J. Heller,* and *A. S. Dreiding* from 1,5-cyclooctanedione by treatment with 4 mol. equiv. of phenyltrimethylammonium tribromide and heating of the resulting isomers of 2,4,6,8-tetrabromo-1,5-cyclooctanedione *(1a)* and *(1b)* (m.p. 225 to 226 and 196–198 °C, resp.; joint yield 53%) with copper powder in a high vacuum to 150 °C. *(1a)* affords 70% of *(2a)* (m.p. 179–180 °C) and 5% of *(2b)* (m.p. 100–101 °C), the corresponding yields from *(1b)* being 25% and 13%. The *syn*



(1) *(2a)* *(2b)*

and *anti* forms were assigned by reduction to the diols, which were examined by NMR spectroscopy. / Chimia *23*, 411 (1969) / —Ma. [Rd 127 IE]

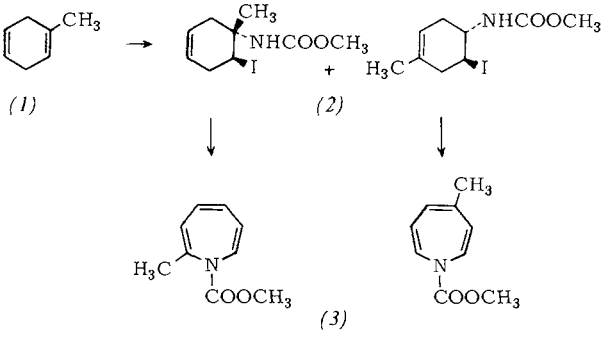
The catalytic cyclodimerization of allene, the first known example of a metal-catalyzed cyclodimerization in the vapor phase, has been described by *F. W. Hoover* and *R. V. Lindsey jr.* A phosphine-modified carbonyl-Ni catalyst having the empirical formula $(C_6H_5)_2PC_6H_4P(C_6H_5)_2 \cdot Ni(CO)_2$, which was prepared from an equimolar mixture of 1,4-bis(diphenylphosphino)benzene and $Ni(CO)_4$, converts a stream of allene diluted with helium at 200 °C into 1,3- and 1,2-dimethylenecyclobutane (60 and 13%, resp.), and 27% of trimer, predominantly 1,2,4-trimethylenecyclohexane. Attempted thermal dimerization in the liquid phase (THF) with the same catalyst effected cyclomerization to a tetramer, a pentamer, and higher oligomers, without formation of any dimers. The pentamer is 1,2,4,6,8- or 1,2,4,6,9-pentamethylenecyclodecane. / J. org. Chemistry *34*, 3051 (1969) / —Ma. [Rd 128 IE]

μ-Oxodifluorophosphoryldifluorophosphine *(1)*, a phosphorus oxide fluoride whose P atoms are in different oxidation states (+3 and +5), has been obtained by *D. D. DesMarteau* by photolysis (λ = 2537 Å) of $P(O)F_2Br$ in the presence of Hg at 23 °C

$$2\,P(O)F_2Br + Hg\,(excess) \xrightarrow{h\nu} \underset{(1)}{F_2POP(O)F_2} + Hg_2Br_2$$

in 40% yield, alongside POF_3, F_2POPF_2, $P_2O_3F_4$, PF_3, *etc.* Compound *(1)* is a colorless liquid, b.p. 48 °C, m.p. —31 °C, which slowly decomposes at 23 °C. It is extremely sensitive to moisture. Reaction with stoichiometric amounts of HCl at 23 °C proceeds almost quantitatively to give $HOP(O)F_2$ and PF_2Cl. / J. Amer. chem. Soc. *91*, 6211 (1969) / —Ma. [Rd 129 IE]

A general synthesis of 1*H*-azepine derivatives *(3)* is described by *L. A. Paquette, D. E. Kuhla, J. H. Barrett,* and *R. J. Haluska.* Electrophilic addition of iodine isocyanate to readily accessible 1,4-cyclohexadiene derivatives such as *(1)*, followed by cyclization of the resulting carbamates *(2)* with



(1) *(2)* *(3)*

bases to give unsaturated aziridines and subsequent bromination-debromination, affords the 1*H*-azepines *(3)*. They form tricarbonyl-Fe complexes. / J. org. Chemistry *34*, 2866 (1969) / —Ma. [Rd 130 IE]

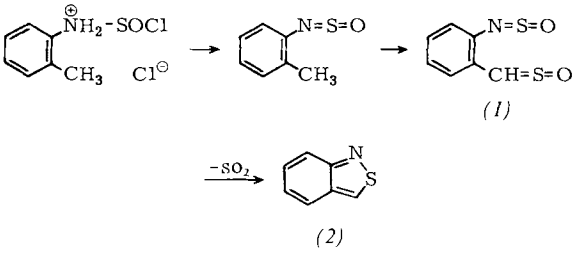
Two cyclic thiocarbonates, 1,3-dioxolane-2-thione *(1)* **and 1,3-oxathiolane-2-thione** *(2)* have now been unambiguously synthesized for the first time by *F. N. Jones* and *S. Andreades. (1)* was obtained directly from thiophosgene and ethylene glycol in boiling THF—CH_2Cl_2 in the presence of K_2CO_3 (yield 33%), and *(2)* from the lead salt of 2-mercaptoethanol and thiophosgene in CH_2Cl_2. *(1)* is a colorless oil, m.p. 55 to 55.5 °C, and *(2)* a pale yellow oil, m.p. *ca.* —20 °C; both are



(1) *(2)*

thermally unstable and sensitive towards acids, bases, and moisture. Halide ions isomerize *(1)* and *(2)* to thio- and dithiocarbonates. Alkylation with alkyl halides affords unstable compounds that rearrange to β-halogenoethylthio- and -dithiocarbonates. On treatment with acids the compounds polymerize to polythio- and polydithiocarbonates. *(1)* and *(2)* react with triphenylphosphine to give ethylene. / J. org. Chemistry *34*, 3011 (1969) / —Ma. [Rd 131 IE]

A new synthesis of benz[c]isothiazole and its derivatives has been accomplished by *M. Davis* and *A. W. White* by reaction of *o*-toluidine and substituted *o*-toluidines with thionyl chloride in boiling xylene, mesitylene, or bromobenzene.



(1)

(2)

Yields of up to 80% are obtained. It is assumed that the unsubstituted compound *(2)* is formed *via* the benzylidenesulfinyl compound *(1)*. 2-Amino-5-nitrotoluene does not give any benzisothiazole. / J. org. Chemistry *34*, 2985 (1969) / —Ma. [Rd 132 IE]

The isomerization of perfluoropyridazines *(2)* has been studied by *C. G. Allison*, *R. D. Chambers*, *Yu. A. Cheburkov*, *J. A. H. MacBride*, and *W. K. R. Musgrave*. Pyrolysis of tetrafluoropyridazine *(2a)* at 820 °C and of bis(heptafluoroisopropyl)pyridazine *(2b)* at 560 °C gave tetrafluoropyrimidine *(3a)* (60% yield) and 4,6-difluoro-2,5-bis(heptafluoroisopropyl)pyrimidine *(3b)* (*ca.* 50%), respectively. This thermal isomerization probably proceeds *via* a fluorinated 1,5-diazabenzvalene that undergoes aromatization. Irradiation of *(2a)* and *(2b)* under a quartz lamp, on the other hand, leads almost



(1) *(2)* *(3)*

(a), R = F
(b), R = iso-C_3H_7

quantitatively to the pyrazine derivatives *(1a)* and *(1b)*, respectively. The photochemical conversion of *(2a)* probably occurs by way of tetrafluorodiazaprismane (formed *via* the Dewar-benzene analog?), scission of the N—N bond, and rearomatization. / Chem. Commun. *1969*, 1200 / —Ma. [Rd 133 IE]

Dinitrogen tetrafluoride occurs below room temperature as a mixture of the centrosymmetric *trans*-form and the *gauche* form in the ratio 53 : 47 according to electron diffraction investigations carried out by *M. C. Cardillo* and *S. H. Bauer*; the *trans* conformation is about 300—500 cal/mole more stable and the rotation barrier has a value of 3—7 kcal/mole. Both rotamers have equal bond lengths: dNN = 1.489 ± 0.007, dNF = 1.375 ± 0.004 Å; the bond angles in the *trans* form are ∢ FNF = 102.9 ± 0.75 and ∢ FNN = 100.6 ± 0.6 °, and in the *gauche* form (dihedral angle 67.1 ± 0.8 °) ∢ FNF = 105.1 ± 1.5, ∢ FNN = 100.1 ± 1.5, and ∢ F′NN = 104.3 ± 1.0 °. / Inorg. Chem. *8*, 2086 (1969) / —HB. [Rd 135 IE]

Formation and decomposition of carbonic acid in aqueous solution has been investigated by *M. J. Welch*, *J. F. Lifton*, and *J. A. Seck* using a method involving determination of the exchange of ^{15}O between water and carbon dioxide. ^{15}O, which has a half-life of 2 min, is suitable as tracer when very small amounts of CO_2 are being investigated; the reaction can therefore be investigated over a wide pH range without addition of buffers which change the rate of reaction. A value of $\ln(10^3 k_1) = 34.69 - 9252/T$ was found for the constant k_1 in the reaction

$$CO_2 + H_2O \rightleftharpoons H_2CO_3$$

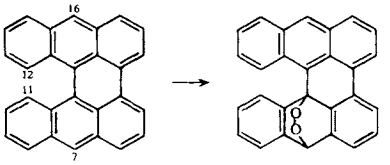
and $\ln(10^6 k_{-2}) = 48.08 - 12720/T$ for k_{-2} in the reaction

$$HCO_3^{\ominus} \rightleftharpoons OH^{\ominus} + CO_2$$

/ J. physic. Chem. *73*, 3351 (1969) / —Hz. [Rd 140 IE]

The structure of the Se_8^{2+} ion in $Se_8(AlCl_4)_2$ is similar to that of bicyclo[3.3.0]octane and is derived from the Se_8 ring in the crown form by linkage of a 1,5 bond and flipping of the Se-3 atom into a *syn-cis-anti* conformation. Se_8^{2+} can be regarded as intermediate between the 48-electron systems Se_8 and S_8 and the 44-electron system S_4N_4, in which two S atoms are situated above and two below the N_4 plane and are linked transannularly by 1,5 and 3,7 bridges. The Se—Se distances of 2.32 ± 0.03 Å are the same as those in Se_8; the Se—Se—Se angles are about 98 °, except at atoms 3 and 7 where they are about 90 °. The single crystals of $Se_8(AlCl_4)_2$ studied by *R. K. McMullan*, *D. J. Prince*, and *J. D. Corbett* were prepared by transport in the gas phase; they are orthorhombic, having space group $Pca2_1$ with a = 14.92 ± 0.02, b = 10.67 ± 0.01, and c = 13.22 ± 0.01 Å; Z = 4. / Chem. Commun. *1969*, 1438 / —HB. [Rd 143 IE]

The structure of the photo-oxide of dibenzo[*a*,*o*]perylene has been established by *H. Brockmann* and *F. Dicke*. Dibenzo[*a*,*o*]perylene *(1)*, prepared by dehydrogenation of its 7,16-dihydro derivative in the gas phase at 300 °C (red prisms containing 1.13% of CS_2, 50% yield), is converted on irradiation of its red solution in carbon disulfide into a yellow



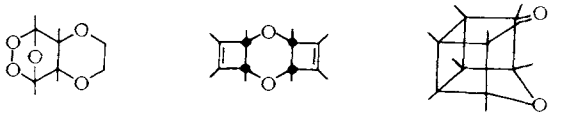
(1) *(2)*

solution of the photo-oxide *(2)* (yellow prisms containing 1.43% of CS_2, 70% yield). The structure was derived from the electronic spectra and the NMR spectrum. Neither *(1)* nor *(2)* is planar. / Chem. Ber. *103*, 7 (1970) / —Kr. [Rd 146 IE]

Dioxabicyclo[*n*.2.0]alkenes *(1)*—*(4)* have been prepared by *R. Criegee* and *R. Rucktäschel* for studies on valence isomerism and ozonization. Conrotatory opening of the 4-membered ring must give a *trans* double bond which is possible



(1)-*(3)*, n = 2-4 *(4)*

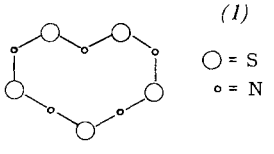


(5) *(6)* *(7)*

without any marked strain only when the resulting ring contains at least 10 members. *(1)*, *(2)*, and *(4)* can be prepared, *inter alia*, from ethylene glycol, 1,3-propanediol, and pyrocatechol, respectively, and tetramethylcyclobutene-1,2-diol; *(3)* is formed by cyclization of the ether formed from 3-chloro-1,2,3-trimethyl-4-methylenecyclobutene and the monosodium salt of 1,4-butanediol. *(1)—(4)* each gave two (*endo*/*exo*) monomeric ozonides; for example, the ozonide *(5)* was formed from *(1)*. A *cis*-linkage in *(1)—(4)* is deduced from the ozonide formation. On heating the tetramethyl-1,2-cyclobutenediols with acids in inert solvents the authors obtained three isomeric tricyclic compounds, of which *(6)* (m.p. 171 °C) is converted into the dioxabishomocubane derivative *(7)* on irradiation. / Chem. Ber. *103*, 50 (1970). / —Kr.

[Rd 147 IE]

Preparation and structure of the cyclopentasulfur pentanitride cation *(1)* are reported by *A. J. Banister*, *P. J. Dainty*, *A. C. Hazell*, *R. G. Hazell*, and *J. G. Lomborg*. The sulfur nitrides S_2N_2, S_4N_4, and $(SN)_x$ can be considered as members of the series SN^+, S_2N_2, $S_3N_3^+$, S_4N_4, $S_5N_5^+$, S_6N_6 . . . $(SN)_x$. The first cation of this series to be obtained was the cation $S_5N_5^+$; it was prepared in the form of the tetrachloroaluminate, $S_5N_5AlCl_4$ (yellow prismatic crystals, m.p. 181 °C), by adding S_4N_4 to a solution of $AlCl_3$ in $SOCl_2$ over a period of 48 h with stirring at room temperature followed by fractional crystallization (by concentration). According to X-ray crystallographic investigations, *(1)* forms a ten-membered ring that is almost planar and has an approximate symmetry

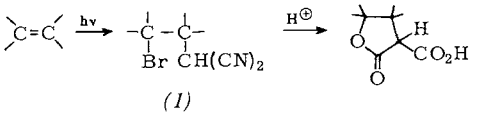


(1)

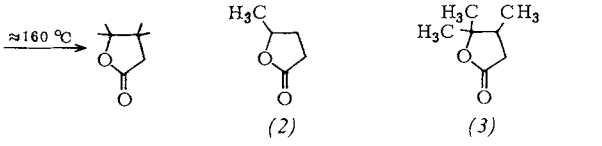
mm2. The average S—N bond length of 1.55 Å is indicative of considerable double bond character. / Chem. Commun. *1969*, 1187 / —Ma.

[Rd 149 IE]

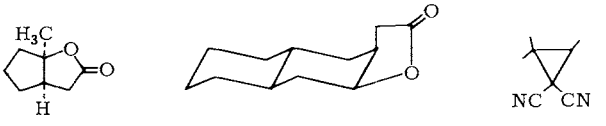
Synthesis of γ-lactones from alkenes has been described by *P. Boldt*, *W. Thielecke*, and *J. Etzemüller*. Addition of bromodicyanomethane to alkenes in methylene chloride leads, on irradiation, to 1-bromo-2-dicyanomethylalkanes *(1)*, which can be converted directly by hydrolysis and decarboxylation into γ-lactones in good yield. Cyclohexene gives the



(1)



(2) *(3)*



(4) *(5)* *(6)*

cis-lactone stereoselectively. The lactones *(2)—(5)* can be obtained from propene, 2-methyl-2-butene, 1-methylcyclopentene, and *trans*-1,2,3,4,4a,5,8,8a-octahydronaphthalene in 78, 68, 66, and 81% yields, respectively. Compounds *(6)* likewise give γ-lactones on hydrolysis and decarboxylation. / Chem. Ber. *102*, 4157 (1969) / —Ma.

[Rd 152 IE]

BOOK REVIEWS

Chemische Thermodynamik (Chemical Thermodynamics). By *A. Münster*. Verlag Chemie GmbH, Weinheim Bergstr. 1969. 1st Edit., x, 261 pp., 34 figs., paper, DM 29.—.

A new book on thermodynamics is assessed by how much it is better than the others. The principles of thermodynamics should be explained with impeccable logic, and the applications should be real ones.

That the good points of the present book outweigh its failings is due to the pedagogic experience of the author, who follows Gibbs' method consistently, introduces the main laws as (experimentally validated) axioms, and derives all further relations by relatively simple mathematics.

To find a successful description of Carathéodoric axiomatics in such a small booklet is surely sensational. On a second reading of the relevant chapter the reader recognizes the pedagogic value of *Carathéodory*'s work, which is presented in a considerably more readable form by *Münster* than in the original. It is shown that *Carathéodory*'s first law (anywhere near a given state of a system is a neighbor state that is not accessible from it by an adiabatic route) becomes equivalent to the second law only after addition to it of a further law (one of experience).

Description of the general conditions for equilibrium and stability is followed by the customary applications of thermodynamics to phase equilibria, chemical equilibria, critical phases, electrochemical equilibria, matter in a gravitational and in a centrifugal field.

The paragraph on the Nernst heat law in the chapter on chemical equilibria deserves special mention. *Münster* has here not only explained the various formulations of this law critically, but he has also consistently avoided the usual recourse to statistical considerations.

The book's weaknesses perhaps result from its advantages. Thus in the classical formulation of the main laws, *Münster* avoids the classical introduction of heat and temperature, possible though this is, and reserves it for the later section on Carathéodoric axiomatics. This applies also to the clear definitions of the concepts "adiabatic" and "quasistatic". The tendency to express physical connections in mathematical terms has adverse effects on the readability, particularly for the beginner who has not acquired perspective; unusual symbolisms (rot $\vec{R}$ = grad × $\vec{R}$) are partly to blame for this. The more experienced reader will turn gladly to this book for advice on presenting the axiomatics of thermodynamics.

Kl. Schäfer [NB 850 IE]

Differentialthermoanalyse (Differential Thermal Analysis). By *D. Schultze*. Verlag Chemie GmbH, Weinheim Bergstr. 1969. 1st Edit., 335 pp., 196 figs., 42 tables, plastic cover, DM 58.—.

Chemical changes of materials usually go hand in hand with thermal effects. Since thermal effects can be measured with a considerable degree of accuracy by modern electronic meth-

ods, the field of differential thermal analysis (DTA) has developed rapidly during the last 10 years, particularly in Anglo-Saxon countries and in the Soviet Union.

There has unfortunately not previously been any review in the German language that does justice to the importance of this method. The possible uses and the results had to be looked for tediously in the original papers in the most varied journals and in manufacturers' literature.

This gap is now closed by the monograph to be discussed here. After a concise historical introduction and an accurate explanation of the fundamental principles, the author describes the measuring equipment and the influence of the experimental parameters. He then considers the applications and so comes to the quantitative evaluation of DTA diagrams, where there is some unavoidable overlap with a similar discussion in the chapter on experimental conditions.

It is to be welcomed wholeheartedly that the author has compared the various theories and their fields of application clearly and critically. The last remnants of a previous prejudice that differential thermal analysis is a too empirical and somewhat inaccurate and uncritical method (this being due to its involving relatively complicated heat-conductivity relations as well as thermodynamics and reaction kinetics) have only been dispersed by the provision of a firm theoretical basis. It must, however, be emphasized that these objections do not apply to the liquid system studied by *Borchardt* and *Daniels*, and that, *e.g.*, contrary to the assumption on p. 74, the signal height can often be used for approximate calculation of the heat of reaction. In view of the sensitivity of modern methods of temperature measurement the possibility of working in solution is very attractive for the organic chemist.

The last part of the book gives a good impression of the varied applications of DTA and related methods, *e.g.*, to problems of metallurgy, mineralogy, semiconductor physics, the chemistry of complexes, organic chemistry (in particular that of high polymers and fuels), and the study of explosives and catalysis.

With its many instructive illustrations and tables and a comprehensive list of references, this book will offer much new information to the expert, and it is to be hoped that it will convince many non-expert readers that thermoanalytical methods are more generally applicable than might be assumed from glances at individual papers in the field.

E. *Koch* [NB 849 IE]

Chemie der Heterocyclen (Chemistry of Heterocycles). By *A. R. Katritzky* and *J. M. Lagowski*. Springer-Verlag, Berlin-Heidelberg-New York 1968, 1st Edit., xii + 183 pp., bound DM 48.—.

This book is intended as a textbook for the chemistry of heterocycles. It is divided into seven chapters. An introduction (chapter 1) is followed by an account of the chemistry of six-membered heterocycles (chapters 2 and 3). Chapter 4 deals with five-membered heterocycles. In chapter 6 the heterocyclic three- and four-membered rings are dealt with (5 pages) and in chapter 7 the physical properties of heterocyclic compounds (7 pages).

Each chapter is divided into a general part (nomenclature, occurrence, important individual compounds, schematic synthetic principle), and a special part (syntheses, reactivity, reactions). The production is careful; printing errors and errors of fact are rare. The extensive material is clearly and sensibly arranged, aided in particular by the many formulas and the fact that they can be easily traced by their consecutive numbering. Cross-references to other parts of the book are, however, not easy to trace; for example, page 25 would have been preferable to 2.II.C.2.c.2.

The authors have attempted to give a complete, logical survey of heterocyclic chemistry, and they have succeeded. But who will use the book? The student will be discouraged by the large number of isolated facts that are not essential for him. On the other hand, most reaction sequences are too briefly described (*e.g.* the azulene synthesis, p. 46). Also, there is often no mention of reaction conditions, even for important syntheses; and the chemist working in the field of heterocycles will feel the lack of references to original literature. For these reasons this book can be given only limited recommendation. *H. Ahlbrecht* [NB 852 IE]

Problems in Organic Reaction Mechanism. By *F. M. Menger*. From the "Appleton-Century-Crofts Series in Chemistry". Edited by *W. C. Agosta*. Appleton-Century-Crofts, New York 1969. 1st Edit., vii + 121 pp., numerous formulas, bound $ 2.95.

One often has to admire the ease with which Americans write books. The present work by *F. M. Menger*, however, has been compiled with such a light hand as to give the impression of being a set of lecture notes rather than a serious book.

The first part (19 pp.) contains formulas representing 55 organic reactions for which the student is required to state a reaction mechanism. Twenty-one examples are taken from the period 1956–1960, and 26 from 1961–1967.

The solutions to the problems are given in the second part. The examples are also intended to acquaint the student with some of the basic concepts of organic chemistry, such as resonance, tautomerism, electronegativity, acidity, reactive intermediates (carbonium ions, carbanions, free radicals, carbenes, arynes, *etc.*). Certain fundamental problems are discussed in greater detail in connection with the answers to the first 20 examples. Only formulas are given by way of solutions to examples 21—55.

Such an attempt to deal with the principles of organic chemistry in a few pages can scarcely hope to convey even a partial understanding of the many complex reactions involved. In other words, this "introduction" to organic chemistry, which takes up almost half of the book, could well have been left out altogether.

The presentation of the material lacks the diligence required in a book intended for the beginner. Apart from a whole series of misleading printing errors, one is annoyed by, for example, equations being written out in full for some reactions, while in other cases ions, atoms, or molecules that are added or split off have simply been omitted. Teachers will find the book useful for the references cited on pages 120 and 121. The shortcomings mentioned render it unsuitable for students. *F. Effenberger* [NB 844 IE]

Noble-Gas Chemistry. By *J. H. Holloway*. Methuen & Co. Ltd., London 1968. 1st Edit., xiii + 211 pp., numerous illustrations, bound 40s.

J. H. Holloway has written an excellent survey of the chemistry of noble gases.

Part I (29 pages) is devoted to the elements, and Part II (35 pages) to species (such as He_2^+) that are only known spectroscopically, clathrates, and biological effects (*e.g.* solubility of xenon in the blood).

Part III (101 pages) is divided into nine chapters concerned with the chemistry of noble gases proper, beginning with the history of their compounds. We then have chapters on binary fluorides (36 pages), oxides and oxide fluorides (28 pages), complex compounds, xenon chlorides, and compounds of krypton and radon. A separate chapter is devoted to the xenon compounds such as XeO_3 and XeF_6 which are dangerous from the point of view of explosion hazards: Chapter 8 deals with the chemical bonding in noble-gas compounds, and Chapter 9 with their use.

The very full bibliography, with but few gaps, merits special mention.

The numerous illustrations and tables enhance the value of this book, which combines experiment, theory, and individual results (including crystal structure and crystal chemistry). The reviewer has read it with considerable interest, and has formed the opinion that it will be found very useful by student and teacher alike.

R. Hoppe [NB 845 IE]

The Molecular Orbital Theory of Organic Chemistry. By *M. J. S. Dewar*. From the "McGraw-Hill Series in Advanced Chemistry". McGraw-Hill Book Corp., New York 1969. 1st Edit., xiv + 484 pp., numerous figures and tables, bound, approx. DM 74.—.

The book is highly ambitious right from the word go. It represents an attempt to derive organic chemistry from the principles of quantum mechanics. By bringing in such heavy artillery as *Dirac*'s Bra-Ket formalism in the very first chapter the author risks frightening away readers who would be quite capable of following the rest of the book. Quantum-chemical approximation methods are discussed in Chapter 2, semi-empirical methods of quantum chemistry in Chapter 3, and an outline of the theory of atoms and small molecules is presented in Chapter 4. Two-thirds of the book deals with the properties of organic molecules, *e.g.* their bond energies and their stability, as well as the problem of aromatic character (Chapter 5), and the mechanisms of chemical reactions (Chapter 8). The theory of UV spectra is deliberately omitted, but on the other hand we find something on the MO theory of electron spin resonance (Chapter 7). A separate chapter (9) is reserved for aromatic systems with heteroatoms, and finally, in Chapter 10, we are told something of the topical field of the quantum chemistry of σ-bonds.

As regards methods, the central position in the book is occupied by *Dewar*'s version (*i.e.* the one parametrized for properties of the ground states) of the semi-empirical Pariser-Parr-Pople method for π-electrons, abbreviated by the author to "Pople method", for the usefulness of which he adduces convincing comparisons from experiment and theory. However, the justification for the Pople method (in particular for the neglect of differential overlapping) is not entirely convincing. The Hückel MO (HMO) method is very elegantly derived from that of Pople, the derivation clearly revealing both the limitations and the possibilities of the HMO method (provided, of course, that one has previously allowed oneself to be persuaded of the admissibility of *Pople*'s approximations).

As an alternative to the Pople method the author offers a perturbation-theory simplification of the HMO method (called PMO), which makes use in particular of the properties of alternant hydrocarbons. This method is very neat and no doubt quite useful since it yields important results without computation, but it is not so straightforward as one might think after reading Chapter 6.

The book disposes of a number of traditional misconceptions, although the discussions sometimes tend to get out of hand.

One will not begrudge the author his tendency to highlight his own work, in many cases to excess, but he would have done better to resist the temptation to include the "SPO method", which can claim no more than historical interest either in its first or in its second formulation.

Despite any reservations that one may have on points of detail, one must in fairness admit that there exists no other textbook of theoretical organic chemistry on a comparable level.

Werner Kutzelnigg [NB 859 IE]

The Chemistry of the Nitro and Nitroso Groups. Part 1. Edited by *H. Feuer*. From the series "The Chemistry of Functional Groups". John Wiley and Sons Ltd., London-New York 1969. 1st Edit., xii + 771 pp., numerous formulas and tables, 281 s.

This book, the first of two volumes to be devoted to the nitro and nitroso groups, forms part of the series "The Chemistry of Functional Groups" edited by *S. Patai*. It contains nine chapters, written by a total of ten authors, on theoretical aspects of C—NO and C—NO_2 bonding, the spectroscopy and photochemistry of the two groups, the formation and the reactions of the nitroso group, the formation of aliphatic and alicyclic nitro compounds, of nitronic acids and esters, and of nitroamino groups. There is also a chapter on the activation of nucleophilic aromatic substitution by nitro groups. The introduction includes a summary of the chapters and authors of the still awaited second volume. Among other things, it indicates that the formation of aromatic nitro compounds, the effect of nitro groups on electrophilic and radical aromatic substitutions, and the Meisenheimer complexes of nitro compounds will be discussed only in this future volume. It can be seen that the final topic of the first volume fits more properly within the overall framework of the second. From remarks in the preface it may be gathered that this faulty arrangement of chapters is due to the late arrival of some of the manuscripts. In our opinion the publisher should have found a way of avoiding this fundamental weakness of multi-author publications. Since a critical discussion of the first (fragmentary) volume without a knowledge of the contents of the second volume would not be altogether fair to the authors whose contributions have already appeared, the review of the entire work will be held over until the publication of the second volume.

Heinrich Zollinger [NB 858 IE]

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The Chemical Behavior of Active Nitrogen

By R. Brown and C. A. Winkler[*]

Active nitrogen, which is formed on passage of an electric discharge through a stream of nitrogen, is detected by a characteristic yellow afterglow. It can be determined quantitatively, e.g. by gas phase "titration" with nitric oxide. Active nitrogen reacts with many chemical elements, as well as with organic and inorganic compounds. Although nitrogen atoms are responsibe for many of the reactions of active nitrogen, electronically excited molecules also play a role.

1. Introduction

Morren, in 1865, first reported the now well-known yellow nitrogen afterglow that results when an electrical discharge is passed through molecular nitrogen [1]. Subsequently, *Lewis* confirmed its relatively long lifetime, and identified the banded spectrum of the emission with that of molecular nitrogen [2–4]. From 1911 to 1913, *Strutt* published several papers in which he showed that the glowing gas possesses a marked chemical reactivity, as a consequence of which he referred to it as active nitrogen [5–8]. He recognized that many of its properties could be attributed to nitrogen atoms. Since that time, however, the chemical activity has been ascribed also to such species as molecular nitrogen ions, and various electronically or vibrationally excited nitrogen molecules. Progress in resolving the resulting controversies was hindered for many years by uncertainties in the experimental values for the dissociation energy of ground state molecular nitrogen, and probably continues to be hindered by a greater sensitivity of active nitrogen systems to experimental conditions than has generally been recognized.

Mitra made a comprehensive review of the work on active nitrogen prior to 1945 [9]. The available information led him to suggest that the chemical activity of active nitrogen was due to N_2^+, but he later recognized that this was inconsistent with experimental evidence [10]. *Evans*, *Freeman*, and *Winkler* proposed a "unified" mechanism to account for the more significant experimental observations [11]. Data available at that time suggested that the lifetimes of *electronically* excited molecular species were too short for them to be important participants in the reactions. Consequently, it was concluded that, while nitrogen atoms are the predominant chemically active species in the yellow (Lewis-Rayleigh) afterglow, *vibrationally* excited ground state $N_2(X\,^1\Sigma_g^+)$ molecules might be responsible for certain reactions in which nitrogen atoms seemingly do not participate [12]. However, recent data on the lifetimes of electronically excited nitrogen molecules suggest that their participation could be significant [12a, 12b].

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Subsequent reviews have examined the main spectroscopic and chemical features of active nitrogen [13–17]. The present discussion will, therefore, be directed largely to the information that has become available during the past few years. The discussion will be further limited to reactions involving uncharged nitrogen species in the region of the Lewis-Rayleigh afterglow. No attempt will be made to discuss more transient nitrogen afterglows and reactions of atomic and molecular nitrogen ions.

2. Experimental Methods

Most studies of the reactions of active nitrogen have been made in conventional, fast flow, low pressure (< 10 torr) systems of the type shown schematically in Figure 1. Comprehensive surveys of the methods applicable to such systems, and their limitations, have been made [18–20]. Generally, the active nitrogen is produced by either a microwave or a condensed DC discharge, although other methods, such as shock tube and vacuum ultraviolet photolysis [17a], have been tried with varying degrees of success [17]. It has been suggested that the reactions of N atoms can also be studied by γ-irradiation of dilute solutions of reactant in liquid nitrogen [20a, 20b].

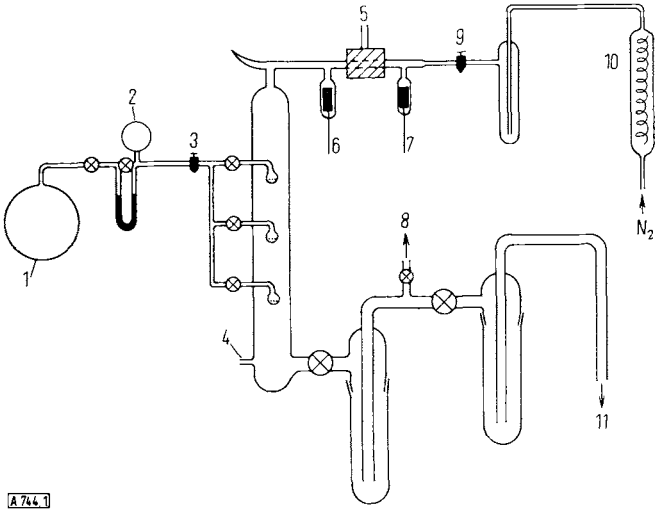


Fig. 1. Apparatus for production and investigation of active nitrogen. 1, storage. 2, calibrated volume. 3, flow control. 4, pressure gauge. 5, microwave source. 6 and 7, condensed discharge. 8, analysis. 9, flow control. 10, copper furnace. 11, vacuum.

The active nitrogen concentration is generally assumed to be given by the concentration of atomic nitrogen, and may be estimated by either physical or chemical methods. Such methods as ESR, mass spectrometry, and photometric measurements have the advantage of minimum interference with the actual system, but they generally do not give an absolute measurement of [N]. The measuring equipment is usually calibrated with reference to some chemical reaction, such as the gas phase "titration" with NO (see Section 4.2.1.) [15–17]. The method depends upon the very high rate of reaction of NO with N and certain well-defined color changes that occur essentially at the equivalence point.

It has also been proposed that the N atom concentration may be given by the maximum yield of HCN from the reaction of active nitrogen with C_2H_4 and some other hydrocarbons [21–28]. However, the value of [N] measured by the NO "titration" is usually considerably greater than that by the maximum HCN production from the hydrocarbons, *i.e.* a ratio NO/HCN >1 [29–31]. This discrepancy is probably due to complications in the hydrocarbon reactions [15, 32, 33].

A recent report that maximal HCN production might, under certain conditions, be greater than the amount of NO destroyed (NO/HCN <1) has now been shown to be due to back diffusion [17, 34]. It has been found that, with a system presumed to be "unpoisoned", back diffusion of reactants or products into the discharge zone, in amounts as little as one part in 5 million of N_2, may treble the production of N atoms. The problems associated with the estimation of the active nitrogen concentration have been discussed in detail elsewhere [15, 17].

3. The Nitrogen Afterglow

The Lewis-Rayleigh afterglow consists predominantly of certain bands of the first positive [*] system ($B\,^3\Pi_g \rightarrow A\,^3\Sigma_u^+$), together with some of the "Y" bands ($B'\,^3\Sigma_u^- \rightarrow B\,^3\Pi_g$). Despite many investigations, the

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[*] The sign + or − as superscript describes the symmetry behavior on reflection in a plane through the symmetry axis of the molecule.

mechanism by which the afterglow is produced is not fully understood (c.f. earlier theories[14,17]). This is due, in part, to conflicting experimental evidence.

There seems to be general agreement that the intensity of the first positive bands is second order in [N], but the effect of total pressure is not as well understood[35–38]. "Pressure jump" experiments have shown that, at about 0.04 torr, the intensity is pressure dependent[39,39a,39b]. Recent evidence seems to indicate, however, that the intensity is independent of pressure at higher pressures, at least in the range 1 to 10 torr[35,36,38]. As the pressure is increased, there appears also to be a change from first to zero order dependence of the intensity on [M], the third body concentration[39]. *Gross* used a glow discharge shock tube to study the dependence of the intensity (I) on pressure (0.25–1.5 torr) and on temperature in the range 300 ° to 2400 °K[36]. He found

$$I = 0.60 \times 10^{-17} \left(\frac{T}{300}\right)^{-0.90} [\mathrm{N}]^2 \text{ photons cm}^{-3} \text{ sec}^{-1}$$

Berkowitz, Chupka, and *Kistiakowsky*[40] proposed that the afterglow is produced by

$$\mathrm{N}(^4\mathrm{S}) + \mathrm{N}(^4\mathrm{S}) + \mathrm{M} \rightleftarrows \mathrm{N}_2(^5\Sigma_g^+) + \mathrm{M} \quad (1)$$

$$\mathrm{N}_2(^5\Sigma_g^+) + \mathrm{M} \rightarrow \mathrm{N}_2(\mathrm{B}\,^3\Pi_g,\ v = 12) + \mathrm{M} \quad (2)$$

$$\mathrm{N}_2(\mathrm{B}\,^3\Pi_g) \rightarrow \mathrm{N}_2(\mathrm{A}\,^3\Sigma_u^+) + h\nu \quad (3)$$

The $\mathrm{N}_2(\mathrm{B}\,^3\Pi_g)$ state is assumed to be populated by predissociation from the $(^5\Sigma_u^+)$ state in a collision-induced radiationless transition.

Benson[41] has suggested that the production of the first positive emission depends upon the primary reaction

$$\mathrm{N}(^4\mathrm{S}) + \mathrm{N}(^4\mathrm{S}) \rightleftarrows \mathrm{N}_2^*(^5\Sigma_g^+) \rightleftarrows \mathrm{N}_2^*(\mathrm{B}\,^3\Pi_g,\ v = 12) \quad (4)$$

Assuming that the curve-crossing transition has a probability between 10^{-1} and 10^{-2}, this reaction represents an equilibrium between free N(4S) atoms and rotationally "hot" molecules in the twelfth vibrational level of the B state. No third body is required. The vibrationally "hot" B state molecules can decay to the $\mathrm{A}^3\Sigma_u^+$ state by radiation, or undergo some form of relaxation – rotational, vibrational, or electronic. *Benson* showed that, for the intensity to be independent of pressure, it is kinetically required that the relaxation processes be much faster than the radiation process. It seems reasonable that rotational relaxation should be rapid, especially at pressures $\geqslant$ 1 torr[42]. Vibrational relaxation would occur by a stepwise process, and might be relatively inefficient[43–45]. On the other hand, recent studies seem to indicate rapid electronic quenching of the B state molecules by ground state N_2 molecules ($k = 6.2 \times 10^{-11}$ cm^3 molec^{-1} s^{-1})[39,46–48]. *Young* and co-workers have determined the quenching efficiencies of various gases for $\mathrm{N}_2(\mathrm{A}\,^3\Sigma_u^+)$ and $\mathrm{N}_2(\mathrm{B}\,^3\Pi_g)$[48a]. The Stern-Volmer type quenching of the B state by added gases can also be explained by this mechanism[35,38,49–52].

A somewhat similar mechanism for the production of the nitrogen after-glow, based on a collision induced population of the $\mathrm{B}\,^3\Pi_g$ state from the $\mathrm{A}\,^3\Sigma_u^+$ state, was proposed by *Campbell* and *Thrush*[38]. *Benson* pointed out, however, that the proposed population of $\mathrm{B}\,^3\Pi_g$ levels by collision from the $\mathrm{A}\,^3\Sigma_u^+$ level is inconsistent with the kinetic aspects of afterglow production[41]. This conclusion has been disputed by *Jonathon* and *Petty*[39b] in their study of the pressure dependence of the nitrogen afterglow. It has also been suggested that oxygen interacts with vibrationally excited $\mathrm{N}_2(\mathrm{A}\,^3\Sigma_u^+)$ to produce $\mathrm{N}_2(\mathrm{B}\,^3\Pi_g)$[52a].

The absence of the Vegard-Kaplan bands (*i.e.* $\mathrm{A}\,^3\Sigma_u^+ \rightarrow \mathrm{X}\,^1\Sigma_g^+$) in the nitrogen afterglow has been of considerable interest, since the $\mathrm{A}\,^3\Sigma_u^+$ state is continually populated by the first positive system. The Vegard-Kaplan bands have recently been detected in systems containing a large concentration of $\mathrm{A}\,^3\Sigma_u^+$ molecules in the absence of significant quantities of nitrogen atoms[53,54]. They have also been detected in the absorption spectrum of N_2[54a]. The emission was

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destroyed by addition of nitrogen atoms [53]. This is consistent with a rapid reaction

$$N_2(A\,^3\Sigma_u^+) + N(^4S) \rightarrow N_2(X\,^1\Sigma_g^+) + N(^4S) \quad (5)$$

The rate constant at room temperature was estimated to be $k_5 = 5 \times 10^{-11}$ cm^3 particle^{-1} s^{-1}. Indirect proof for the occurrence of this reaction has been obtained from beam studies [55] and from mercury emission in an active nitrogen stream [56].

It has been pointed out that the reverse reaction can also occur [57], with a rate constant estimated from shock tube studies to be $k_{-5} = 1.9 \times 10^{-6}\ T^{-3/2}$ exp $(-142\ \text{kcal}/RT)$ cm^3 particle^{-1} s^{-1} [57a]. By combining these results with data from an earlier study by *Noxon* [58], a value has been calculated for k_5 that is in excellent agreement with the experimentally determined value [59].

4. Chemical Reactions of Active Nitrogen

Since studies of the reactions of active nitrogen prior to 1967 have already been extensively reviewed [17], the present discussion will be concerned primarily with progress since that time.

4.1. Recombination of Nitrogen Atoms

Of the reactions that may involve atoms produced by the gas phase dissociation of a stable diatomic molecule, the simplest is their recombination, either heterogeneously or by a three-body homogeneous process.

4.1.1. Heterogeneous Recombination

At low pressures (< 1 torr) in glass vessels, the heterogeneous recombination of nitrogen atoms becomes a significant factor in active nitrogen reactions [15, 60]. Its extent may be largely reduced by a strong "poisoning" by trace impurities in the nitrogen stream, or by coating the walls with a suitable "poison", such as phosphoric acid.

Early studies indicated that the heterogeneous recombination process was probably first order in [N] [61–63]. The values obtained for the first order rate constant varied from 4.0 s^{-1} to 4.2×10^{-2} s^{-1} for an unheated, clean glass surface [30, 64]. The corresponding value of γ, the recombination coefficient, varied between 10^{-4} and 10^{-5} for glass surfaces.

More recently, *Campbell* and *Thrush* have applied photometric methods to a flow system and found that the heterogeneous recombination is a second order process, with $k = 7.3 \times 10^{-16}$ cm^3 molec^{-1} s^{-1} [38]. Their observations have been confirmed by *Clyne* and *Stedman*, who found that two heterogeneous recombination processes may occur [65]. One of these is first order and predominates for low [N]. The other is second order in [N], and predominates in an unheated, clean pyrex vessel. Under such conditions, however, the first order process was appreciable at 90 °K and 611 °K, and the second order wall reaction could be virtually eliminated in an unheated vessel by coating the wall with phosphoric acid.

It is found, in general, that metal surfaces are more efficient than glass in promoting heterogeneous recombination [17]. The value of γ for metals can be fitted to the expression $\gamma = a/(bP + c)$, where P is the pressure and b and c depend on the surface [66]. Thus, for clean Mo sputtered on a glass surface, γ decreases from 0.22 at 0.09 torr to 0.04 at 1.35 torr [60]. The high efficiency of metals or their oxides, especially "spongy" cobalt and copper oxide, in causing heterogeneous N atom recombination has made them useful in the preparation of surfaces to terminate gas phase reactions [67].

4.1.2. Homogeneous Recombination

It is generally accepted that the homogeneous recombination of nitrogen atoms is a termolecular process

$$N + N + M \rightarrow N_2 + M \quad (6)$$

Homogeneous recombination has special importance as a major source of electronically excited nitrogen molecules, the precursors of the nitrogen afterglow. At pressures greater than about 3 torr, the rate of homogeneous recombination largely determines the rate of nitrogen atom disappearance.

Clyne and *Stedman* have recently followed the disappearance of N atoms by gas phase "titration" with NO, making an appropriate correction for the heterogeneous recombination [65]. They estimated a termolecular rate constant of $k_6 = 0.96 \times 10^{-32}$ cm^6 molec^{-2} s^{-1}. By combining their results with earlier data, they showed that the temperature variation of k_6 was given by the simple Arrhenius expression, with $A = 10^{-32.81}$ cm^6 molec^{-2} s^{-1} and $E = 1000$ cal mole^{-1} [38, 68, 69].

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It is interesting that the mechanism proposed by *Benson* for the first positive emission is not consistent with the third order kinetics observed for the homogeneous recombination of N atoms. This seems to suggest that reactions leading to first positive emission are of minor importance relative to the total extent of homogeneous recombination. This observation is supported by calculation of the relative rates of photon emission [36] and termolecular recombination [65] which show only one photon emitted as a consequence of 51 recombinations at 1 torr and 300 °K.

The variation in rate of recombination with change in M, the third body, has not yet been reliably determined. This is partly due to the fact that in such studies the intensity of afterglow emission has been used as a measure of N atom concentration. This is probably not a reliable method because a change in M can cause a change in intensity due to a shift in relative importance of the relaxation processes and the radiation process in afterglow production. It is well known that NH_3 and CH_4, for example, strongly quench first positive emission, presumably by rapid electronic quenching of one of the precursors of the afterglow [35, 38, 51, 70]. On the other hand, Ar and He increase the emission from the vibrational levels ($v < 12$) in the B state because of fast vibrational quenching [35, 43]. With Ar as a third body, the recombination rate appears to be unchanged [38], although a recent shock tube study of the reverse reaction [71]

$$N_2 + M \rightarrow 2\,N + M \qquad (7)$$

showed that the relative efficiencies of N, N_2, and Ar as third bodies are in the ratio 1 : 4.4 : 12. The rate of N atom production was obtained from vacuum UV absorption.

4.2. Inorganic Reactants

4.2.1. Nitric Oxide

Of all the reactions of active nitrogen with either inorganic or organic reactants, that with NO is perhaps best understood. The primary reaction of active nitrogen with NO almost certainly involves N atoms:

$$N + NO \rightarrow N_2 + O; \quad \Delta H^0 = -75 \text{ kcal mole}^{-1} \qquad (8)$$

This reaction probably occurs on an attractive potential energy surface since the heat of reaction seems to appear mainly as vibrational energy in the nitrogen produced [72–75]. It has been suggested that the infrared chemiluminescence that accompanies this reaction comes from NO excited by vibrationally excited N_2 [75a]. Reaction (8) has little or no activation energy, and proceeds at close to collision rates ($k_8 = 2 \times 10^{-11}$ cm^3 molec^{-1} s^{-1}) [76–79]. Because of its simplicity, this reaction has been used as a source of O atoms, especially when the presence of excess O_2 may cause undesirable complications [80].

When [NO] < [N], there is complete reaction of the available NO. Unreacted N atoms then react with O atoms produced in reaction (8), with emission of the β and γ bands of NO:

$$N + O + M \rightarrow NO^* + M \qquad (9)$$

$$NO^* \rightarrow NO + h\nu \qquad (10)$$

The emission may range in color from purple to blue as the concentration of N atoms decreases relative to that of O atoms.

The rate constant of reaction (9) at room temperature has been estimated to be $k_9 = 1.1 \times 10^{-32}$ cm^6 molec^{-2} s^{-1} [81, 82]. It has been reported that a sensitive measure of the N atom concentration can be obtained from the intensity of the β bands [38, 81]. Direct estimates of [N] have recently been made possible from a determination of the variation of the absolute intensity of the β, γ, and δ bands with temperature and pressure [83].

When [NO] is greater than [N], the N atoms are rapidly and completely consumed. The resulting O atoms then react with the excess NO:

$$NO + O + M \rightarrow NO_2^* + M \qquad (11)$$

The greenish-yellow NO_2 bands of the "air afterglow" are then emitted by a mechanism which is not yet fully understood [84].

At the equivalence point, *i.e.* [NO] = [N], reactions (9) and (11) are not possible, and there is no emission. Accordingly, a gas phase "titration" to this dark endpoint makes is possible to estimate [N] by visual or photometric methods. The results agree well with those obtained from maximum destruction of NO [29].

Fontijn and *Vree* have observed that chemi-ionization and formation of electronically excited species (such as NO(A $^2\Sigma$, B $^2\Pi$) and O(^{1}S)) is catalyzed by addition of certain carbon-containing compounds to systems containing N and O atoms [85]. As a result, the intensity of certain bands in the NO system is increased,

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and the authors warn that "caution should be exercised in the use of the NO afterglow intensity for atom concentration measurements in the presence of a third reactant" [86].

4.2.2. Nitrogen Dioxide

To explain the experimental features of the fast reaction of active nitrogen with NO_2, it has been postulated that four primary reactions occur simultaneously [87]:

$$N + NO_2 \rightarrow N_2O + O \quad (43\%) \qquad (12)$$

$$N + NO_2 \rightarrow 2\,NO \quad (33\%) \qquad (13)$$

$$N + NO_2 \rightarrow N_2 + 2\,O \quad (13\%) \qquad (14)$$

$$N + NO_2 \rightarrow N_2 + O_2 \quad (10\%) \qquad (15)$$

The rate constant for removal of NO_2 by N atoms at room temperature was estimated to be $k = 1.85 \times 10^{-11}$ $cm^3\ molec^{-1}\ s^{-1}$. A study of the emission from the N_2O formed by reaction (12) showed that the bending mode ν_2 is not excited but the stretching modes ν_1 and ν_3 are vibrationally excited [88]. This seems to suggest that the reaction occurs on a repulsive potential energy surface.

4.2.3. Other Oxides of Nitrogen

Unlike the reactions of active nitrogen with NO and NO_2, the corresponding reactions with N_2O and with N_2O_5 are extremely slow. Mass spectrometric studies indicate that the rate constant for the reaction of N_2O_5 is $\leqslant 10^{-15}$ cm^3 $particle^{-1}$ s^{-1} [89].

The reaction of active nitrogen with N_2O does not appear to involve N atoms. The slight reaction that is observed has been attributed to reaction with electronically excited N_2 molecules, either in the $B\ ^3\Pi_g$ or the $A\ ^3\Sigma_u$ state [90, 91]. N_2O seems to be particularly effective as a third body for relaxation of vibrationally excited N_2 molecules [72, 73, 92, 92a]. It has been pointed out by *Rubin* that the cross-section for vibrational deexcitation of N_2 by N_2O, measured by *Morgan* and *Schiff*, was actually a cross-section for two processes [73, 93]

$$N_2(v = 1) + M \rightarrow N_2 + M + \text{kinetic energy} \qquad (16)$$

$$N_2(v = 1) + M \rightarrow N_2 + M^* \qquad (17)$$

followed by

$$M^* + N_2 \rightarrow M + N_2 + \text{kinetic energy} \qquad (18)$$

A rapid reaction of N atoms with NOCl has been reported recently [93a].

4.2.4. Hydrogen

Campbell and *Thrush* have studied the reaction of H_2 in a system containing both N and O atoms, produced by a partial "titration" of active nitrogen with NO [94]. Since no primary reaction is observed when H_2 is added to active nitrogen, the initial reaction in this system can be attributed to the reaction of O atoms with H_2 [95]:

$$O + H_2 \rightarrow OH + H \qquad (19)$$

From photometric measurements of the rate of consumption of O and N atoms, they were able to show that the rate of

$$N + OH \rightarrow NO + H \qquad (20)$$

is 1.4 times the rate of the corresponding reaction of O atoms.

4.2.5. Oxygen and Ozone

N atoms react with O_2 by [97, 98]

$$N + O_2 \rightarrow NO + O \qquad (21)$$

NO_2 and N_2O were also obtained as products [96]. The rate of reaction (21) at room temperature has been estimated to be $k_{21} \approx 1 \times 10^{-16}$ $cm^3\ molec^{-1}$ s^{-1} and has an activation energy of about 7 kcal $mole^{-1}$ [97–101, 101a]. It is interesting to note that N atoms react much more rapidly with $O(^1\Delta_g)$ than with ground state O_2 [101b].

The overall reaction of N atoms with O_3 has been postulated to be [78]

$$2\,N(^4S) + O_3 \rightarrow N_2 + O_2 + O(^3P) \qquad (22)$$

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The rate of this reaction at room temperature has been estimated as $k_{22} = 5.7 \times 10^{-13}$ cm^3 molec^{-1} s^{-1} [78]. Although upstream addition of N_2O does not affect the O_3 reaction, about 75% of the N_2^* formed by reacting N atoms with NO are capable of destroying O_3 [74, 78].

4.2.6. Phosphorus

The reaction of active nitrogen with white phosphorus is fast ($k \simeq 2 \times 10^{-13}$ cm^3 molec^{-1} s^{-1}) and produces nitrogen-phosphorus polymers [102]. The P/N ratio of the polymeric product was found to vary with the relative concentrations of reactants. The N atom flow rate inferred from the amount of nitrogen incorporated into the polymer agreed well with that estimated by the NO "titration".

4.2.7. Ammonia and Hydrazine

The high activation energy ($\geqslant 17$ kcal mole^{-1}) thermodynamically required for hydrogen abstraction from NH_3 by N atoms makes its occurrence highly improbable. This is supported by mass spectrometric studies, which indicate that N atoms are not consumed in the presence of NH_3 [103]. It has been suggested, therefore, that the observed decomposition of NH_3 by active nitrogen [15, 17] is due to energy transfer from electronically excited nitrogen molecules.

Because of its relatively long lifetime, $N_2(A\,^3\Sigma_u^+)$ has frequently been postulated as the species responsible for the destruction of ammonia [104–106]. However, since the nitrogen afterglow may be quenched by NH_3, it is possible that a precursor of the afterglow, $N_2(^5\Sigma_g^+)$ or $N_2(B\,^3\Pi_g)$, might be involved [15], and that destruction of NH_3 might be represented as

$$N_2^* + NH_3 \rightarrow NH + 2\,H + N_2 \qquad (23)$$

followed perhaps by

$$NH + H \rightarrow H_2 + N \qquad (24)$$

$$NH + N \rightarrow N_2 + H \qquad (25)$$

Apparently, the reaction

$$NH + NH \rightarrow N_2 + 2\,H \qquad (26)$$

does not occur since $^{14}N^{15}N$ is produced exclusively during the reaction of ^{14}N active nitrogen with $^{15}NH_3$ [105]. Reaction (26) has been postulated to account for the rapid disappearance of NH radicals during gas phase radiolysis of NH_3, but the possible contribution of reaction (24) was not considered [107].

The fact that the N atom concentration remains virtually unchanged when NH_3 is added to active nitrogen might imply that reactions (24) and (25) occur to approximately the same extent. Since [H] < [N], it would follow that $k_{24} > k_{25}$.

When H atoms are added to excess active nitrogen, NH_3 is produced in amounts directly proportional to [H] [108]. Moreover, $NH(A\,^3\Pi \rightarrow X\,^3\Sigma^-)$ emission occurs during this reaction, which shows that NH radicals are present as an intermediate [109, 110]. Hence, the reaction

$$N + H \xrightarrow{M} NH \qquad (27)$$

must compete favorably with reactions (24) and (25). Further evidence for the importance of such a reaction is provided by the production of NH_3 during the reaction of active nitrogen with C_2H_4, where it is appreciable only when $[C_2H_4] < [N]$ [32].

Kinetic studies of the active nitrogen-NH_3 reaction indicate that it is not truly first order in $[NH_3]$ and tends to zero order as $[NH_3]$ is increased [104, 111]. This might be a "pseudo" zero order behavior with NH_3 in large excess if N atoms are continually regenerated as in reaction (24). It is also possible, however, that the reaction is partially heterogeneous, comparable with that observed at −196 °C [112].

The rate constant for the reaction of N atoms with N_2H_4, to produce NH_3 and H_2 [112a], has been estimated as 1.2×10^{-13} cm^3 molec^{-1} s^{-1} at 298 °K [34, 112b].

4.2.8. Phosphine

The reaction of active nitrogen with the phosphorus analog of NH_3, *i.e.* PH_3, is probably a reaction of N atoms [113]. The strength of the H_2P-H bond is such that H atom abstraction is thermodynamically possible, *i.e.*,

$$N + PH_3 \rightarrow NH + PH_2 \qquad (28)$$

The main products of the reaction are H_2 and the α-form of $(PN)_n$. No red phosphorus is formed.

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4.2.9. Sulfur and Compounds of Sulfur

Although the reactions of active nitrogen with sulfur and with the various compounds of sulfur have been rather extensively studied, the formation of solid, polymeric products has tended to make interpretation of the results difficult. A great deal of spectroscopic work has been done on the reactions of active nitrogen with sulfur [5, 6, 114–124], CS_2 [6, 114, 125–128], H_2S [6, 123, 127, 129–132], SCl_2 [133–135, 135a], and S_2Cl_2 [8, 132, 135a, 136] (and also on $SeCl_4$ [134, 135, 137, 138]).

Spectroscopic studies clearly show that the NS radical is formed as an intermediate during the reaction of active nitrogen with sulfur. Various nitrides of sulfur, including $(NS)_x$ polymer, have also been identified as reaction products [136, 139].

Since S_8 is one of the products of the reaction of active nitrogen with H_2S it is not surprising that $(NS)_x$ polymer is also found as a product of this reaction [127, 136]. Other products identified were NH_3, S_7NH [136], and H_2.

Polymeric $(NS)_x$ is the only nitrogen-containing product that has been identified among the products of the reaction of active nitrogen with CS_2 and with COS [136]. A black polymer, resembling paracyanogen, was also formed during the CS_2 reaction [127], in accord with the spectroscopic observation of certain emissions of the CN system [126].

It has been found that N atoms react rapidly with SO, ($k = 0.8 \times 10^{-12}$ cm^3 molec^{-1} s^{-1} at room temperature), to form NO and S [140, 140a]. A similar, but slower O atom abstraction, ($k = 5.4 \times 10^{-16}$ cm^3 molec^{-1} s^{-1} at room temperature), occurs when N atoms react with SO_3 to form SO_2 and NO [140]. The SO_2 molecule appears to be too stable to be directly attacked by N atoms. However, a limited decomposition of SO_2, somewhat analogous to the NH_3 reaction, has been observed under appropriate conditions [140, 141]. It has been suggested that this is due to energy transfer from an electronically excited nitrogen molecule, since ESR measurements have indicated no decrease in [N] when SO_2 is added to active nitrogen [142, 143].

The reaction of active nitrogen with $SOCl_2$ was found to yield NOCl, N_2O, SO_2Cl_2, Cl_2, and small amounts of sulfur [136]. No sulfur nitrides could be detected. The main products of the reaction with the chlorides of sulfur, SCl_2 and S_2Cl_2, were NSCl and Cl_2 [136].

4.2.10. Oxides of Carbon

The interaction of active nitrogen with CO and CO_2 has received special attention recently because of the observed laser action in these systems. (The exchange of energy from vibrationally excited $N_2(X\,^1\Sigma_g^+)$ molecules to CO, CO_2, N_2O and similar molecules has been considered in detail elsewhere [92, 93, 144–150]).

Avramenko and *Krasnen'kov* have reported a rate constant, $k_{29} = 3.2 \times 10^{-13} \exp(-3.4\ \text{kcal}/RT)$ cm^3 molec^{-1} s^{-1}, for the reaction [151]

$$N + CO_2 \rightarrow NO + CO \qquad (29)$$

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The production of NO, as well as $^{13}N-N$ and N_2O, was also reported to occur as a result of the reaction of recoil ^{13}N with CO_2 [152]. However, this is in disagreement with the observed laser action, which is not accompanied by CO_2 decomposition. Moreover, earlier studies reported only slight decomposition of CO_2 that appeared to be a result of a reaction with electronically excited nitrogen molecules [90, 91]. In an attempt to resolve this discrepancy, *Herron* and *Huie* have reinvestigated this reaction, using a mass spectrometer to follow reactant concentrations [153]. They were unable to detect any reaction at room temperature and concluded that $k_{29} \leqslant 1.7 \times 10^{-16}$ cm^3 molec^{-1} s^{-1}.

It has been suggested that the disagreement might be due to considerable heterogeneous reaction under the conditions used by the Russian workers [18]. This is perhaps also indicated by their report that the rate of the reaction of active nitrogen with H_2 to produce NH_3 is independent of temperature [154]. As mentioned earlier, other workers have been unable to detect any reaction with H_2 [94, 108].

A mass spectrometric study indicated only relatively small decomposition of C_3O_2 by active nitrogen (at room temperature $k = 2.3 \times 10^{-15}$ cm^3 molec^{-1} s^{-1}) to produce "dicyanogen" as the only detected gas phase product [155]. Intense emissions from the CN red and violet systems accompanied the reaction.

4.2.11. Halogens and Halogen Acids

Much of the present knowledge of the reactions of active nitrogen with halogens can be attributed to studies by *Phillips* and co-workers. In general, no stable products are formed, although N atoms do disappear, possibly by the sequence [57, 156–160]

$$N + X_2 \rightarrow NX + X \quad (30)$$

$$NX + N \rightarrow N_2^* + X \quad (31)$$

It might be expected, and spectroscopic data suggest, that the efficiency of the halogens in promoting recombination of N atoms follows the order $I_2 > Br_2 > Cl_2$.

A kinetic analysis has been made of the vacuum ultraviolet emissions observed during the reaction of active nitrogen with IX compounds (X = I, Br, Cl, or CN). The results indicate that, in certain cases at least, the N_2^* produced in reaction (31) was $N_2(^3\Delta_u)$ [57]. An analysis of energy requirements suggested that this state has an energy of 185 ± 3.5 kcal mole^{-1}. This value is considerably greater than that (171 kcal mole^{-1}) derived from a direct spectroscopic measurement of $^3\Delta_u \rightarrow B\,^3\Pi_g$ transition [161].

From a study of infrared emission, *Phillips* has shown that the intensity of the first positive bands increases markedly with addition of trace amounts of I_2 [162]. This effect has also been observed when other reactants, such as O_2, CH_4, and C_2H_4, are added to an active nitrogen stream [51].

A mass spectrometric study of the reaction of active nitrogen with Cl_2O indicated a rapid reaction of N atoms [163]. For long reaction times and $[Cl_2O] = 5[N]$ the ratio of Cl_2O consumed to N consumed was 0.93 ± 0.10. A rate constant at room temperature, $k_{32} = 9.1 \times 10^{-12}$ cm^3 molec^{-1} s^{-1}, was estimated for the postulated primary attack by N atoms:

$$N + Cl_2O \rightarrow NCl + ClO \quad (32)$$

The final products contained N_2, O_2, and Cl_2, but not NO. Similarly, a spectroscopic study of the reaction of active nitrogen with ClO_2 gave no evidence for the reaction [164]

$$N + ClO_2 \rightarrow NO + ClO \quad (33)$$

The reactions of active nitrogen with the halogen acids HI, HBr, and HCl clearly show the importance of bond energy in determining the course of a reaction. Both HI and HBr react quite readily, probably according to [165–168]

$$N + HX \rightarrow NH + X \quad (34)$$

to give free halogen and the ammonium salts, NH_4I and NH_4Br, respectively. Addition of Br_2 or H_2 during the HBr reaction causes a decrease in the rate of HBr destruction.

However, for HCl, reaction (34) would be highly endothermic and direct attack by N atoms is not likely [25]. Only slight decomposition of HCl to produce H_2 and Cl_2 is observed. It is possible that this is due to energy transfer from excited N_2, or, alternatively, to the catalyzed recombination of N atoms

$$HCl + N \rightarrow [HCl \cdot N] \xrightarrow{N} N_2 + H + Cl \quad (35)$$

[152] *M. J. Welch*, Chem. Commun. *1968*, 1354.

[153] *J. T. Herron* and *R. E. Huie*, J. physic. Chem. *72*, 2235 (1968).

[154] *L. I. Avramenko* and *V. M. Krasnen'kov*, Izvest. Akad. Nauk SSSR, Ser. Chim. *1966*, 417; Bull. Acad. Sci. USSR, Div. chem. Sci. (English translation) *1966*, 1394.

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[161] *H. L. Wu* and *W. Benesch*, Physic. Rev. *172*, 31 (1968).

[162] *L. F. Phillips*, Canad. J. Chem. *46*, 1450 (1968).

[163] *C. G. Freeman* and *L. F. Phillips*, J. physic. Chem. *72*, 3028 (1968).

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[168] *R. H. Ewart* and *W. H. Rodebush*, J. Amer. chem. Soc. *56*, 97 (1934).

The addition of small amounts of HCl to reactions of active nitrogen with hydrocarbons, *e.g.*, CH_4 or C_2H_6, has been found to increase markedly the HCN production from such reactions [32,169]. There is no net consumption of HCl. The probable mechanism is

$$Cl + RH \rightarrow R + HCl \quad (36)$$

followed by a rapid reaction

$$R + N \rightarrow HCN + R' \quad (36a)$$

4.2.12. Hydrogen Cyanide and Cyanogen

Both HCN and $(CN)_2$ are too strongly bonded to be attacked directly by N atoms. Thus, any apparent reaction is probably the result of a reaction with excited N_2 molecules.

Only slight decomposition of HCN by active nitrogen appears to occur, to produce H_2 and $(CN)_2$ [142,170]. Although it has been reported that the addition of HCN to active nitrogen does not significantly decrease the N atom concentration [142], it has been found that upstream addition of HCN greatly decreases the ability of active nitrogen to react with CH_3Cl [171].

The decomposition of $(CN)_2$ by active nitrogen produced large quantities of a black polymer on the walls of the reaction vessel [172]. A substance with $m/e = 76$, corresponding to $C_2(CN)_2$, was also formed [142]. Addition of H_2 or CH_4 to the reaction mixture was found to yield HCN [172].

The $(CN)_2$ reaction is probably initiated by $N_2(A\,^3\Sigma_u^+)$ [143] and might involve C atoms in its overall mechanism [170]:

$$(CN)_2 + N_2^* \rightarrow N_2 + 2\,CN \quad (37)$$

$$CN + N \rightarrow N_2 + C \quad (38)$$

$$C + (CN)_2 \rightarrow C_2N + CN \quad (39)$$

$$C_2N + N \rightarrow 2\,CN \quad (40)$$

The reaction is inhibited by certain additives [173], the relative efficiencies of which ($O_2 \gg CH_4 > N_2O > CO > CO_2 > SF_6$) might reflect their competitive reactions with either CN or C, *e.g.*,

$$CH_4 + CN \rightarrow CH_3CN + H \quad (41)$$

$$CH_4 + CN \rightarrow HCN + CH_3 \quad (42)$$

$$C + O_2 \rightarrow CO + O \quad (43)$$

The addition of O atoms favors the reaction and intensifies CN emission.

[169] *D. R. Safrany, P. Harteck,* and *R. R. Reeves jr.*, J. chem. Physics *41*, 1161 (1964).

[170] *D. R. Safrany* and *W. Jaster*, J. physic. Chem. *72*, 3305 (1968).

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[173] *D. R. Safrany* and *W. Jaster*, J. physic. Chem. *72*, 3318 (1968).

4.2.13. Metals and Metallic Compounds

The effects of adding metals to an active nitrogen stream in the region of the Lewis-Rayleigh afterglow have been studied in considerable detail [17]. Nitride formation has been observed with some metals, *e.g.*, Hg, K, or Ca [174,175]. However, emission from excited metal atoms is a much more general result. From studies of these emission, early workers made estimates of the energy content of active nitrogen. Active nitrogen has also been used for many years as a low energy source for excitation of line and band spectra of many molecules [5,176]. The production of Ba^+ when Ba is added to active nitrogen at 1125 °K suggests that N_2^+ is responsible for this reaction [176a].

Reactions of the more volatile metal halides with active nitrogen are usually accompanied by emissions from excited metal atoms [17], probably as a result of a collision with an electronically excited nitrogen molecule, perhaps in the $(^5\Sigma_g^+)$ state [176,177].

The enhancement of the first negative system of N_2, and Na line emission, have been observed during the reaction of active nitrogen with anhydrous Na_2SO_4 [178] The enhancement of the first negative system of N_2 and Na line emission, have been observed during the reaction of active nitrogen with anhydrous Na_2SO_4 [178]. These observations suggest simultaneous production of a neutral Na atom and a N_2^+ ion.

The reactions of active nitrogen with metal carbonyls result in a rapid, stepwise degradation of the carbonyls by the reaction [49]

$$M(CO)_n + N \rightarrow M(CO)_{n-1} + NCO \quad (44)$$

These reactions are accompanied by intense metal atom emission.

The reactions of active nitrogen with organometallic compounds have received only limited attention. In the temperature range 130 to 330 °C, a rapid, temperature-independent production of HCN was observed during the reaction of active nitrogen with $Hg(C_2H_5)_2$ [179]. It was suggested that the HCN resulted from a reaction of N atoms with C_2H_5 radicals, the presence of which was indicated by the production of small amounts of saturated hydrocarbons.

Both HCN and NH_3 (more HCN than NH_3) were obtained as products of the reaction of active nitrogen with methyl silanes [180,181]. Maximum HCN production increased with increase in temperature. Similarly,

[174] *J. Okubo* and *H. Hamada*, Philos. Mag. [7] *8*, 375 (1928).

[175] *A. E. Ruark, P. D. Foote, P. Rutnick,* and *R. L. Chenault*, J. opt. Soc. America Rev. sci. Instruments *14*, 17 (1927).

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[181] *H. A. Dewhurst*, J. physic. Chem. *63*, 1976 (1959).

the main product of the reaction of active nitrogen with $[(CH_3)_2SiO]_7$ was also HCN [182].

Spectroscopic studies of the reactions of active nitrogen with certain organometallic compounds suggest that transfer of energy from an electronically excited nitrogen molecule causes dissociation of the organometallic compound, and excitation of the products [183, 184]. The observed emissions from the excited metal atoms and from vibrationally excited CN suggest that the species concerned might be $N_2(^5\Sigma_g^+)$.

4.3. Organic Reactants

The reactions of active nitrogen with organic compounds have been reviewed in some detail a number of times [11, 15–17]. In general, the qualitative features of these reactions are fairly well understood, but relevant kinetic data are limited and the mechanisms that have been proposed are still dubious.

4.3.1. Alkenes

The reactions of active nitrogen with alkenes have been studied in considerable detail. They are of particular interest as a basis for much of our present knowledge of the reactions of active nitrogen with organic compounds. Until quite recently, the olefins, especially ethylene, were used as a chemical titrant for N atoms and have, therefore, been of special interest.

When alkenes are allowed to react with active nitrogen, HCN is rapidly formed as a major product. The amounts of alkene reacted and HCN produced increase linearly at first, then reach a constant ("plateau") value as the flow of alkene is increased [23, 185, 186]. For alkenes, this "plateau" value is generally independent of temperature. Similar behavior is observed for the active nitrogen reactions with many organic compounds. The attainment of such a temperature-independent "plateau" for HCN production from the olefins prompted the suggestion that it represented a measure of the N atom concentration in the system.

Although HCN generally constitutes more than 95% of the N-containing products from reactions of active nitrogen with alkenes, appreciable quantities of CH_3CN and $(CN)_2$ are also formed [187–190]. When [N] > [alkene], NH_3 production may also be significant [32]. Small quantities of CH_4, C_2H_6, C_2H_2, and possibly a C_3 hydrocarbon, are also found as products of the reaction of active nitrogen with C_2H_4 [23, 187].

The reaction with propene produces significant quantities of C_2H_4 as well as smaller amounts of C_2H_6 and C_3H_8 [187, 188, 190, 191]. Experiments with labeled C_3H_6 showed that some of the C_3H_6 recovered is resynthesized from hydrocarbon fragments produced during the reaction with active nitrogen [189].

In the reactions of active nitrogen with the butenes, the same "plateau" value for HCN was observed, but whereas butane is the main hydrocarbon product of the reaction with isobutene, both 1-butene and *cis*-2-butene produce mainly C_2 and C_3 hydrocarbons [*] [192].

The reactions of active nitrogen with alkenes are moderately fast ($k \geqslant 10^{-14}$ cm^3 molec^{-1} s^{-1} at room temperature) and have low activation energies ($E < 2$ kcal mole^{-1}) [187, 193, 194].

Rate constants for the reaction of active nitrogen with C_2H_4 have recently been calculated from photometric measurements of the intensities of the first positive and second positive systems of the nitrogen afterglow [195]. The value found from the second positive emission was about six times that estimated from the first positive emission. Although the significance of these results was not discussed the difference might be due to different rates of reaction of $N(^4S)$ and $N(^2D)$ with ethylene, as reported earlier [196].

A "unified" mechanism of the type

$$N + C_2H_4 \rightarrow [C_2H_4N] \quad (45)$$

$$N + [NC_2H_4] \rightarrow N_2 + C_2H_4 \quad (46)$$

$$[NC_2H_4] \rightarrow HCN + CH_3 \quad (47)$$

$$N + CH_3 \rightarrow HCN + 2\,H \quad (48)$$

was first proposed to explain the main features of these reactions [11]. More recently, *Herron* has suggested that the discrepancy between the N atom concentration measured by the NO "titration", and that inferred from the C_2H_4 reaction, may be explained by a mechanism that involves H atoms as an essential component [33], *e.g.*,

$$H + C_2H_4 \rightarrow C_2H_5 \quad (49)$$

$$N + C_2H_5 \rightarrow NH + C_2H_4 \quad (50)$$

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[*] Recent results indicate that the "plateau" HCN yields from the reactions of active nitrogen with isobutene and 2-methyl-2-butene are considerably less than those from reactions with the other alkenes [34].

[192] *H. Gesser, C. Luner*, and *C. A. Winkler*, Canad. J. Chem. *31*, 346 (1953).

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$$H + C_2H_5 \rightarrow 2\,CH_3 \quad (51)$$

$$N + NH \rightarrow N_2 + H \quad (25)$$

$$N + CH_3 \rightarrow HCN + 2\,H \quad (52)$$

A loss of N atoms might be expected from reaction (50) followed by reaction (25).

Safrany and *Jaster* studied the effect of adding H atoms from a second discharge to the active nitrogen-ethylene reaction [32]. They found that the maximum HCN produced under these conditions is in essential agreement with the NO "titration" made in the presence of the added H atoms, which probably catalyze N atom recombination (see below). This would be in qualitative agreement with *Herron*'s mechanism since the addition of H atoms would favor reaction (51) and thus increase HCN production. They also found that, assuming CH_4 to be produced from CH_3 radicals and C_2H_6 from C_2H_5 radicals, HCN was produced mainly from the C_2H_6 precursor. They suggested that this is due to a rapid "cracking" reaction

$$N + C_2H_5 \rightarrow HCN + CH_3 + H \quad (53)$$

which would be faster than reaction (51). This does not imply that HCN production from the reaction of N atoms with CH_3 radicals is slow. These reactions were studied under conditions of an excess of hydrocarbon, which would favor reaction (53). There is experimental evidence that the corresponding reaction with CH_3 radicals is also fast [197]. This is supported by the rapid production of HCN from the HCl-catalyzed reaction of active nitrogen with CH_4, which must result from reaction of N atoms with CH_3 radicals (32).

Safrany and *Jaster* suggested that, under ordinary conditions, the disappearance of N atoms could proceed *via* NH radicals according to

$$NH + NH \rightarrow N_2 + 2\,H \quad (26)$$

The effect of adding H atoms could then be explained if the reaction

$$NH + H \rightarrow H_2 + N \quad (24)$$

could regenerate N atoms at a rate appreciably faster than the rate of N_2 formation by reaction (26).

Safrany has suggested that the reactions of H, O, and N atoms proceed by similar mechanisms, and that the difference in the final products obtained is simply a result of the different valences of the atoms [198]. He reinterpreted his earlier results on this basis, and concluded that H_2CN must be an important reaction intermediate in the reactions of active nitrogen with hydrocarbons. The possibility that this species might be involved in the mechanism of the reaction with ethylene had been suggested earlier [23]. Important steps of the overall mechanism might then be

$$N + C_2H_5 \rightarrow H_2CN + CH_3 \quad (54)$$

$$N + CH_3 \rightarrow H_2CN + H \quad (55)$$

$$N + H_2CN \rightarrow NH + HCN \quad (56)$$

$$H + H_2CN \rightarrow HCN + H_2 \quad (57)$$

When $[N] \gg [H]$, the formation of NH by reaction (56) would lead to loss of N atoms by reaction (25), while addition of H atoms, so that $[N] \approx [H]$, would suppress formation of N_2 by increasing the importance of reaction (57).

The reactions of active nitrogen with higher alkenes are assumed to be reduced essentially to reactions of N atoms with either CH_3 or C_2H_5 radicals by the intervention of "cracking" reactions.

Several features of the reactions of active nitrogen with alkenes cannot be explained adequately by this mechanism. Perhaps the most striking discrepancy lies in the formation of NH_3 as a product when $[C_2H_4] < [N]$. If the loss of N atoms were caused entirely by reaction (25), the loss of NH, with formation of N_2, should become more pronounced when N atoms are in excess. Furthermore, spin considerations suggest that reaction (24) should be at least four times as important as reaction (25) [12].

Reaction (25) should not be dismissed as of no significance. It has been shown that, when H atoms from a second discharge are added to active nitrogen, the concentration of N atoms (NO "titration") is decreased by about 17% [32, 193]. Since no known reaction of NO with H atoms could possibly compete with its very fast reaction with N atoms, it seems likely that the NO "titration" remains valid under these conditions, hence that H atoms may catalyze N atom recombination.

These mechanisms are also not adequate to explain the observed pressure dependence of the NO/HCN ratio [29, 139, 199]. This might, in part, be explained by a reaction of the type

$$N + H + M \rightarrow NH + M \quad (58)$$

It has been reported that HCN can be produced when mixtures of C_2H_4, or other hydrocarbons, with N_2 are allowed to react in a shock tube [200]. The temperature was too low (1400–6000 °K) to produce a significant number of N atoms. It was postulated, therefore, that HCN is produced by the reaction of a vibrationally excited nitrogen molecule with hydrocarbon radicals. The measured activation energies for the process involved are in the range 23 to 54 kcal $mole^{-1}$, much higher than those for corresponding N(^{4}S) reactions.

HCN has also been obtained from the radiolysis, with ^{60}Co γ-rays, of a gas phase mixture of nitrogen and C_2H_4 [201]. It is interesting to note that HCN production is insignificant when *trans*-2-butene is used instead

[197] *D. A. Armstrong* and *C. A. Winkler*, Canad. J. Chem. *33*, 1649 (1955).

[198] *D. R. Safrany*, personal communication.

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[200] *V. V. Rao*, *D. Mackay*, and *O. Trass*, Canad. J. Chem. Engng. *45*, 61 (1967).

[201] *T. Oka*, *R. Kato*, *S. Sato*, and *S. Shida*, Bull. chem. Soc. Japan *41*, 2192 (1968).

of C_2H_4. Furthermore, the presence of butene inhibits production of HCN from C_2H_4 in such systems. It has also been shown that HCN is not necessarily the major product when alkene-liquid nitrogen solutions are irradiated with γ-rays [20a, 20b].

4.3.2. Alkanes

The reactions of active nitrogen with the saturated hydrocarbons are similar in many respects to those with alkenes. However, the initiation reactions are probably different, especially for the lower members of the series, such as CH_4, C_2H_6, and cyclopropane.

At room temperature, the production of HCN from the reactions with the lower alkanes is appreciably decreased when NH_3 or SO_2 is added to the active nitrogen stream between the discharge and the point of hydrocarbon addition [140, 202]. It has also been found that the Arrhenius plots for the reactions of active nitrogen with certain alkanes have a definite change of slope [22]. These observations indicate that the alkane reactions are initiated by excited N_2 molecule reactions such as

$$N_2^* + RH \rightarrow N_2 + R + H \qquad (59)$$

To conserve spin, the N_2^* would have to be in either a singlet or a triplet state. The alkyl radical formed in such an initial step should react rapidly with N atoms.

As with the alkenes, the main product of the reactions of active nitrogen with alkanes is HCN. Other N-containing products that have been identified are NH_3, $(CN)_2$, and CH_3CN [30, 196, 198, 202, 203]. These are generally accompanied by various hydrocarbons [17].

At room temperature, the reactions with CH_4 or C_2H_6 showed an "induction" effect in the yield of HCN with hydrocarbon flow rate, which was overcome, however, by the addition of H atoms. Temperatures above, 200 °C were required to obtain "plateau" values for HCN production from C_2H_6 and C_3H_8 [30, 32, 204]. The "plateau" value was then identical with that obtained from the reactions with alkenes [30]. It should, perhaps, be noted that the rate of H atom attack on CH_4, or C_2H_6, is quite slow at temperatures below about 200 °C [205, 206]. Thus, the behavior of the active nitrogen reactions may be based on the change in rates of H atom attack on the alkanes with increase in temperature.

The presence of secondary C atoms in the butanes or higher alkanes increases the rate of reaction with active nitrogen, and "plateau" values for HCN production are observed even at room temperature [130, 207].

The rate constants for the reactions of active nitrogen with alkanes are lower than those for the reactions with alkenes ($k \simeq 10^{-15}$ cm^3 molec^{-1} s^{-1} at room temperature), and activation energies are higher [22, 203].

4.3.3. Alkynes

Recent studies indicate that the reactions of active nitrogen with alkynes should be divided into two groups: (a) the reaction with acetylene; (b) the reactions with other alkynes.

Unlike the reactions with most other hydrocarbons, the reaction of active nitrogen with C_2H_2 produces considerable amounts of $(CN)_2$ as well as the usual product, HCN [208, 209]. The reaction is also accompanied by deposition of a brown polymer (C = 65%, N = 27%, H = 7%) on the walls of the reaction vessel [170, 208]. Other N-containing products obtained are NH_3 and cyanoacetylene (C_2HCN) [186, 203].

It has been reported that the initial attack of C_2H_2 by N atoms is a slow process (for $[C_2H_2]/[N]$ 0.05, $k \approx 5 \times 10^{-15}$ cm^3 molec^{-1} s^{-1} at 300 °K) [170, 194, 211, 211a]. It was found, however, that the rate of reaction increased rapidly with increase in $[C_2H_2]$ ($0.05 < [C_2H_2]/[N] < 1$). When $[C_2H_2]/[N] > 1$, a comparatively slow reaction is observed [211a].

The mechanism of this reaction is probably quite complex [186]. The formation of C_2HCN, identified mass-spectrometrically, indicated that displacement reactions might be important, *e.g.*,

$$CN + C_2H_2 \rightarrow C_2HCN + H \qquad (60)$$

Safrany and *Jaster* have suggested that the overall behavior of the reaction is greatly influenced by the presence of $(CN)_2$ as a product [170]. Although the production of HCN is increased by about 50% by the upstream addition of NH_3 [210] it has little effect on the rate of the slow reaction ($[C_2H_2]/[N] > 1$) but decreases the rate of the fast reaction [211a]. In their study of the kinetics of this reaction, *Kistiakowsky* and co-workers [211a] suggest that the slow reaction ($[C_2H_2]/[N] > 1$) proceeds by a mechanism similar to the "unified" mechanism of *Evans*, *Freeman*, and *Winkler*. They also suggest that $N_2(A^3\Sigma_u^+)$ may initiate the fast reaction.

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The reaction of active nitrogen with propyne and 2-butyne resemble the analogous reactions with alkenes. Both compounds produce significant quantities of $(CN)_2$ (about 50% of total HCN), but relatively little polymer. The Arrhenius parameters for the reactions of active nitrogen with alkynes other than acetylene are comparable with those for the corresponding reactions with alkenes [194].

The reactions of active nitrogen with isomeric allene and propyne were found to be remarkably similar [212]. Both reactions produce significant quantities of C_2H_2. Addition of H atoms to these reactions increased the yields of both HCN and C_2H_2, and it was suggested that production of C_2H_2 in the active nitrogen systems results from H-atom reactions, *e.g.*,

$$CH_2{=}C{=}CH_2 + H \rightarrow CH_3{-}C{\equiv}CH + H \quad (61)$$

$$CH_3{-}C{\equiv}CH + H \rightarrow CH_3 + C_2H_2 \quad (62)$$

4.3.4. Aromatic Hydrocarbons

The reactions of active nitrogen with aromatic compounds have not been studied in detail. The production of tars and solids, which deposit on the walls of the reaction vessel, seem to be characteristic of these reactions [181, 213–215]. Small yields of phenyl isocyanide, benzonitrile, and pyridine (but no aniline) were obtained from the reaction of active nitrogen with C_6H_6 [181, 215].

The emission spectrum recorded during the reaction of active nitrogen with solid benzene shows the vibrational structure of the phosphorescence spectrum of C_6H_6 shifted to higher wavelengths [216]. This was attributed to reaction with $N_2(A\,^3\Sigma_u^+)$.

4.3.5. Other Organic Compounds

The reactions of active nitrogen with several alkyl halides have been studied in considerable detail. The perfluorinated alkenes C_2F_4, C_3F_6, and perfluoro-2-butene yield a polymer (C = 26%, F = 65%, N = 9%) as the major N-containing product [217]. Fluorocarbons are also obtained, together with small quantities of FCN. It was suggested that the yield of FCN might be reduced by its reaction with the parent alkene to form a polymer, *e.g.*,

$$C_2F_4 + FCN \rightarrow (C_3F_5N)\ \text{polymer} \quad (63)$$

The main features of these reactions were explained by a mechanism similar to the "unified" mechanism for the reaction of active nitrogen with ethylene, proposed earlier by *Evans, Freeman,* and *Winkler* [11].

The kinetics of the reaction of active nitrogen with perfluoro-2-butene were studied by the diffusion flame technique [218]. The rate constant was estimated to be 7×10^{-14} cm^3 molec^{-1} s^{-1} at 313 °K, which does not agree with the value suggested by a mass-spectrometric study, *i.e.*, $k \leqslant 6 \times 10^{-15}$ cm^3 molec^{-1} s^{-1} at 500 °K [194].

The reactions of active nitrogen with the chlorinated methanes, except CCl_4, produce HCl and HCN as the main products [27, 219]. These reactions are unusual in that the maximum HCN yield seems to be temperature-dependent. It is possible that the HCl produced acts as a "catalyst" in a manner similar to that observed when HCl is added to the reactions of active nitrogen with certain hydrocarbons [32, 169].

The reaction of active nitrogen with CCl_4 is accompanied by an intense reaction flame and produces CNCl and Cl_2 [219]. The rate constant has been estimated as $k = 2 \times 10^{-12} \exp(-2.1\ \text{kcal}/RT)$ cm^3 molec^{-1} s^{-1} from an analysis of the product distributions [220].

The reactions of active nitrogen with CH_3OH and C_2H_5OH produced HCN and H_2O as the main products [221, 222]. The activation energies for these reactions were estimated to be 3.1 and 3.4 kcal mole^{-1}, and the steric factors to be 1.7×10^{-3} and 3.6×10^{-3}, respectively.

The reaction of active nitrogen with CH_3CHO showed no evidence for hydrogen abstraction by N atoms [223]. The main products of the reaction are HCN, H_2, and CO, with small amounts of glyoxal and substances with $m/e = 43$ and $m/e = 86$. The reaction with CH_3CDO does not seem to produce any DCN, and the H_2:HD:D_2 ratios are 1:0.88:0.33. The proposed mechanism was

$$N + CH_3CHO \rightarrow HCN + H_2 + CHO \quad (64)$$

$$CHO + CH_3CHO \rightarrow CO + H_2 + R \quad (65)$$

To account for the $m/e = 43$ peak, it was suggested that R might be CH_2CHO. The rate constant for reaction (65) was estimated to be $k_{65} = 2.0 \times 10^{-14}$ cm^3 molec^{-1} s^{-1} at 296 °K.

A qualitative study of the corresponding reaction with C_2H_5CHO suggested that it probably reacts by a similar mechanism [223].

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The reactions of active nitrogen with CH_3NH_2 and CH_3CN typically produce HCN as the main product [28,181,224]. For both reactions, the "plateau" value for HCN production apparently increases with temperature.

5. CN Emission

The reactions of active nitrogen with C-containing compounds are generally accompanied by a characteristic CN emission. Both the red ($A\,^2\Pi \rightarrow X\,^2\Sigma$) and violet ($B\,^2\Sigma \rightarrow X\,^2\Sigma$) bands of CN have been observed in the flames that accompany such reactions [70], and they have been studied in considerable detail in an attempt to elucidate the mechanism by which these electronically excited states of CN may be populated.

It was noted earlier that $(CN)_2$ production from most of the active nitrogen-hydrocarbon reactions is small and, as *Strutt* pointed out, the intensity of the reaction flames need give no indication of the extent to which the main reactions occur to yield HCN as the final product [5,8]. This observation has recently been confirmed by *Avramenko* and *Krasnen'kov*, who showed that the rates of $(CN)_2$ or HCN formation are not related to the intensity of the emission spectra of CN, CH, and C_2 from the reactions of active nitrogen with CH_4, C_2H_2, C_2H_6, CH_3OH, and CCl_4 [225].

The mechanism for the population of electronically excited CN radicals in active nitrogen reactions is complex. Intensity measurements of the CN emissions, from reactions with cyanogen derivatives or halogenated hydrocarbons, showed three distinct vibrational energy population distributions in both the $A\,^2\Pi$ and the $B\,^2\Sigma$ states [226]. Three distinct mechanisms were proposed to account for these distributions. The first population distribution was observed mainly during reactions with cyanogen derivatives, YCN, at pressures < 0.1 torr and was attributed to either

$$N + N + YCN \rightarrow CN^*(A\,^2\Pi \text{ or } B\,^2\Sigma) + N_2(X\,^1\Sigma_g^+) + Y \quad (66)$$

or

$$N_2^* + YCN \rightarrow CN^* + N_2(X\,^1\Sigma_g^+) + Y \quad (67)$$

A second distinct population distribution was observed with halogenated hydrocarbons at higher pressures and fairly high reactant concentration. Excitation of CN was attributed to

$$N + CX \rightarrow CN^* + X \quad (68)$$

A third population distribution was observed in the reactions of cyanogen derivatives and halogenated hydrocarbons under "blue" flame conditions, *i.e.*, low reactant concentrations, when the first positive system of active nitrogen is still visible and emission results from excitation of previously formed CN according to

$$N + N + CN \rightarrow CN^* + N_2(X\,^1\Sigma_g^+) \quad (69)$$

or

$$N_2^* + CN \rightarrow CN^* + N_2(X\,^1\Sigma_g^+) \quad (70)$$

Absolute intensity measurements and the overall kinetics suggest that the N_2^* species of reaction (70) is $N_2(A\,^3\Sigma_u^+)$, or possibly $N_2(X\,^1\Sigma_g^+)$ in a high vibrational level (with energy > 149 kcal mole^{-1}) [227].

This mechanism has been confirmed by results of optical absorption measurements of ground state CN in active nitrogen flames [228].

6. The $N_2(A^3\Sigma_u^+)$ State

In the past, reactions of active nitrogen which could not be adequately explained in terms of N atom reactions have often been attributed to reaction with $N_2(A\,^3\Sigma_u^+)$ molecules. Because decay to the ground state $N_2(X\,^1\Sigma_g^+)$ by light emission is spin forbidden, $N_2(A\,^3\Sigma_u^+)$ molecules are relatively long-lived, and afford a particularly attractive choice as a second reactant [12a,17]. Several workers have recently obtained significant concentrations of the $N_2(A\,^3\Sigma_u^+)$ species in systems which contain a relatively small number of N atoms [53,54,143].

As mentioned previously [Section 3, eq. (5)], perhaps the most important reaction of $N_2(A\,^3\Sigma_u^+)$ molecules is the rapid reaction with N(^{4}S) atoms to produce vibrationally excited ground state molecules [53]. The rate of this reaction may be very sensitive to the vibrational energy of the A state molecules [228a]. Energy pooling by

$$N_2(A\,^3\Sigma_u^+) + N_2(A\,^3\Sigma_u^+) \rightarrow N_2(X\,^1\Sigma_g^+) + N_2(C\,^3\Pi_u) \quad (71)$$

has also been observed [228b]. The initial production of H atoms in reactions of active nitrogen with organic compounds might well be due to energy transfer from $N_2(A\,^3\Sigma_u^+)$. This species, with energy of 142–146 kcal/mole, may also serve as a triplet sensitizer [143]. With reactants having low-lying triplet levels, such as $(CN)_2$, SO_2, or CS_2, reaction of $N_2(A\,^3\Sigma_u^+)$ generally leads to emission from the reactant due to a rapid triplet-triplet transition. Other reactants, such as N_2O

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or O_2, are partially dissociated by $N_2(A\,^3\Sigma_u^+)$ molecules [104, 143]

Excitation of NO by $N_2(A\,^3\Sigma_u^+)$ has been shown to occur efficiently by

$$N_2(A\,^3\Sigma_u^+) + NO(X\,^2\Pi) \rightarrow N_2(X\,^1\Sigma_g^+) + NO(A\,^2\Sigma^+) \quad (72)$$

Excitation of NO results in approximately one-half of the de-exciting collisions of $N_2(A\,^3\Sigma_u^+)$ with NO [229].

It has been suggested that the mercury 2537 Å emission might be used as a test for $N_2(A\,^3\Sigma_u^+)$ [56, 230–232].

The importance of $N_2(A\,^3\Sigma_u^+)$ molecules in active nitrogen is, however, somewhat limited by their relatively low concentration, which is estimated to be $\approx 10^{-3}$ [N] [204].

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Magnetic Resonance of Paramagnetic Complexes

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The line width of the ESR and NMR signals of paramagnetic transition metal complexes is determined mainly by the electron spin-lattice relaxation time τ_e. Values of τ_e greater than 10^{-9} lead to ESR spectra that are readily resolved, while values smaller than 10^{-11} give NMR spectra having small line widths. Since fast relaxation processes are effective in nearly all transition metal complexes with several unpaired electrons and in all complexes having an orbitally degenerate ground state, the NMR method has a wider scope. The sign and magnitude of the electron-nucleus coupling can be determined with great sensitivity from the NMR spectra, whereas only the magnitude of this interaction can be determined from the ESR spectra. Free spin densities can be found very accurately from the NMR shifts, and the method can therefore be advantageously applied to kinetic measurements, e.g. on short-lived contact complexes.

1. Introduction

The use of both the electron spin resonance (ESR) and the nuclear magnetic resonance (NMR) effects can lead to the solution of a number of chemical problems in connection with paramagnetic transition metal complexes. Several reviews of both methods have been published in recent years, and results for transition metal complexes have also been discussed [1–8], but their *combined* application to paramagnetic complexes has been largely ignored. A question of prime interest to chemists is when to use NMR measurements in practice, and when ESR.

2. Theoretical Principles

2.1. Resonance Conditions

The problems will be considered on the basis of the simplest possible system, *i.e.* hydrogen atoms, assuming at first that these atoms are not influenced by their neighbors, so that it is possible to discuss the resonance properties of a single hydrogen atom.

It is well known that the hydrogen atom consists of one proton and one electron. Each of these elementary particles has a characteristic angular momentum (spin), which, according to the quantum theory, can only assume certain specific values. The angular momentum J, which differs in magnitude for the two particles in question, is therefore, figuratively speaking,

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restricted to two definite directions in space. Thus there are only two possible (±) spin states for the proton and for the electron ($J = 1/2$).

Owing to the electric charge carried by the elementary particles, the angular momentum is associated with a magnetic moment, which can be calculated from

$$\beta = e_0 \hbar/2 m c \qquad (1)$$

where e_0 is the charge on the elementary particle, m is its mass, c is the velocity of light, and $\hbar$ is the Planck constant divided by 2π. However, the moments calculated from this equation, which are known as the nuclear magneton and the Bohr magneton ($\beta = \mu_N$ and μ_B) respectively, do not coincide with the magnetic moments found for the proton and for the electron in resonance experiments. These are given by the product of the magneton (β) with a purely empirical correction factor, the g factor.

$$\mu = g\beta \qquad (2)$$

Like the angular momentum vectors, the magnetic moments of the proton and the electron are also restricted to two directions. These two states, which are represented by antiparallel arrows, have the same energy provided that no external magnetic field is acting, *i.e.* the energy levels of the oppositely oriented magnetic vectors are degenerate (Fig. 1, a). In a strong external magnetic field H_0, the energy of the state in which the magnetic moment is parallel to the external field is reduced by a certain amount, while the energy of the state with the antiparallel orientation of the magnetic moment is increased by the same amount, *i.e.* the degeneracy is lost (Zeeman effect).

The splitting (ΔE_1 or ΔE_2) is proportional to the magnetic moment and to the strength of the external field (Fig. 1, b):

$$\Delta E \sim \mu H_0 \qquad (3)$$

Since the magnetic moment of the electron, according to eq. (1), is greater by a factor of $\approx 10^3$ than the moment of the proton, the splitting of the degenerate energy levels for electrons in accordance with eq. (3) is $\approx 10^3$ times as large as the corresponding splitting for nuclei. Figure 1 thus gives only a hint of the true state of affairs.

2.2. Resonance Spectrum of a Hydrogen Atom

Absorption or emission spectroscopy can now be carried out on the system chosen as our example. If electromagnetic energy corresponding to the difference between the magnetic electronic or nuclear levels (ΔE_1 and ΔE_2 respectively) is supplied to the system from a suitable source, the elementary particles with the parallel spin can be raised to the higher levels, with reversal of their magnetic moment into the antiparallel state. Two discrete frequencies are absorbed from a broad frequency spectrum in accordance with

$$\Delta E = h\nu = g\beta H_0 \qquad (4)$$

Since the transitions between the magnetic electronic levels have a much higher energy than those between the magnetic nuclear levels, ESR absorptions occur in the microwave region ($\nu \approx 10^9$–10^{10} Hz; $H_0 \approx 10^3$ gauss), while NMR absorptions, even at higher field strengths, occur in the radio wave region ($\nu \approx 10^6$ Hz; $H_0 \approx 10^4$ gauss). According to eq. (3), the magnitude

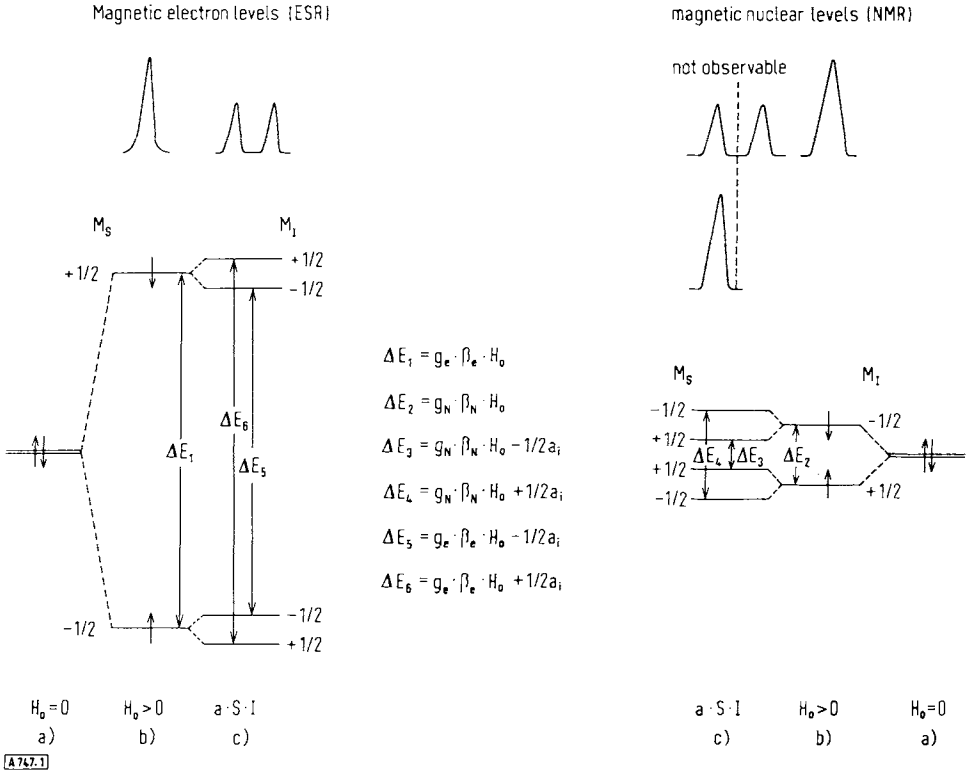


Fig. 1. Zeeman levels of a hydrogen atom in a strong external field H_0.

of the splitting of the levels is determined purely by the magnetic moments of the particles; this leads to differences in the methods used in ESR and NMR experiments. Nevertheless, the usual distinction between ESR and NMR spectroscopy does not seem to be justified merely on the basis of experimental peculiarities. The rules applicable to the two methods are qualitatively the same. The chemist is interested only in the parameters of the spectra that contain essentially chemical information; these are above all the shifts of the resonance signals in NMR, which correspond in practice to the g factor measured in ESR.

It has been assumed so far that the magnetic moments of the electron and of the proton do not influence each other. However, this is not so. There is in fact a strong "contact interaction" between these magnetic dipoles, which was first postulated by *Fermi* for the interpretation of optical spectra [9]. This interaction has a finite value only if the unpaired electron can be described by an orbital function with a finite probability for the position of the nucleus, as *e.g.* for unpaired electrons in s orbitals. The strength of the interaction depends on the spin quantum operators of the electron $\vec{S}$ and of the interacting nucleus $\vec{I}$, as well as on the absolute probability of finding the unpaired electron in the position of the nucleus ($|\psi(0)|^2$):

$$\mathscr{H} = a\,\vec{I}\,\vec{S};\quad a = \frac{8\pi}{3}\, g_e\beta_e g_N\beta_N|\psi(0)|^2 \qquad (5)$$

This results in further splitting of the electronic and nuclear levels. The electronic moments are now exposed to two different magnetic fields, *i.e.* the external field H_0 plus the magnetic moment of the nucleus with the nuclear moment parallel to the field direction on the one hand, and H_0 minus the nuclear moment with antiparallel orientation on the other. On insertion of the electron-nucleus interaction, therefore, we obtain the diagram shown in Figure 1, c, with the result that further transitions become possible. The orientation of the nuclear moment parallel to H_0 corresponds to $M_I = +1/2$, while the parallel orientation of the electronic moment, because of the opposite charge, corresponds to $M_S = -1/2$. Thus a large number of independent hydrogen atoms would give a resonance spectrum of four "allowed" lines. (Selection rules: $\Delta M_I = \pm 1$, $\Delta M_S = 0$ for nuclear transitions; $\Delta M_S = \pm 1$, $\Delta M_I = 0$ for electronic transitions.) The absorption line of the nuclear transition and the absorption line of the electronic transition exhibit splitting corresponding to equal energy differences. Two ESR lines should be observed in the microwave region and two NMR lines in the radio wave region (Fig. 1, c).

2.3. Relaxation

Unfortunately, this last view is still not sufficiently close to reality, since the hydrogen atoms are also appreciably influenced by time-dependent fields of their environment. Each atom executes thermal motions with a speed that varies with the temperature. Since the atom has magnetic dipoles, this motion produces an alternating electromagnetic field. If the frequency ν_w of this alternating field satisfies the resonance condition (4), a resonance transition is induced by this radiation in neighboring atoms. In the spectral region considered, induced emission and absorption are equally probable, so that both emission and absorption are stimulated by the electromagnetic "stray field". Thermal lattice energy can thus be converted into spin energy and *vice versa*. Fast transitions between the levels thus become possible, since a particle that has been transferred to a higher level by absorption of energy can return to the ground state by radiationless loss of energy to the "lattice". The lifetime of a given state is consequently shortened, sometimes to such an extent that according to the Heisenberg uncertainty relation

$$\Delta E \cdot \Delta t \geqslant \hbar \qquad (6)$$

its energy becomes uncertain. The line width of the resonance signal increases considerably. With very short lifetimes, this may have the result that the transitions can no longer be observed. Since the magnetic moments of electrons are very large, a very strong electromagnetic stray field prevails in paramagnetic systems, as in our example of hydrogen atoms or in dilute solutions of organic radicals, and causes extremely short nuclear lifetimes and hence broadening of the NMR lines. The two absorptions expected in the radio wave region cannot be detected. This led to the assumption that NMR spectra could not be recorded for paramagnetic compounds. However, this is incorrect above all for inorganic complexes [1–8]; on the contrary, NMR lines of adequate sharpness are the rule in this case.

The fact that the resonance signals of such compounds can be detected experimentally is the result of fast transitions between the *electronic* levels. If, for example, many such transitions occur during a specific thermal motion of a hydrogen atom, *i.e.* if the electron spin of this hydrogen atom changes its direction several times during the motion, the influence of the stray field produced by the thermal oscillation of the magnetic dipoles on nuclear relaxation decreases. Only a time average of all possible spin directions acts during a translation or rotation.

For a quantitative treatment of this intuitive model, it is necessary to define the relaxation time, *i.e.* the time after which 1/e of the excited spins have returned radiationlessly to the ground state. If the spins are very strongly coupled to the "lattice", *i.e.* if a fast exchange takes place between the energy of the spin system and degrees of freedom of the environment, the spin-lattice relaxation times are short. According to the relation (6), resonance absorptions should then be absent or extremely broad, as has been indicated for the NMR absorption of the hydrogen atom.

If, however, unpaired electrons have extremely short *electron* spin-lattice relaxation times, as in many

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transition metal complexes, *i.e.* if the direction of their spin is reversed rapidly in comparison with the correlation time of the particles in the solution, the coupling of the nuclear spin with the lattice is largely eliminated; the *nuclear* spin-lattice relaxation times again become longer, and the line width of the NMR signals accordingly decreases. No ESR spectra are observed in such cases. Thus in solutions of paramagnetic compounds, the question when NMR and when ESR studies are possible is determined by the *electron* spin-lattice relaxation time [10–14]. With relatively long electron spin relaxation times (down to about 10^{-9} s), usable ESR spectra can be recorded, but only very broad-lined NMR spectra. With relaxation times shorter than 10^{-11} s, on the other hand, *i.e.* with extremely short electron spin relaxation times, only NMR spectra (usually with small line width) can be recorded. The two methods thus complement each other excellently [15].

In addition to the intramolecular transitions, fast intermolecular processes also have a similar averaging effect on the time-dependent internal fields. If, for example, the unpaired electrons in a molecule are strongly delocalized, the orbitals, which have a broad probability distribution, may overlap slightly in concentrated solution; an exchange interaction, in which the spin can also reverse rapidly, becomes possible. The requirements for this are often satisfied by organic radicals [16–18], but less often by complex compounds.

3. Electron Spin-Lattice Relaxation Times

We are thus faced with the question of the parameters that govern the electron spin-lattice relaxation times of metal complexes, in order to clarify whether to carry out NMR and/or ESR studies. The interpretation of the electron spin relaxation times of paramagnetic transition metal complexes has been discussed only quite recently [19], so we will confine ourselves here to just the essential aspects. Since the mechanisms are more complicated for an effective relaxation in complexes containing several unpaired electrons (zero-field splitting), it seems reasonable to confine the discussion to compounds with $S = 1/2$, *i.e.* with only one free electron spin. As a rough simplification, we can say that NMR absorptions with small line widths should be obtained for most complexes containing several unpaired electrons (the only exceptions are ions with an S ground state, such as Mn^{2+} and Fe^{3+}). These complexes are therefore particularly suitable for NMR studies [20–26].

On the other hand, in complexes having only one unpaired electron, the electron spin-lattice relaxation time is largely dependent on the symmetry and strength of the ligand field. According to an empirical relation [27]

$$\tau_e = \frac{\Delta^6 \cdot 10^4}{\lambda^2 H^2 T^7} \qquad (7)$$

the electron spin-lattice relaxation time τ_e is determined mainly by the energy difference between the highest occupied and the lowest unoccupied electron levels (Δ) and by the temperature. Reference was made earlier to the dependence of the line width on the spin-orbital coupling constant λ in complexes with varying λ values [28]; its effect on the relaxation time need not be considered further here.

At the same temperature and at comparable magnetic field strengths, τ_e for various metal complexes depends mainly on Δ. In paramagnetic complexes with orbitally degenerate ground states, the highest occupied and the lowest unoccupied levels have the same energy, so that Δ should be zero. Though thermal motion and fields of neighboring molecules cause slight splitting, all metal complexes with *orbitally degenerate* ground states, according to eq. (7), have extremely short electron spin-lattice relaxation times. ESR spectra should therefore be expected only at extremely low temperatures (a few °K), whereas NMR spectra should be very easy to record for compounds of this type.

To clarify this point further a short discussion of the splitting of d orbitals in transition metal complexes having different ligand field symmetries is given. According to a simple (electrostatic) ligand field scheme [29], the five d states (Fig. 2) split up into an undistorted or tetragonally distorted octahedral ligand field, as shown in Figure 3.

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[18] *K. H. Hausser, H. Brunner,* and *J. C. Jochims,* Molecular Physics *10,* 253 (1966).

[19] *W. B. Lewis* and *L. O. Morgan,* Transition Metal Chem. *4,* 33 (1968).

[20] *G. N. La Mar* and *L. Sacconi,* J. Amer. chem. Soc. *89,* 2282 (1967).

[21] *G. W. Everett jr.* and *R. H. Holm,* Inorg. Chem. *7,* 776 (1968).

[22] *P. K. Burkert, H. P. Fritz, W. C. Gretner, H. J. Keller,* and *K. E. Schwarzhans,* Inorg. nuclear Chem. Letters *4,* 31 (1968).

[23] *F. A. Hart, J. E. Newberry,* and *D. Shaw,* Chem. Commun. *1967,* 45.

[24] *R. W. Kluiber* and *W. De W. Horrocks jr.,* J. Amer. chem. Soc. *88,* 1399 (1966).

[25] *J. Happe* and *R. C. Ward,* J. chem. Physics *39,* 1211 (1963).

[26] *G. N. La Mar,* J. Amer. chem. Soc. *87,* 3567 (1965).

[27] *G. Schoffa*: ESR in der Biologie. Verlag G. Braun, Karlsruhe 1964, p. 29.

[28] *K. H. Hausser,* Naturwissenschaften *48,* 426 (1961); Z. Elektrochem., Ber. Bunsenges. physik. Chem. *65,* 636 (1961).

[29] *C. J. Ballhausen*: Introduction to Ligand Field Theory. McGraw-Hill, New York 1962.

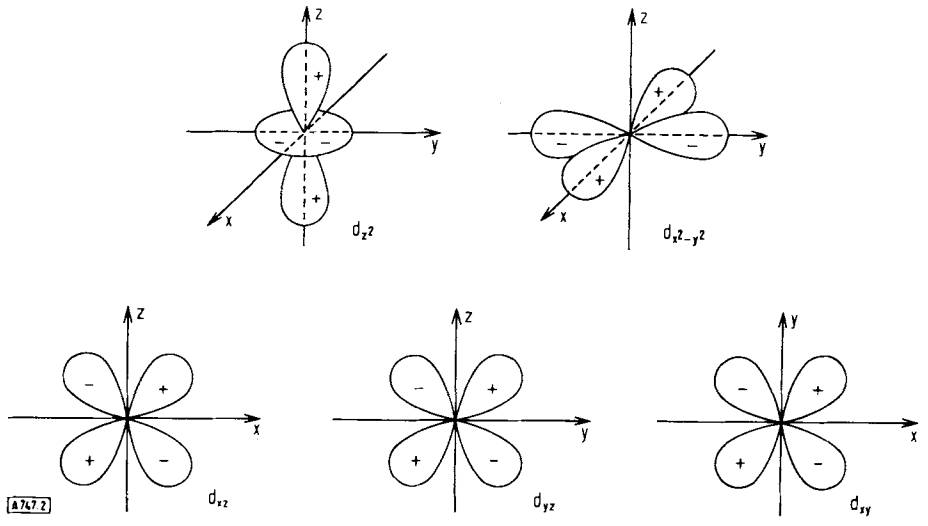


Fig. 2. d orbitals (schematic).

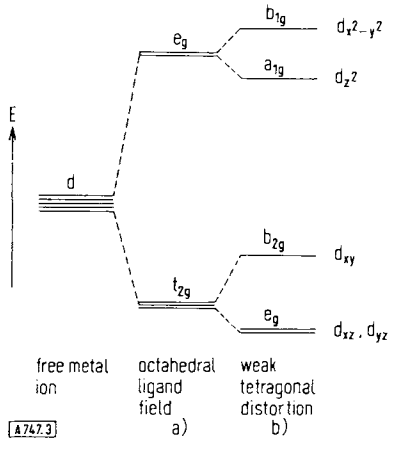


Fig. 3. Splitting of the five d orbital functions in an octahedral field (a) and with tetragonal distortion (b).

If the lower T_{2g} states contain 1,2,4, or 5 electrons and the higher E_g states 1 or 3 electrons, the result is an orbitally degenerate ground state with $\Delta \approx 0$. This situation is found *e.g.* in regular octahedral complexes of Ti^{III}, V^{IV}, or Cr^{II} and in regular tetrahedral complexes of Cu^{II}, Ti^{III}, and V^{II}, to give only a few examples.

If the regular arrangement of the ligands is disturbed, *e.g.* by a Jahn-Teller effect, the degenerate orbital functions fan out farther, the distance Δ between them increasing with increasing distortion. The electron spin-lattice relaxation time is thus a function of the degree of distortion. The line width in the NMR and/or ESR spectra can accordingly be used indirectly to deduce the arrangement of the ligands. For example, on transition from an octahedral to a planar arrangement in d^1 or d^2 complexes, the ESR lines are expected to become narrower while the NMR lines should become broader.

This expectation can be confirmed for $Cu^{II}(d^9)$ complexes with various ligand field symmetries. Cu^{2+} in regular tetrahedral coordination, similarly to the octahedrally coordinated Ti^{3+} ion, is in a triply degenerate $^2T_2$ state [29] (Fig. 4, a); ESR spectra of such complexes are extremely difficult to obtain [30–33]. On distortion of the ligands toward a planar arrangement, the levels split into an E and a B_2 state (Fig. 4, b). The ground state is not further orbitally degenerate, so the width of the ESR lines must decrease with increasing distortion, while that of the NMR lines increases, since τ_e increases with Δ [eq. (7)]. The field of the ligands can be varied in the bis(2-alkyliminomethylphenolato)copper(II) compounds *(1)* (Fig. 5) by varying the *N*-substituent [34].

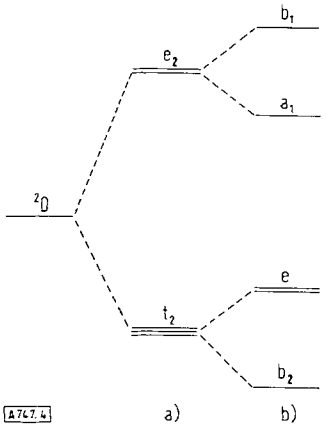


Fig. 4. Energy of the one-electron orbital functions of a tetracoordinate d^9 ion in the regular tetrahedral (a) and distorted tetragonal (b) ligand fields.

In the comparison of the *N-tert*-butyl *(1a)* with the isopropyl derivative *(1b)* (Fig. 5), the former was expected, on steric grounds, to exhibit a greater angle of twist between the planes of the practically planar ligands [35], and hence also to give a greater ESR line width.

[30] *C. A. Bates, W. S. Moore, K. J. Standly*, and *K. W. H. Stevens*, Proc. physic. Soc. *79*, 73 (1962).

[31] *C. A. Bates*, Proc. physic. Soc. *83*, 465 (1964).

[32] *M. Sharnoff*, J. chem. Physics *42*, 3383 (1965).

[33] *R. E. Dietz, H. Kamimura, M. D. Sturge*, and *A. Yariv*, Physic. Rev. *132*, 1559 (1963).

[34] *H. P. Fritz, B. M. Golla*, and *H. J. Keller*, Z. Naturforsch. *21b*, 1015 (1966).

[35] *T. P. Cheeseman, D. Hall*, and *T. N. Waters*, Nature (London) *205*, 494 (1965).

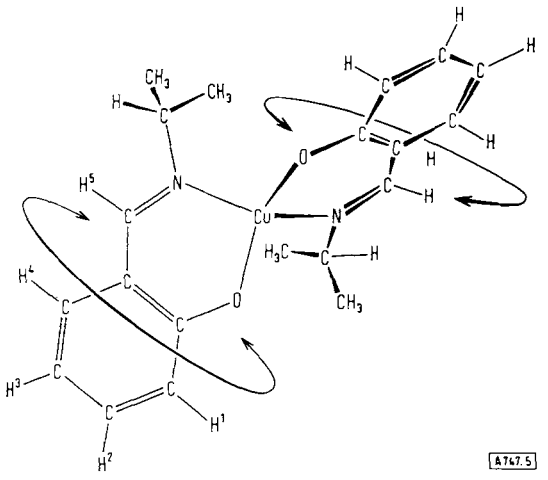


Fig. 5. Structure of bis(2-isopropyliminomethylphenolato)copper(II) *(1b)*.

As is shown in Figure 6, the two complexes give very different line widths at the same temperature (77 °K), *i.e.* 1.5 and 40 gauss respectively. Contrary to expectation, therefore, *(1a)* appears to have a more coplanar arrangement of the ligands, despite the expected

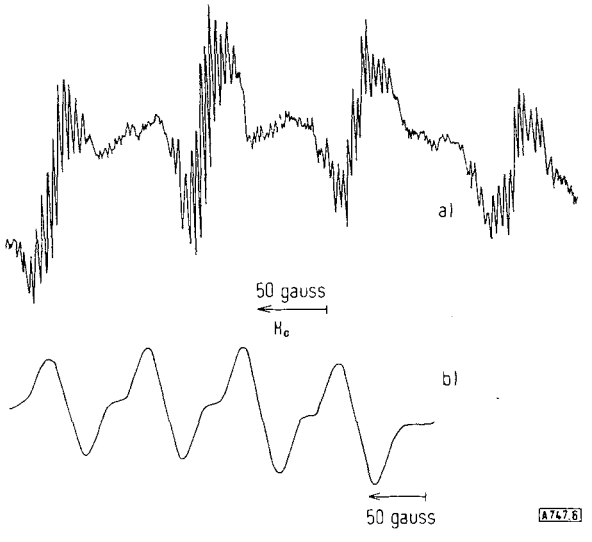


Fig. 6. ESR spectra of (a) bis(2-*tert*-butyliminomethylphenolato)-copper(II) *(1a)* and (b) bis(2-isopropyliminomethylphenolato)copper(II) *(1b)* incorporated into the corresponding Zn^{II} complexes in the direction $H_0 \parallel c$ at 77 °K.

enhanced steric hindrance. This surprising result was confirmed by X-ray studies, which show that the twist angle is 45° in *(1a)* [36], as compared with 60° in *(1b)* [37]. The line width of the ESR absorptions thus provides important information about the symmetry of the ligand field.

The observed large ESR line widths at room temperature suggest, on the other hand, that the compounds *(1)* with an approximately tetrahedral ligand field should give NMR spectra with reasonable line widths. ^{1}H-NMR absorptions of these complexes are in fact

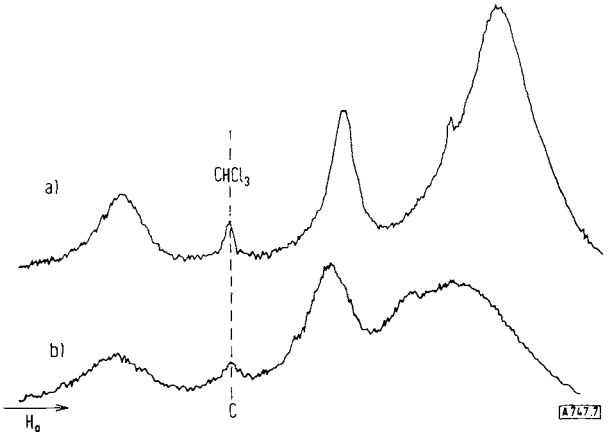


Fig. 7. ^{1}H-NMR spectra of bis(2-isopropyliminomethylphenolato)-copper(II) *(1b)* in $CDCl_3$ at 70 (a) and 20 °C (b).

readily observed having a line width of about 100 Hz (20 °C) [38] (Fig. 7, b).

These observations confirm the conclusion that the NMR and ESR line widths of the spectra of paramagnetic complexes in solutions of equal concentration are roughly inversely proportional to one another [15]. This can be said of complexes which are accessible by only one method as well as of species for which both methods can be used [38–41].

The dependence of the line width on the temperature can be seen from what has been said already. According to eq. (7), a temperature rise considerably shortens the electron spin-lattice relaxation time. Complexes *(1)* with an approximately tetrahedral ligand field give a very broad ($\approx$ 1000 gauss) structureless signal in the ESR spectrum at room temperature, while the NMR absorptions have line widths of about 100 Hz, which become narrower with rising temperature (Fig. 7, a). Well resolved NMR spectra are obtained at higher temperatures, and well resolved ESR spectra at lower temperatures, since the unstructured ESR line observed at room temperature has a distinct hyperfine structure at 77 °K. Both NMR and ESR studies can therefore be carried out on complexes of this type by varying the temperature.

It should be noted that τ_e is large for complexes with "strong" ligands; in these complexes, the orbital moment, and hence the cause of effective relaxation, is eliminated by substantially covalent metal-ligand bonds. Thus most of the paramagnetic organometallic complexes have long electron spin relaxation times and behave in resonance experiments as free organic radicals [42,43].

[36] *T. P. Cheeseman, D. Hall*, and *T. N. Waters*, J. chem. Soc. (London) *A 1966*, 685.

[37] *P. L. Orioli* and *L. Sacconi*, J. Amer. chem. Soc. *88*, 277 (1966).

[38] *H. P. Fritz, B. M. Golla, H. J. Keller*, and *K. E. Schwarzhans*, Z. Naturforsch. *21b*, 725 (1966).

[39] *R. Prins, P. Biloen*, and *J. D. W. van Voorst*, J. chem. Physics *46*, 1216 (1967).

[40] *Y. S. Karimow, V. M. Tschibrikin*, and *I. F. Schtschegolew*, J. Physics Chem. Solids *24*, 1683 (1963).

[41] *H. P. Fritz, F. H. Köhler*, and *K. E. Schwarzhans*, J. organometallic Chem. *16*, 14 (1969).

[42] *H. J. Keller*, Z. Naturforsch. *23b*, 133 (1968).

[43] *H. J. Keller* and *H. Wawersik*, Z. Naturforsch. *20b*, 939 (1965).

Attempts to compare the line width of NMR absorptions of different nuclei in a given paramagnetic complex show that the line width is influenced above all by the magnitude of the nucleus-electron coupling, *i.e.* the interaction measured by the value of a_i. Results of NMR experiments on organic radicals suggest that the line width increases with the value of a_i^2 [1,11,13,18,44]. This is obviously also true of the paramagnetic transition metal complexes. Owing to a "direct" interaction (cf. Section 2.6), the protons nearest to the metal ion often have the largest spin density, and hence also the greatest value of a_i. Fig. 8 shows the ^{1}H-NMR spectrum of bis(salicylaldehydato)bis(pyridine)nickel(II) (Fig. 9).

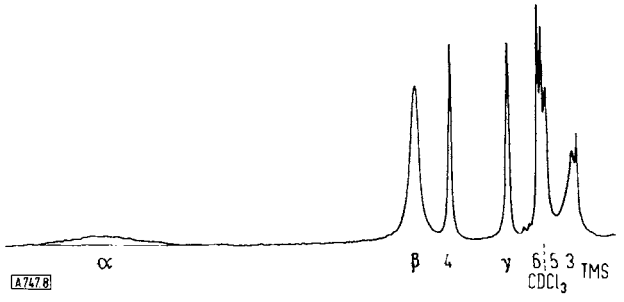


Fig. 8. ^{1}H-NMR spectrum of bis(salicylaldehydato)bis(pyridine)-nickel(II).

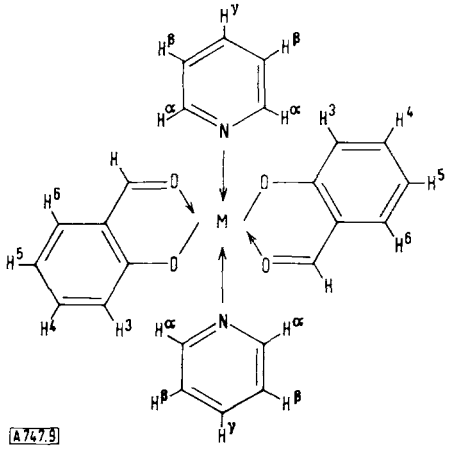


Fig. 9. Structure of bis(salicylaldehydato)bis(pyridine)nickel(II).

The signals of the high spin density protons close to the metal ion exhibit more pronounced broadening; this is true in particular of the signals of the pyridine protons in the α position, which almost dive into the electron cloud of the Ni^{II}. The line width can be used for identification of the protons if the structure of the complex is approximately known [45–47].

4. Number and Position of the ESR and NMR Absorptions

It can be seen from the above discussion that though the magnetic levels of the nuclei are greatly influenced by the strong magnetic electronic dipoles, the nuclear dipoles have only a small effect on the electron levels. They have an effect of second order on the position of the ESR absorptions, but the number of lines observed is determined by the number and nature of the nuclei that interact with the unpaired electron. "Hyperfine splitting" (measured as a_i in the units gauss or Hz) appears (Fig. 6), the magnitude of this splitting increasing with the probability of finding the unpaired electron in the position of the nucleus with which it is in interaction [1,7,8].

As was mentioned earlier, narrow NMR lines can be recorded only if the *electron* spin relaxation times are extremely short, *i.e.* if the transitions between the electron levels are extremely fast. This leads to the observation that a nucleus situated in the neighborhood of such a rapidly relaxing electron spin experiences only an averaged magnetic field due to the unpaired electron, and includes also the hyperfine fields if the electron spin relaxation time is very short in relation to that of the reciprocal nucleus-electron interaction (a_i).

$$\tau_e \ll 1/a_i \qquad (8)$$

For example, a proton cannot then distinguish between the various electron spin orientations. The NMR splitting (Fig. 1, c) disappears. Only one absorption signal is then observed, situated at the center of gravity of the intensities of the two original lines, which had unequal intensity [48]. This stems from the fact that according to

$$N_-/N_+ = \exp(-g\beta H_0 M/kT_s) \qquad (9)$$

the population of the lower levels is significantly greater at room temperature than that of the higher levels. The transition with the higher energy (ΔE_4 in Fig. 1, c) thus gives a higher absorption intensity than that with the lower energy (ΔE_3), which joins levels with smaller differences in population. The center of gravity of the intensities of the two lines is thus not given by the arithmetic mean, but is situated at somewhat lower field strengths. Pictorially speaking, there are more electrons with orientation parallel to the external field than with the antiparallel orientation in the neighborhood of the nuclei. The external field is reinforced, and the process corresponds to shielding, which results in a displacement to lower field strengths. The displacements increase with falling temperature [eq. (9)], and increase with the number of unpaired electrons per molecule. They show the same trend as the susceptibility of paramagnetic compounds [49].

$$\frac{\Delta H_i}{H} = -a_i \frac{\gamma_E g \beta S(S+1)}{\gamma_H 3kT} \qquad (10)$$

[44] *K. H. Hausser*, Proc. XIV. Colloque Ampére, Ljubljana 1966, p. 1169.

[45] *H. P. Fritz, W. C. Grentner, H. J. Keller*, and *K. E. Schwarzhans*, Z. Naturforsch. *23b*, 906 (1968).

[46] *H. P. Fritz, B. M. Golla, H. J. Keller*, and *K. E. Schwarzhans*, Z. Naturforsch. *22b*, 216 (1967).

[47] *H. P. Fritz, H. J. Keller*, and *K. E. Schwarzhans*, J. organometallic Chem. *6*, 652 (1966).

[48] *H. M. McConnell* and *D. B. Chesnut*, J. chem. Physics *28*, 107 (1958).

[49] *H. M. McConnell* and *C. H. Holm*, J. chem. Physics *28*, 749 (1958); *27*, 314 (1957).

For comparison with the order of magnitude of ESR splitting, one can define a paramagnetic shift δ_p [18], which at room temperature is

$$\frac{\delta_p}{a_i}(RT) = \frac{75 \text{ ppm}}{\text{gauss}} \quad (11)$$

Free spin densities can thus be measured much more accurately by the NMR method, since shifts of up to 0.01 ppm are readily detectable, whereas an ESR splitting of less than 0.05 gauss cannot be detected. Moreover the direction of the shift gives the sign of the constant a_i, and hence of the coupling, which is not given by ESR spectra. The use of the NMR method for paramagnetic complexes thus offers two important advantages over ESR studies.

5. NMR Results

The first successful experiments were carried out on various paramagnetic bis(π-cyclopentadienyl)metal complexes [49].

Of the many examples reported so far [2,4,50-56], only a few typical measurements on bis(aminotropinoiminato)nickel(II) complexes will be discussed at first. The metal ions have a $^3T_2$ ground state (Fig. 4, a) in the tetrahedral ligand field, but a diamagnetic $1\,A_{1g}$ ground state with a square-planar arrangement of the ligands. The NMR line widths are a few hertz [26]. The activation energy of the change from the paramagnetic to the diamagnetic conformation and back can be determined from the shifts found at various temperatures [2].

The spin density at various points in the molecule can be calculated from the paramagnetic shifts of the protons, so that it has been possible to clarify the nature of the transfer of free spin density [*] to the ligands. Both σ and π bonds between the central metal and the ligand may be involved.

Whereas the spin densities on the aromatic ligands in the tetrahedral nickel(II) complexes mentioned, which have alternating signs, clearly point to transfer by π-orbital functions [2], predominant σ delocalization was postulated in particular for the hexacoordinate nickel(II) and cobalt(II) complexes [25].

However, the argument used to distinguish between σ and π delocalization seems questionable at first. In addition to spin transfer *via* metal-ligand bonds, strong direct metal-hydrogen interactions are also possible. By overlap of suitable metal orbitals with hydrogen orbitals of adjacent ligand protons, spin density can be transferred "directly" to these protons. The relationships are particularly clear in the bis(π-cyclopentadienyl)metal complexes [57-59].

According to the usual rules, which are based either on MO or on VB models, some of the unpaired electrons of the central metal ions should be distributed, *via* the metal-ligand bond, over the molecular orbitals involving the carbon p_z functions of the rings. These orbital functions would then have a considerable "positive" spin density, which should lead to strong deshielding of the carbon nuclei, and hence to displacements to lower fields for any ^{13}C absorption observed. Neighboring protons are not affected by this interaction.

Differentiation between "positive" and "negative" spin densities is found to be necessary when the interaction between protons and free electrons in carbon orbitals is also taken into account. As is shown in particular by the ESR spectra of organic radicals [1], the magnetic electron levels are split by the moments of adjacent protons (as shown in Figure 1, c for the hydrogen atom). According to eq. (5), this is possible only if the orbital function by which the unpaired electron can be described has a non-zero value at the position of the proton.

The problem is solved mathematically by admixture of electronically excited states with the ground state (configuration interaction) with the result that free

Table 1. ^{1}H-NMR data for paramagnetic bis(π-cyclopentadienyl)-metal complexes.

	δ (ppm) [a]			
	Ring	α-CH_2	β-CH_2	-CH_3
$V(C_5H_5)_2$	−307.5			
$V(C_5H_4-CH_3)_2$ [b]	−337			−120
$Cr(C_5H_5)_2$	−314.1			
$Cr(C_5H_4-CH_3)_2$	−364			− 36
	−310			
$Co(C_5H_5)_2$	53.8			
$Co(C_5H_4-CH_3)_2$	72.3			− 10.4
	49			
$Ni(C_5H_5)_2$	254.8			
$Ni(C_5H_4-CH_3)_2$	253.8			−200.5
$[Fe(C_5H_5)_2]^{\oplus}$	− 24.8			
$[Fe(C_5H_4-CH_3)_2]^{\oplus}$	− 30.0			11.3
$[Fe(C_5H_4-C_2H_5)(C_5H_5)]^{\oplus}$	− 29.7	14.9		13.7
$[Fe(C_5H_4-C_2H_5)_2]^{\oplus}$	− 29.6	15.1		11.1
$[Fe(C_5H_4-C_3H_7)_2]^{\oplus}$	− 28.2	18.5	7.1	0.0
$[Fe(C_5H_4-C(O)CH_3)(C_5H_5)]^{\oplus}$	− 16.0			9.0
$[Fe(C_5H_4-C(O)CH_3)_2]^{\oplus}$	decomp.			
$[Fe(C_5H_4-C(O)C_3H_7)_2]^{\oplus}$	− 18.1		8.0	0.5
$[Fe(C_5H_4-C_4H_9)_2]^{\oplus}$	− 28.3	16.3	5.4	0.6

[a] At room temperature; the shifts are given relative to the corresponding protons in 1,1'-dimethylferrocene with the positive sign toward higher field strengths.
[b] *M. F. Rettig* and *R. S. Drago*, Chem. Commun. *1966*, 891.

[50] *R. J. Fitzgerald* and *R. S. Drago*, J. Amer. chem. Soc. *90*, 2523 (1968).
[51] *G. N. La Mar*, Inorg. Chem. *6*, 1921 (1967).
[52] *B. B. Wayland* and *R. S. Drago*, Inorg. Chem. *7*, 628 (1968).
[53] *F. Röhrscheid*, *R. E. Ernst*, and *R. H. Holm*, Inorg. Chem. *6*, 1607 (1967).
[54] *B. B. Wayland* and *W. L. Rice*, Inorg. Chem. *5*, 54 (1966).
[55] *P. B. Burkert*, *H. P. Fritz*, *W. Gretner*, *H. J. Keller*, and *K. E. Schwarzhans*, Inorg. nuclear Chem. Letters *4*, 237 (1968).
[56] *D. Shaw* and *E. W. Randall*, Molecular Physics *10*, 41 (1965).
[*] The absolute magnitude of the probability of finding an unpaired electron at a given point is generally referred to as the "free spin density".
[57] *H. P. Fritz*, *H. J. Keller*, and *K. E. Schwarzhans*, Z. Naturforsch. *22b*, 891 (1967).
[58] *H. P. Fritz*, *H. J. Keller*, and *K. E. Schwarzhans*, J. organometallic Chem. *7*, 105 (1967).
[59] *H. P. Fritz*, *H. J. Keller*, and *K. E. Schwarzhans*, Z. Naturforsch. *23b*, 298 (1968).

spin density is transferred *via* the C–H σ bond into suitable hydrogen orbitals. However, the positive spin density in the p_z orbital of carbon is so strongly polarized by the paired electrons involved in the C–H bond that the sign of the spin density at the proton is reversed. The *negative* spin density shields the proton from the field, with consequent signal displacement to *higher* fields. It is clear from the ^{1}H-NMR shifts given in Table 1 for bis(π-cyclopentadienyl)metal complexes that this model is unsatisfactory. Since these results also cannot be explained by a "pseudo-contact interaction" [58] or by polarization of the bonding electrons [60], a novel mechanism was postulated.

According to a simple term diagram (Fig. 10), the resonance properties depend solely on the number of electrons in the degenerate non-bonding metal orbitals σ_g' and δ_g and in the antibonding molecular orbital of π_g^* type.

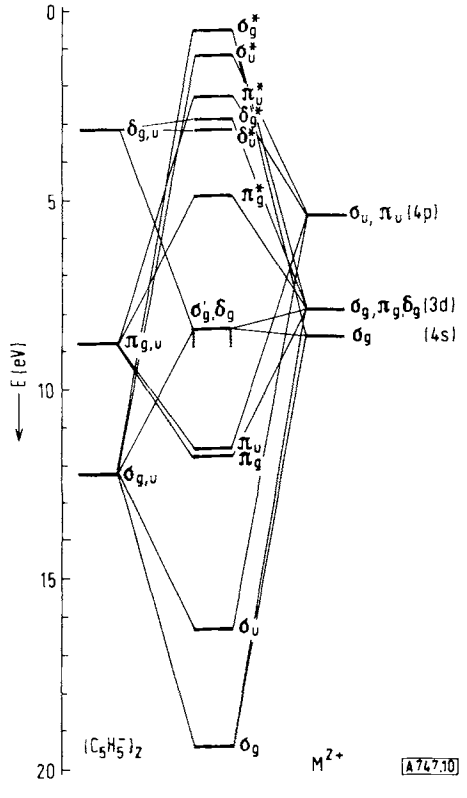


Fig. 10. Term diagram for $[M(C_5H_5)_2]$ (M = 3d metal).

In $V(\pi\text{-}C_5H_5)_2$, three electrons are distributed over the three orbitals of symmetry σ_g' and δ_g; these projecting vanadium orbitals, which are situated between the cyclic ligands, can overlap with the sterically favorable hydrogen orbitals of the ligand protons. The hydrogen-metal combination is occupied by an unpaired electron. Unlike in the above-mentioned transition *via* the carbon atoms, *positive* spin density can be transferred "directly" to the hydrogen atom in this way. The protons of the ligand thus experience strong deshielding, and the resonance signal appears at a *lower* field strength. This is true of all complexes with unfilled metal orbitals of σ_g and δ_g type. "Direct" spin transfer is no longer possible if these metal orbitals, which can interact favorably with the ring protons, are fully occupied by electron pairs (ferrocene). According to the term diagram given, further electrons (in the complexes $Co(\pi\text{-}C_5H_5)_2$ and $Ni(\pi\text{-}C_5H_5)_2$) are packed into the antibonding molecular orbitals of the type π_g^*. The free spin density in these orbitals which involves the ligand p_z carbon functions and metal functions comes from the central metal ion without spin reversal, so that, as in the model described earlier, the ring C atoms have a positive spin density, which is then transferred to the H atoms with sign reversal. The protons are thus strongly shielded, and signal displacements to higher field strengths result. The data in Table 1 are as expected. The shifts of protons of substituted cyclopentadienyl ligands and paramagnetic bis(π-benzene)-metal complexes also agree with this model [59].

It seems worth mentioning the result of an electron diffraction study on bis(π-cyclopentadienyl)metal complexes [61], according to which the H atoms are bent out of the plane of the ring and toward the central metal atom. This could be explained by weak hydrogen bonding between M and C.

On the basis of considerations such as this, it is at least questionable whether it is possible to distinguish between σ delocalization *via* metal-ligand bonds and the direct metal-hydrogen interaction corresponding to "through-space" electron-nucleus coupling [45]. The decay of positive spin densities with increasing distance from the central metal ion has until now been regarded as a typical characteristic of σ delocalization. However, the same is to be expected for direct M–H interaction, which is probably often the main cause of shifts of the ^{1}H-NMR signals. The direct interaction can be averaged out, for example, in the rapidly rearranging "tetrahedral" nickel(II) complexes, and pure π delocalization has in fact been found for these compounds [2]. Thus though very small spin densities can be detected experimentally, it is possible only in a few cases to determine definitely how the unpaired electrons are transferred to ligand atoms. From the chemist's point of view, however, it is usually most interesting to know how many unpaired electrons are present and how they are distributed, whilst the mechanism of transfer is of less importance. Altogether, the small contact shifts (a few ppm), though important in structure analysis, are not suitable as a source of information on the reactivity of a part of a molecule.

5.1. Pseudo-Contact Shifts

The NMR spectra of paramagnetic complexes are influenced additionally by possible pseudo-contact interactions [14], whose magnitude in accordance with

$$\frac{\Delta H}{H} = \frac{\beta^2 S(S+1)\,(3\cos^2 a_i - 1)}{27\, r_i^3\, kT}\,(g_\parallel + 2\,g_\perp)\,(g_\parallel - g_\perp) \qquad (12)$$

[60] *D. A. Levy* and *L. E. Orgel*, J.molecular Physics *3*, 583 (1961).

[61] *I. A. Ronova* and *N. V. Alekseew*, Ž. strukturnoj Chim. *7*, 886 (1966).

depends mainly on the steric relation of the nuclei to the central metal ion and on the anisotropy of the g factor. However, appreciable signal shifts occur only for compounds in which the unpaired electrons are largely localized on the central ion. These include complexes of the lanthanides [22,23] and of the actinides [62,63], in which the unpaired electrons remain in "inner" orbitals that are only slightly affected by the ligands, and complexes of 3d metals with "weak" ligands. It seems unlikely [67] from recent ^{14}N-NMR investigations on some ion associates [55] that the ^{1}H-NMR shifts observed for these substances are really due to pseudo-contact interactions [64–66].

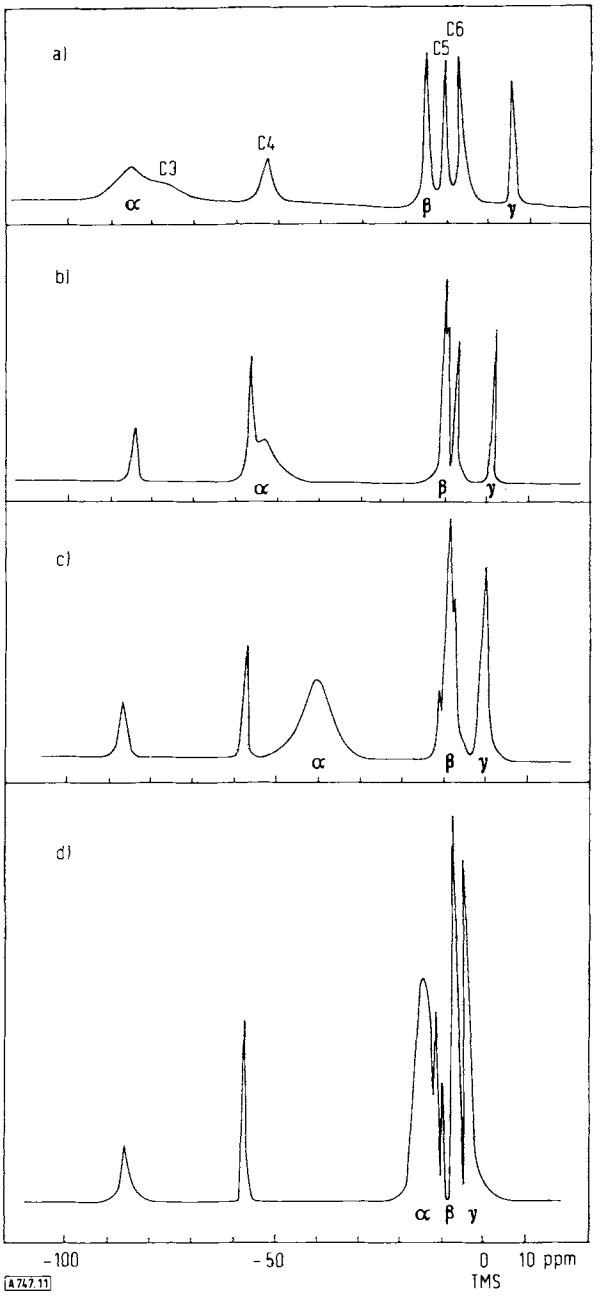


Fig. 11. ^{1}H-NMR spectra of bis(salicylaldehydato)bis(pyridine)-cobalt(II) with excess pyridine.

5.2. Time-Dependent Systems

Since even small changes in spin density cause relatively large NMR shifts, it is possible to detect even very short-lived complexes between a paramagnetic and a diamagnetic molecule [2,4,54,55]. It is particularly advantageous here that under the conditions of a fast exchange, *i.e.* when the diamagnetic partner is present in a large excess, the line widths found are relatively small. If, for example, excess pyridine is added to the cobalt(II) complex shown in Figure 9, the absorption signals of the pyridine protons become sharper (Fig. 11).

In the presence of small quantities of paramagnetic metal ions, it is possible in this way to determine the positions in the diamagnetic molecule where the metal ion is particularly readily attached from the line widths and shifts [2,4].

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Structure and Immunogenicity of Synthetic Antigens

By Erwin Rüde [*]

Synthetic antigens are often valuable tools in immunological research. They are usually linear or branched polypeptides, prepared by polymerization of N-carboxy-α-amino acid anhydrides or by polymerization of defined oligopeptides. Owing to their great variability, these simple antigens allow a systematic study of the chemical and physical parameters involved in immunogenicity, i.e. the ability of a substance to initiate an immune response in higher animals. The study of very simple synthetic antigens made possible the first detailed analysis of genetic factors controlling the immunogenicity of a substance. The results have led to a better understanding of many immunological phenomena, and have helped to explain the complex processes initiated by antigens that lead to a specific immune response.

1. Introduction

Many microorganisms (bacteria and viruses) are known to induce specific immunity in higher animals. In 1890, *von Behring* and *Kitasato* [1] demonstrated that immunity to diphtheria was associated with the presence of protective substances in the serum. These substances were called *antitoxins* since they were able to specifically neutralize diphtheria toxin. Subsequently, many additional antitoxins (*antibodies*), which are highly specific in their ability to react with the original invading organisms or their toxins, have been described.

Antibodies are serum proteins which, on the basis of their electrophoretic migration were classified in 1938 by *Tiselius* and *Kabat* [2] as γ-globulins. However, immunity and antibody formation can be induced not only by infection with living bacteria or viruses but also by injection of killed microorganisms, by macromolecular constituents of these microorganisms, and in general by many exogenous substances (usually macromolecular) of natural or synthetic origin. Those substances responsible for the induction of antibodies are known as *antigens*, or more recently also as *immunogens* (see below). Antigens not only induce the formation of antibodies, which circulate in the serum, but may also initiate defensive reactions that are mediated directly by certain cells. Like antibodies, these cells are specifically directed against the antigen in question, presumably with the aid of antibody-like receptors on the cell surface. This cellular immunity is of great importance in many immunological reactions, such as the rejection of transplanted foreign tissues or delayed hypersensitivity reactions.

In general, a substance must be foreign to the host in order to induce an immune response. Thus, the host is *immunologically tolerant* to its own constituents. Rare exceptions are seen in certain diseases known as autoimmune diseases. Tolerance toward exogenous substances that normally act as antigens can, however, also be produced experimentally. In the tolerant state the host is unable, for a limited period or for life, to form antibodies against the exogenous substance in question. The formation of antibodies to other foreign substances, on the other hand, is not affected. Thus, tolerance, like immunity, is very specific.

It is of great theoretical and practical interest to clarify the cellular and biochemical mechanisms of these processes. One of the most intriguing facets of this topic is the high specificity of all immunological reactions, which must ultimately depend upon the structure of the antigens and antibodies (or of the postulated antibody-like cell receptors).

When *Karl Landsteiner* [3] started his investigations on immunological specificity and its chemical foundations at the beginning of the present century, it was impossible to establish the structure of antibodies or of natural antigens, most of which are macromolecular substances. *Landsteiner* was, therefore, the first to use artificial antigens which were prepared by linking low molecular weight compounds (*e.g.* by azo coupling) to natural antigens, mostly proteins (cf. *e.g.* [4, 5]). After injection of proteins modified in this way, experimental animals formed antibodies that reacted specifically with the low molecular weight group introduced, as well as antibodies against the protein carrier itself. It was thus possible to vary the structure of the groups introduced into an antigen and to study the variation of the antibodies formed. Experiments of this nature led to the important discovery that antibodies are directed, not against the macromolecular antigen as a whole, but against specific structural subunits known as determinant groups. According to

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[1] See *W. Hennessen*, Dtsch. med. Wschr. *90*, 2181 (1965).

[2] *A. Tiselius* and *E. A. Kabat*, Science (Washington) *87*, 372, 416 (1938); *E. A. Kabat*, J. exp. Medicine *69*, 103, 119 (1939).

[3] *K. Landsteiner*: The Specificity of Serological Reactions. 2nd Edit., Harvard University Press, Cambridge, Mass., 1945.

[4] *O. Westphal* in *E. Lehnartz* and *B. Flaschenträger*: Physiologische Chemie. Springer, Heidelberg 1957, Vol. II/2b, p. 894.

[5] *O. Westphal*, Naturwissenschaften *46*, 50 (1959).

recent investigations, the active sites of antibody molecules are complementary to structures or determinant groups having a maximum size of about a hexasaccharide or of a tetra- to hexapeptide [6,8].

Extensive studies with artificial antigens have led to the view that antigens consist of two functionally different parts. *The high molecular weight carrier* is responsible for the antigenicity, *i.e.* for the stimulation of antibody formation, while *the determinant groups* determine the specificity of the antibody. Low molecular weight compounds that can function as determinant groups in the intact macromolecular antigen are themselves usually incapable of inducing antibody formation. These low molecular weight compounds can, however, be specifically bound by homologous antibodies. The same is true of many larger fragments of antigens. Serologically active substances of this type that are not themselves antigenic are known as *haptens*.

The structures of the determinant groups of natural antigens have been widely investigated during the past few decades. This approach has been particularly successful in establishing the determinants of polysaccharide antigens such as bacterial polysaccharides [4–7] and blood group substances [9]. The task has been more complicated in the case of proteins, since the structure of the determinant groups is determined in many cases by the secondary and tertiary structure of the protein [10].

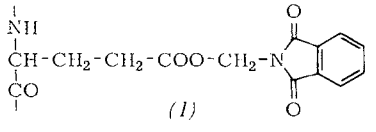
During these investigations, which were almost exclusively concerned with the serological specificity of antigens, the term "antigen" was occasionally used as a general term for substances that react specifically with antibodies, *e.g.* that precipitate them. The primary property of an antigen, *i.e.* its ability to stimulate the formation of antibodies or cellular immunity *in vivo*, was often ignored. It is only recently that growing interest has been shown in the question of the chemical and physical properties that a substance must have in order to be antigenic in the sense of the original definition. The term "immunogenicity" was introduced to allow a clear distinction between this property and "antigenicity" in the sense of serological specificity.

It has been known for a long time from experience with natural antigens that the immunogenicity of a substance can depend in a characteristic manner on its composition and molecular weight [11]. Thus whereas foreign proteins have generally been found to be very effective immunogens, many highly purified polysaccharides are not immunogenic, particularly in rabbits. In addition to chemically modified and partly degraded antigens of natural origin, increasing use has been made since 1960 of completely synthetic polypeptide antigens for the systematic study of immunogenicity [12]. Synthetic polypeptides have a known, relatively simple, and modifiable structure, and so facilitate the interpretation of immunological results.

2. Synthesis of Model Antigens

Synthetic model antigens have, so far, been built up almost exclusively from amino acids. In most cases, these polypeptide antigens have not been synthesized by stepwise methods and, therefore, have no defined amino acid sequence, but are homopolymers or copolymers which can be prepared relatively easily even with high molecular weights. The synthesis of poly-α-amino acids of this type has been reviewed by *Katchalski* and *Sela* [13], and is therefore merely illustrated here with the aid of a few examples.

The monomeric starting materials are *N*-carboxy-α-amino acid anhydrides (Leuchs anhydrides) *(2)*, which are usually prepared by reaction of amino acids with phosgene in inert anhydrous solvents (Fuchs-Farthing method). Functional groups in the side chains of the amino acids are generally blocked by protective groups. Only tyrosine is usually used in unsubstituted form. Benzyl (benzyl esters, benzyl ethers) and benzyloxycarbonyl groups, which can be removed after the polymerization by treatment with hydrogen bromide in glacial acetic acid, are adequate as protective groups in the majority of cases. In the synthesis of polypeptide derivatives of proteins (see Section 2.3), on the other hand, it is necessary to use protective groups



(1)

that can be removed under milder conditions. The trifluoroacetyl group [14] and the phthalimidomethyl group [15] [cf. *(1)*] have been used to protect, respectively, the ε-amino group of lysine and the γ-carboxyl group of glutamic acid; these two protective groups can be removed above pH = 10, *e.g.* by treatment with piperidine in aqueous solution at 0 °C.

2.1. Linear Poly-α-amino Acids

N-Carboxy-α-amino acid anhydrides *(2)* can polymerize in inert solvents in the presence of basic cata-

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[7] *O. Lüderitz, A. M. Staub*, and *O. Westphal*, Bacteriological Reviews *30*, 192 (1966).

[8] *J. W. Goodman, D. E. Nitecki*, and *J. M. Stoltenberg*, Biochemistry *7*, 706 (1968); *J. Haimovich, I. Schechter*, and *M. Sela*, Europ. J. Biochemistry *7*, 537 (1969).

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[10] *J. W. Goodman*, Immunochemistry *6*, 139 (1969).

[11] *E. A. Kabat* and *M. M. Mayer*: Experimental Immunochemistry, 2nd Edit. Charles C. Thomas, Springfield, Ill., 1961, p. 7.

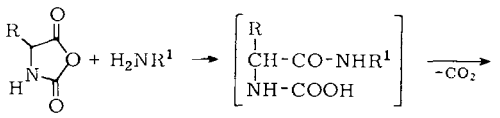
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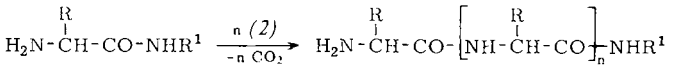
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[15] *M. Wilchek, A. Frensdorff*, and *M. Sela*, Arch. Biochem. Biophysics *113*, 742 (1966).

lysts with loss of carbon dioxide. The products are linear poly-α-amino acids *(3)* [13].



(2)



(3)

Racemization does not occur either in the preparation of the anhydrides or during the polymerization. The average degree of polymerization can be widely varied by variation of the quantity and nature of the basic initiator. Tertiary amines and sodium methoxide generally give high molecular weights 2×10^4—10^6), while secondary and primary amines give lower molecular weights (10^3—2×10^4). Primary and secondary amines are incorporated into the peptide chain as amides at the C-terminal end.

Copolymerization of different *N*-carboxy-amino acid anhydrides yields polymers with an approximately random distribution of the various types of amino acid residues over the polypeptide chain. The solubility of linear polymers and copolymers in water, which is of particular interest for model antigens, is largely dependent on the amino acid composition (hydrophilic or hydrophobic side chains), the secondary structure (random coil, α-helix, or β form "crosslinked" by intermolecular hydrogen bonds), and the molecular weight [13,22]. Highly ordered homopolymers are generally less soluble than copolymers. For example, poly-L-alanine and poly-D-alanine are insoluble in water, whereas the "copolymer" poly-D,L-alanine dissolves very readily.

2.2. Branched Poly-α-amino Acids

The synthesis of branched (multichain) poly-α-amino acids for immunological studies was developed mainly by *Sela et al.* [16]. Usually, poly-L-lysine [*(4)* in Fig. 1] or a linear copolymer containing lysine residues was used as a backbone for such polymers. The ε-amino groups of the lysine residues act as initiators for the polymerization of *N*-carboxy-amino acid anhydrides. Peptide side chains, whose lengths can be varied within wide limits, are polymerized onto the linear backbone.

This reaction can be carried out in aqueous media, since the polymerization proceeds more rapidly than the hydrolysis of the anhydrides. Linear polymers of about the same length as the side chains are formed as by-products; these are separated from the branched high molecular weight polymer by dialysis or gel filtration.

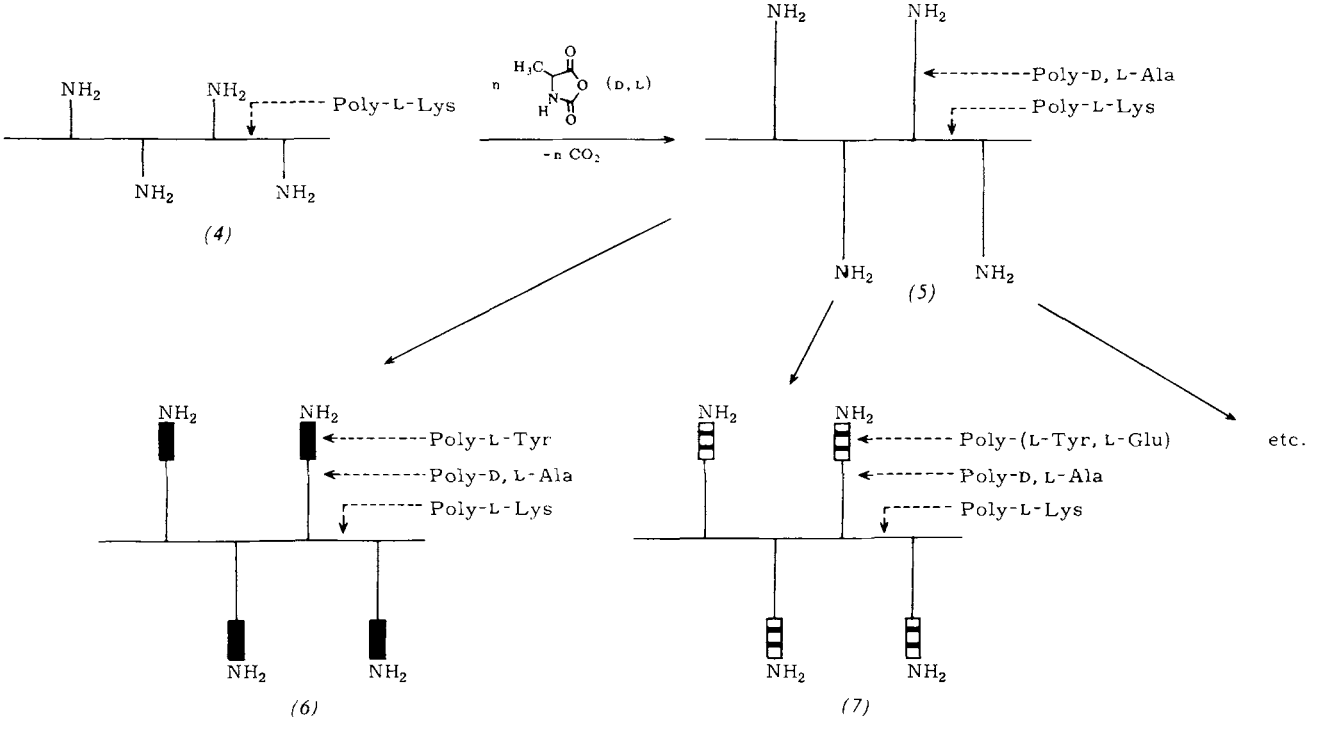


Fig. 1. Preparation of branched poly-α-amino acids according to *Sela* [12], schematic.

A branched polymer frequently used for the synthesis of model antigens is one having a poly-L-lysine backbone and poly-D,L-alanine side chains (on average 15 to 20 alanine residues) [17]. This polymer *(5)* is usually referred to as multichain poly-D,L-alanine. Poly-D,L-alanine side chains, unlike poly-L-alanine or poly-D-alanine side chains, make the polymer water-soluble. Similar polymers with polyproline side chains have recently been synthesized; like linear poly-L-proline or poly-D-proline, these polymers are water-soluble even when composed of amino acids of one optical configuration [18].

[16] *M. Sela, E. Katchalski*, and *M. Gehatia*, J. Amer. chem. Soc. *78*, 746 (1956).

[17] *M. Sela, S. Fuchs*, and *R. Arnon*, Biochem. J. *85*, 223 (1962).

[18] *J. Jaton* and *M. Sela*, J. biol. Chemistry *243*, 5616 (1968).

Each side chain of these branched poly-α-amino acids again ends with an amino group, which can be used as the starting point for the polymerization of any other amino acid, such as tyrosine or short copolymers of tyrosine and glutamic acid [cf. *(6)* and *(7)* in Fig. 1][17–19]. The total number of possible variations is immense.

2.3. Polypeptide Derivatives of Proteins

The ε-amino groups of the lysine residues and the N-terminal amino groups of proteins [*(8)* in Fig. 2] can also act as initiators for the polymerization of *N*-carboxy-amino acid anhydrides. Polypeptide chains are

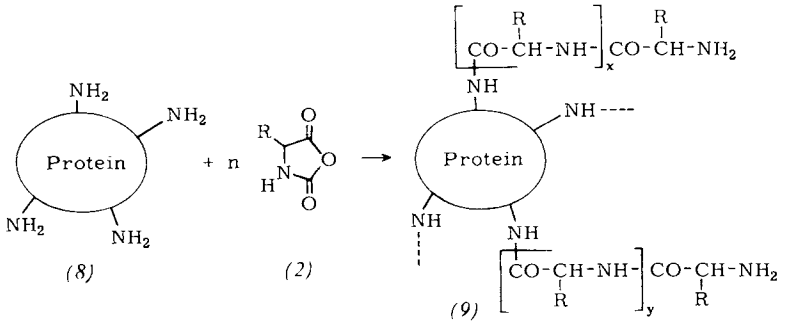


Fig. 2. Preparation of polypeptidyl proteins, schematic.

polymerized onto these amino groups under very mild conditions in aqueous solution at pH = 7[20]. However, all the amino groups of native proteins do not necessarily react with the anhydride, since the reactivities of individual amino groups are dependent on the secondary or tertiary structure of the protein[21]. The properties and the biological activity of polypeptide derivatives of the type *(9)* of enzymes, hormones[22,23], and antibodies[24] are naturally of great interest. Modified proteins of this type may in some cases be more valuable for immunological studies than proteins that contain only relatively small artificial determinants such as dinitrophenyl or arsanilic acid residues[25,26].

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[22] *E. Katchalski*, *M. Sela*, *H. I. Silman*, and *A. Berger* in *H. Neurath*: The Proteins, 2nd Edit. Academic Press, New York 1964, Vol. 2, p. 405.

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[24] *S. Fuchs* and *M. Sela*, J. biol. Chemistry *240*, 3558 (1965); *M. H. Freedman* and *M. Sela*, J. biol. Chemistry *241*, 2383, 5225 (1966); *F. Karush* and *M. Sela*, Immunochemistry *4*, 259 (1967); *K. J. Dorrington*, *M. H. Zarlengo*, and *C. Tanford*, Proc. nat. Acad. Sci. (USA) *58*, 996 (1967).

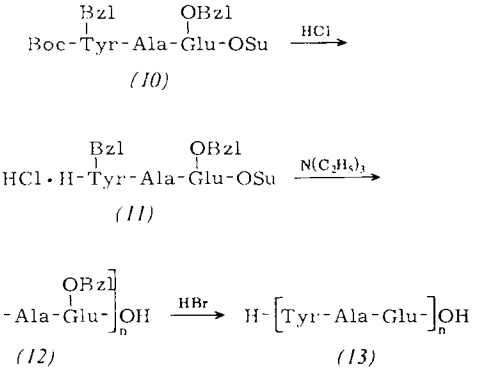
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[26] *I. Schechter*, J. exp. Medicine *127*, 237 (1968).

2.4. Polypeptides of Defined Sequence

The poly-α-amino acids described here are simple in structure but, owing to the method of synthesis, they have a random sequence of the amino acid residues. In many investigations, however, it is necessary to know the precise sequence of the amino acids. The stepwise synthesis of high molecular weight antigens having a specific amino acid sequence is laborious. *Prefabricated oligopeptides of known structure* are, therefore, used as the starting materials and are either converted into branched macromolecules by condensation with a linear backbone polymer, or are polymerized to form linear polymers with periodically repeating amino acid sequences.

E. Haber et al. have condensed the oligopeptide hormones angiotensin (octapeptide) and bradykinin (nonapeptide) onto a poly-L-lysine backbone according to the first method[27]. On average, one oligopeptide side chain was bound to every 33rd or every 5th lysine residue respectively *via* the C-terminal carboxyl group of angiotensin with carbodiimide, and *via* the N-terminal amino group of bradykinin with 1,2-diisocyanato-4-methylbenzene.



Boc = *tert*-butyloxycarbonyl; Bzl = benzyl; OSu = succinimidoxy.

An example of the synthesis of a model antigen *(13)* by the second method employed an oligopeptide whose N-terminal amino group was blocked by the *tert*-butyloxycarbonyl (Boc) residue and whose C-terminal end was activated as the *N*-hydroxysuccinimide ester (OSu) *(10)*. After removal of the Boc group with

[27] *E. Haber*, *F. F. Richards*, *J. Spragg*, *K. F. Austen*, *M. Vallotton*, and *L. B. Page*, Cold Spring Harbor Sympos. quantitat. Biol. *32*, 299 (1967).

hydrochloric acid, polymerization of the oligopeptide *(11)* (which was still protected as the hydrochloride) to *(12)* was started by liberation of the N-terminal amino group with triethylamine[28]; *(13)* was obtained from *(12)* by treatment with hydrogen bromide.

3. Immunological Methods

3.1. Immunization

The immunogenicity of a substance is nearly always determined by *in vivo* experiments. Only recently has it been possible to stimulate antibody formation *in vitro* using cultures of lymphoid cells or small fragments of spleen tissue[29]. To determine whether a substance is immunogenic, one naturally uses the immunization method that is thought, from existing knowledge and experience, to be most effective[30]. Synthetic model antigens are, therefore, nearly always injected together with an adjuvant, usually complete Freund's adjuvant.

Adjuvants increase the immunogenicity of antigens in a non-specific manner; nothing definite is known about their mode of action. Experience has shown that there is no generally applicable optimum immunization method. Antigens may be injected once or repeatedly, at various intervals, and in various doses. The success of a given course of immunization is decisively affected, *inter alia* by the nature of the antigen and the species of animal used. Consequently, statements about the immunogenicity of a substance are valid only for the conditions used in the tests. In particular, the observation that a substance is not immunogenic should not be generalized, since it is quite possible that a different immunization method or simply a different dose of the antigen could lead to antibody formation in another species of animal or in another strain of the same species.

Branched poly-D,L-alanine *(5)*, for example, was long thought to have no immunogenicity. However, antibody formation was detected in about 80% of the test animals (rabbits) when the polymer was injected into many intradermal sites instead of intramuscularly[31].

3.2. Detection of Antibodies

In addition to the immunization method, another important factor in the assessment of the immunogenicity of a substance is the sensitivity of the method for the detection of the antibodies. In investigations with synthetic antigens, generally applicable methods have been used both *in vitro* and *in vivo*[11,32]. The *in-vitro* methods include the precipitin test, passive hemagglutination, the complement fixation reaction, and binding assays with radioactively labeled antigens. Methods used for the detection of antibodies *in vivo* and for the detection of cellular immunity include skin tests. The treated animal is injected intradermally with small quantities of antigen, and if circulating antibodies are present, an allergic skin reaction appears after 15–20 min, possibly giving the typical appearance of the "Arthus' reaction" after about 5–6 hours. If, on the other hand, a skin reaction appears only after 1–2 days it is a delayed-type hypersensitivity (example: tuberculin reaction), which is not due to the presence of circulating antibodies but is mediated directly by specifically reactive cells.

The passive cutaneous anaphylaxis test (PCA test), on the other hand, is not carried out on the immunized animal itself. The serum sample to be tested for antibodies is transferred instead to a normal animal by intradermal injection. The antigen is then injected intravenously, together with a dye that makes the local antigen-antibody reaction visible.

4. Immunological Studies with Synthetic Antigens

4.1. Structural Aspects

Poly-α-amino acids were originally used mainly in physicochemical studies as simple models of the polypeptide chains of proteins[22]. The first observations that completely synthetic macromolecules of this type can also act as immunogens were due to *Stahmann et al.* (1955)[33]. In 1960, *Sela* and *Arnon*[34] synthesized a branched polymer and *Gill* and *Doty*[35] prepared a linear copolymer of amino acids; both of these products were found to be immunogenic. Many similar substances have been examined for immunogenicity in further investigations by various groups of workers (*Gill*, *Sela*, *Maurer*, *Benacerraf*, and others[12]).

4.1.1. Amino Acid Composition

The first question to arise was how the immunogenicity of synthetic polypeptides depended on their amino acid composition. The first systematic studies on this point, however, were carried out not with synthetic polypeptides but with polypeptide derivatives of gelatin, *i.e.* artificial antigens[19,36]. Gelatin itself is

[28] *M. Sela*, *B. Schechter*, *I. Schechter*, and *F. Borek*, Cold Spring Harbor Sympos. quantitat. Biol. *32*, 537 (1967).

[29] See, *e.g.*, *A. Globerson* and *R. Auerbach*, J. exp. Medicine *124*, 1001 (1966); *W. P. McArthur*, *A. J. Hutchinson*, and *M. J. Freeman*, Nature (London) *222*, 84 (1969).

[30] See, *e.g.*, *C. A. Chase* and *M. W. Chase*: Methods in Immunology and Immunochemistry. Academic Press, New York 1967, Vol. 1.

[31] *A. Rimon*, *D. Teitelbaum*, *S. Bauminger*, and *M. Sela*, Immunochemistry *4*, 505 (1967).

[32] *D. M. Weir*: Handbook of Experimental Immunology. Blackwell Scientific Publications, Oxford 1967.

[33] *M. A. Stahmann*, *H. Tsuyuki*, *K. Weinke*, *C. Lapresle*, and *P. Grabar*, C. R. hebd. Séances Acad. Sci. *241*, 1528 (1955).

[34] *M. Sela* and *R. Arnon*, Biochim. biophysica Acta *40*, 382 (1960).

[35] *T. J. Gill III* and *P. Doty*, J. molecular Biol. *2*, 65 (1960).

[36] *M. Sela* and *R. Arnon*, Biochem. J. *75*, 91 (1960); *77*, 394 (1960); *R. Arnon* and *M. Sela*, Biochem. J. *75*, 103 (1960).

only very weakly immunogenic, *i.e.* test animals on immunization produce only very small quantities of specific antibodies. By grafting peptide chains of various compositions onto the gelatin (Fig. 2) it was possible to determine which amino acids increased the immunogenicity of the gelatin (increased production of antibodies). Increased immunogenicity was observed primarily with some aromatic amino acids (tyrosine, phenylalanine), and also with cyclohexylalanine, the non-aromatic analog of phenylalanine. Amino acids such as serine, glutamic acid, and lysine had no effect. It is interesting to note that combinations of these inactive amino acids in the form of copolymers, *e.g.* of glutamic acid and lysine, lead to a pronounced increase in immunogenicity.

The simplest poly-α-amino acids, *i.e.* linear homopolymers *(3)* made from only one type of amino acid residue, appear, with few exceptions, to be non-immunogenic. Polyproline [37], polylysine [38,81], and polyglutamic acid [81], were weakly immunogenic in rabbits or guinea pigs, as demonstrated by the detection of antibodies or by delayed skin reactions (see Section 3.2). The non-immunogenicity of many homopolymers is not, however, due to inability of the animals to synthesize antibodies of suitable specificity. If amino acids in the form of short homopolymer chains were attached to a protein carrier (Fig. 2), antibodies that were directed against the homopolymers could be detected after injection of these artificial antigens, *i.e.* the homopolymers acted as determinant groups [25]. Homopolymers thus usually behave as haptens; they can initiate antibody formation only when combined with an immunogenic carrier.

The binding of linear homopolymers (haptens) to a protein carrier need not be covalent. The essentially non-immunogenic, negatively charged polyglutamic acid forms an insoluble complex with the positively charged methyl ester of serum albumin. Injection of this complex produces antibodies that are specifically directed against polyglutamic acid. Polylysine behaves similarly after complex formation with negatively charged carrier proteins [39]. It is even possible, in this way, to obtain antibodies against nucleic acids and against acidic polysaccharides that are non-immunogenic by themselves [40].

Unlike homopolymers, linear copolymers of two amino acids were found to be immunogenic in certain cases (depending on the amino acid composition and the species of animal examined), but usually not far all individuals of a species (genetic control, see Section 4.2). Finally copolymers of three, and particularly of four, different amino acids were generally effective immunogens [12,41].

Multichain poly-α-amino acids have been used mainly by *Sela et al.* for immunological studies. The starting polymer was usually multichain poly-D,L-alanine *(5)*, which, as mentioned earlier, was not immunogenic under the experimental conditions originally used by these authors. The influence of a variety of amino acids on the immunogenicity of this polymer was investigated by polymerizing them onto the ends of the D,L-alanine side chains (Fig. 1) [12,17,19,42]. Thus an average of 1.7 tyrosine residues bound per side chain was sufficient to convert multichain poly-D,L-alanine into an immunogen [cf. *(6)*]. Particularly effective immunogens were obtained by extension of the D,L-alanine side chains with short copolymers (about 6–7 amino acid residues) of glutamic acid combined with either tyrosine, histidine, or phenylalanine [cf. *(7)* in Fig. 1]. As in the case of gelatin, a combination of glutamic acid with lysine led also to an immunogenic polymer, whereas extension of the side chains with short homopolymers of glutamic acid or lysine alone had no effect.

However, no strict rules for the relation between amino acid composition and the immunogenicity of synthetic polypeptides can be derived from all these experiments. This may be due to the many factors that influence antibody formation *in vivo*. The following empirical rules can however be formulated:

1. Aromatic amino acids appear to be particularly effective in enhancing immunogenicity; however, they are not essential to the immunogenicity of a polymer, since polypeptides that do not contain aromatic amino acids can be effective immunogens.

2. A certain structural complexity appears to be important for immunogenicity. As is shown by the examples mentioned, the probability that a synthetic polypeptide will be immunogenic increases with the number of different amino acid residues present, and hence, in the case of copolymers, with the number of statistically possible amino acid sequences.

Several studies have shown that the induction of an immune response may be stimulated considerably by the cooperation of two types of lymphoid cells in antigen recognition. It has been suggested that these cells, with the aid of antibody-like cell receptors, possibly recognize different determinants of an antigen molecule [43,44]. One might expect, therefore, that substances having a complex structure with several different determinants will be more effective immunogens than very simple molecules such as homopolymers of amino acids.

Substantial agreement has been found between the results and the empirical rules derived from them for polypeptide derivatives of gelatin and for linear and highly branched synthetic poly-α-amino acids. The shape of a macromolecule is thus of no great importance to immunogenicity.

[37] *H. E. Jasin* and *L. E. Glynn*, Immunology *8*, 95 (1965).

[38] *I. Green, W. E. Paul*, and *B. Benacerraf*, J. exp. Medicine *123*, 859 (1966).

[39] *H. van Vunakis, J. Kaplan, H. Lehrer*, and *L. Levine*, Immunochemistry *3*, 393 (1966); *T. J. Gill III* and *H. W. Kunz*, Biochim. biophysica Acta *124*, 374 (1966).

[40] *O. J. Plescia, W. Braun*, and *N. C. Palczuk*, Proc. nat. Acad. Sci. USA *52*, 279 (1964).

[41] See, *e.g.*, *T. J. Gill III* and *P. Doty*, J. biol. Chemistry *236*, 2677 (1961); *P. H. Maurer, B. F. Gerulat*, and *P. Pinchuck*, J. biol. Chemistry *239*, 922 (1964); J. exp. Medicine *119*, 1005 (1964); *P. Pinchuck* and *P. H. Maurer*, J. exp. Medicine *122*, 665 (1965); J. Immunology *100*, 384 (1968).

[42] *S. Fuchs* and *M. Sela*, Biochem. J. *87*, 70 (1963).

[43] *N. A. Mitchison*, Cold Spring Harbor Sympos. quantitat. Biol. *32*, 431 (1967).

[44] *K. Rajewsky, V. Schirrmacher, S. Nase*, and *N. K. Jerne*, J. exp. Medicine *129*, 1131 (1969).

4.1.2. Steric Accessibility of Determinant Groups

Branched polypeptide antigens can be varied not only in their amino acid composition but also in the arrangement of the amino acid residues, so that it is relatively easy to study the influence of the steric accessibility of determinant groups on immunogenicity.

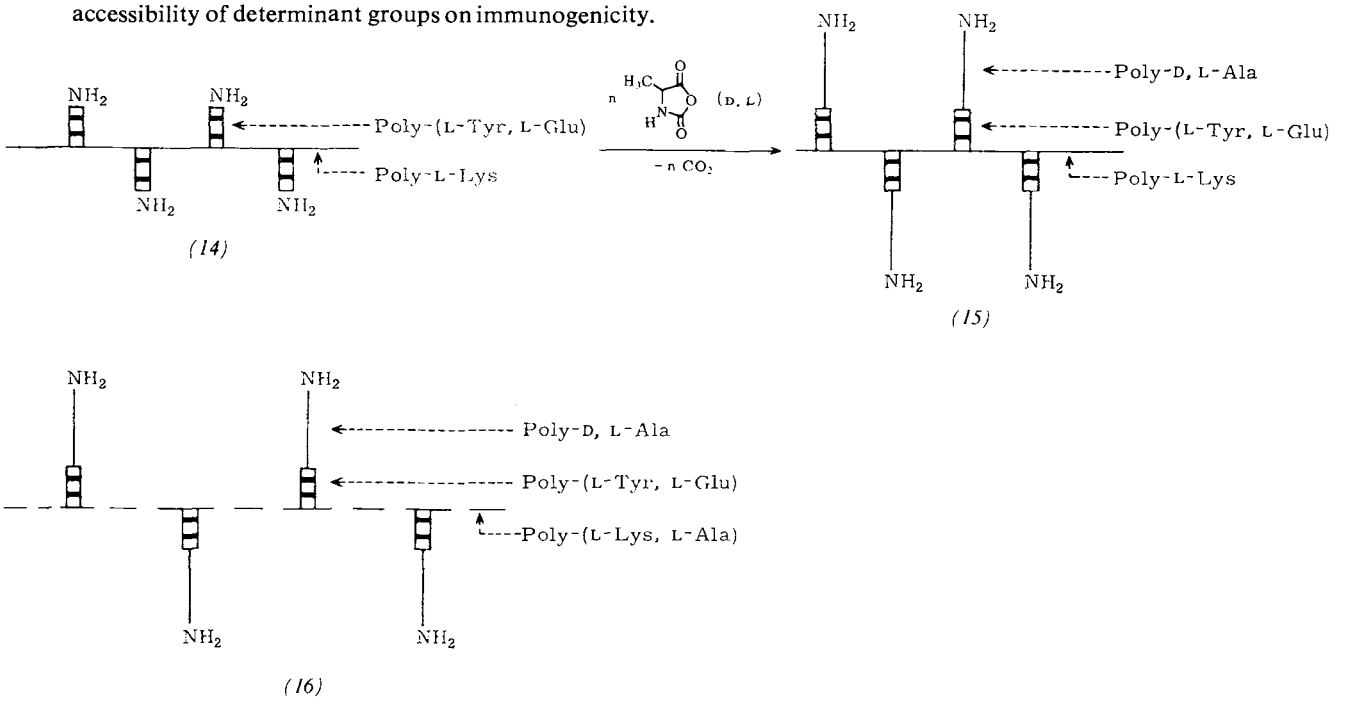


Fig. 3. Synthesis of branched poly-α-amino acids according to *Sela* [12], schematic.

Polymers were synthesized as follows and examined for their ability to initiate antibody formation [17]. Short copolymers of tyrosine and glutamic acid were polymerized directly onto a poly-L-lysine backbone. The resulting branched polymer *(14)* was found to be immunogenic. Extension of the side chains by about 20 D,L-alanine residues then gave a product *(15)* corresponding in molecular weight and in composition to the substance *(7)* described above. The tyrosine-glutamic acid sequences, however, were now in the interior of the molecule instead of on the outside. This polypeptide *(15)* was not immunogenic, though a related polymer with greater average distances between the side chains was. Such a polymer *(16)* was obtained by using a copolymer of lysine and alanine instead of pure poly-L-lysine as the backbone.

It follows from these investigations that those structures that are important to the immunogenicity of a macromolecule must be sterically accessible in order to initiate antibody formation. If this condition is satisfied, it does not appear to be essential that these structures (*e.g.* the Tyr-Glu sequences) are located at the end of, or within, the polypeptide side chains.

4.1.3. Chemical Substitution

In addition to amino acid residues a great variety of other groupings can be introduced into synthetic polypeptides [12]. Thus, the coupling products of poly-α-amino acids with simple aromatic haptens such as 2,4-dinitrophenyl groups [45,46], arsanilic acid [47,48], with penicillin [49], coenzymes [50], nucleosides [51], sugars [52], and glycolipids [52a] have been used as model antigens. Depending on the aim of the investigations, the focal point was either the immunogenicity of the substitution products or the specificity of the antibodies formed.

As was mentioned earlier, linear homopolymers such as poly-L-tyrosine and poly-L-lysine are usually very weakly or non-immunogenic. Immunogenic conjugates were obtained from both homopolymers by introduction of arsanilic acid residues or of dinitrophenyl, *p*-toluenesulfonyl (tosyl), or 5-dimethylamino-1-naphthalenesulfonyl (dansyl) groups respectively. Products containing about one hapten residue to about 20 amino acid residues were more immunogenic than more highly substituted derivatives, some of which were non-immunogenic [45,48].

[45] *F. S. Kantor, A. Ojeda,* and *B. Benacerraf,* J. exp. Medicine *117*, 55 (1963).

[46] *B. B. Levine, A. Ojeda,* and *B. Benacerraf,* J. exp. Medicine *118*, 953 (1963).

[47] *S. Leskowitz,* J. exp. Medicine *117*, 909 (1963); Nature (London) *199*, 85, 291 (1963).

[48] *F. Borek* and *Y. Stupp,* Immunochemistry *3*, 339 (1966).

[49] *C. W. Parker, A. L. deWeck, M. Kern,* and *H. N. Eisen,* J. exp. Medicine *115*, 803 (1962); *B. B. Levine,* Immunology *7*, 527 (1964).

[50] *H. Ungar-Waron* and *M. Sela,* Biochim. biophysica Acta *124*, 147 (1966); *J. C. Jaton* and *H. Ungar-Waron,* Arch. Biochem. Biophysics *122*, 157 (1967).

[51] *H. Ungar-Waron, E. Hurwitz, J. C. Jaton,* and *M. Sela,* Biochim. biophysica Acta *138*, 513 (1967).

[52] *E. Rüde, O. Westphal, E. Hurwitz, S. Fuchs,* and *M. Sela,* Immunochemistry *3*, 137 (1966).

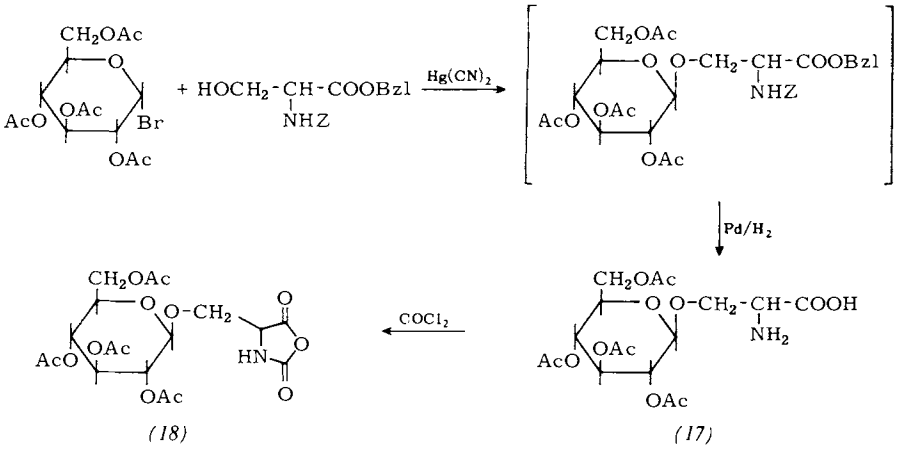
[52a] *R. Arnon, M. Sela, E. S. Rachaman,* and *D. Shapiro,* Europ. J. Biochemistry *2*, 79 (1967).

Sugars are of great importance in determining the serological specificity of many natural antigens [4,5,7,9], and can also function as determinant groups in artificial antigens [52–56]. Pure polysaccharides, however, very often exhibit an immunological behavior which in several respects differs from that of protein and polypeptide antigens. For example, they are usually non-immunogenic in rabbits [11], but function as haptens, which can stimulate the synthesis of polysaccharide-specific antibodies only when combined with an immunogenic carrier (*e.g.* a protein) (see Section 4.1.1). In contrast to protein antigens immunization of mice with capsular polysaccharides of pneumococci, leads to antibody formation only at very low antigen doses, while no antibodies are detectable, at least in the serum of the animals, when the usual higher doses are used.

Higher doses of polysaccharides very readily produce immunological "paralysis" in the animals. As in the state of experimentally induced tolerance, the immunologically paralyzed mice are apparently incapable of forming antibodies against the polysaccharide in question for some time. Recent studies indicate that the state of immunological paralysis may not necessarily be identical with that of tolerance (see Section 4.1.5) [57,58].

In view of these immunological properties of polysaccharides, it appeared to be of interest to examine the influence of sugars on the immunogenicity of synthetic polypeptides. For example, is it possible to convert multichain poly-D,L-alanine *(5)*, which is only slightly immunogenic, into a good immunogen by the attachment of sugars in the same way as by grafting tyrosine peptides?

Since aromatic rings may be sufficient by themselves to confer immunogenicity, it was necessary to develop a method of linking sugars to synthetic polypeptides without the usual aromatic connecting links [53,55]. The sugars were bound to polypeptides *via* *O*-glycosides of serine, which also link the carbohydrate moiety to the peptide chain in many glycoproteins. The *O*-acetylated serine glycosides *(17)* of several mono- and disaccharides were prepared, as illustrated for the case of glucose, and converted into the *N*-carboxy amino acid anhydrides *(18)* by treatment with phosgene [59]. Using these anhydrides, serine glycosides could be polymerized onto the side chains of multichain poly-D,L-alanine *(5)* (an average of 1.5–2.5 glycosyl-serine residues per side chain) in the same way as other amino acids [52].



(18) *(17)*

The resulting sugar-polypeptide conjugates [*(19)* in Fig. 4] were tested for their immunogenicity in rabbits. Under the conditions used, multichain poly-D,L-alanine *(5)* itself was found to be weakly immunogenic for about 50% of the animals, whereas practically no antibody formation was observed on injection of the polymers containing glucose, *N*-acetylglucosamine, or lactose. With polymers containing galactose, rhamnose, or cellobiose, the antibody titer was approximately the same as or slightly higher than that found with multichain poly-D,L-alanine *(5)* [60]. In agreement with the behavior of polysaccharides, therefore, the sugars studied, unlike aromatic amino acids or nucleosides [51], appear to be incapable of significantly increasing the immunogenicity of the carrier polypeptide.

Further experiments were carried out to establish whether the immunogenicity of sugar-polypeptide conjugates could be enhanced by the additional incorporation of long-chain fatty acids as "internal adjuvants". Fatty acids in the form of glycolipids are important constituents of natural adjuvants, such as

[53] *W. F. Goebel* and *O. T. Avery*, J. exp. Medicine *50*, 521 (1929).

[54] *W. F. Goebel*, J. exp. Medicine *68*, 469 (1938); Nature (London) *143*, 77 (1939); J. exp. Medicine *72*, 33 (1940).

[55] *O. Lüderitz*, *O. Westphal*, *A. M. Staub*, and *L. Le Minor*, Nature (London) *188*, 556 (1960); *A. M. Staub*, *S. Stirm*, *L. Le Minor*, *O. Lüderitz*, and *O. Westphal*, Ann. Inst. Pasteur *111* (Suppl.) 47 (1966).

[56] *K. Himmelspach*, Hoppe-Seyler's Z. physiol. Chem. *350*, 5 (1969).

[57] *L. D. Felton*, *G. Kauffmann*, *B. Prescott*, and *B. Ottinger*, J. Immunology *74*, 17 (1955).

[58] *J. G. Howard* and *G. W. Siskind*, Clinical exp. Immunology *4*, 29 (1969); *J. G. Howard*, *J. Elson*, *G. H. Christie*, and *R. G. Kinsky*, Clinical exp. Immunology *4*, 41 (1969).

[59] *E. Rüde* and *M. Meyer-Delius*, Carbohydrate Res. *8*, 219 (1968).

[60] *E. Rüde* and *M. Meyer-Delius*, to be published.

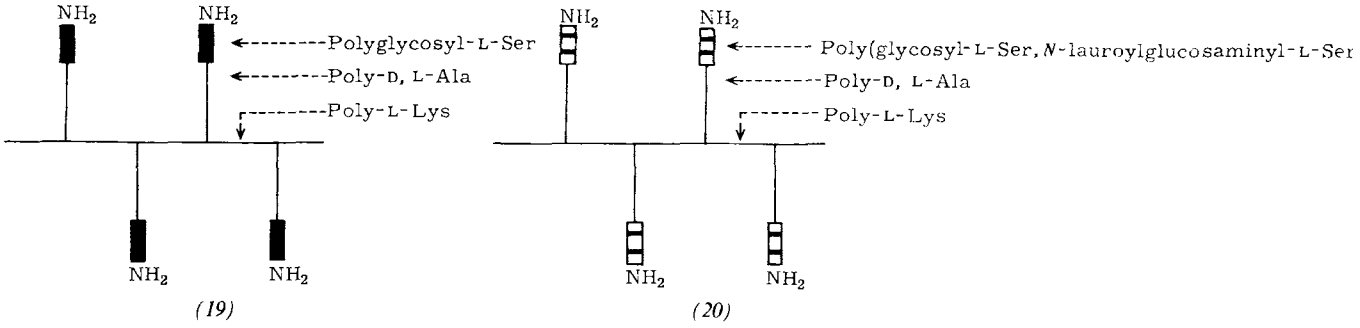
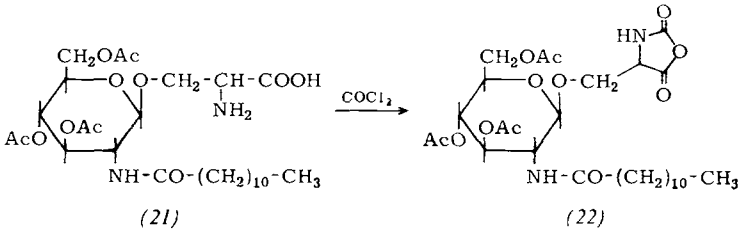


Fig. 4. Synthesis of branched sugar-polypeptide conjugates, schematic; Glycosyl = β-D-glucosyl, β-D-galactosyl, α-L-rhamnosyl, β-D-*N*-acetylglucosaminyl, β-D-lactosyl, or β-D-cellobiosyl.

certain wax fractions from tubercle bacilli [61] or the endotoxins of gram-negative bacteria [62]. By analogy with these natural glycolipids, lauric acid bound to the amino group of glucosamine was linked to synthetic antigens [*(20)* in Fig. 4]. *O*-Peracetylated *N*-lauroyl-glucosaminyl-serine *(21)* was synthesized and polymerized onto the side chains of multichain poly-D,L-alanine [*via* its *N*-carboxy amino acid anhydride *(22)*], together with one of the above-mentioned serine glycosides, in the form of short copolymers (*e.g.* 0.6 *N*-lauroyl-glucosaminyl-serine and 2.0 glucosyl-serine residues per side chain).

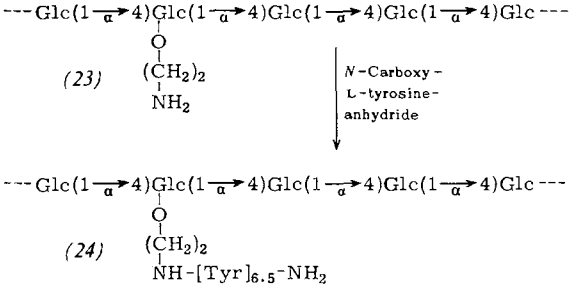


(21) *(22)*

In most cases the resulting conjugates *(20)* containing fatty acids were more effective immunogens than the corresponding ones *(19)* containing simple serine glycosides only [60]. Due to the presence of fatty acid residues these polymers *(20)* were highly aggregated and at a content of about 0.7 *N*-lauroyl-glucosamine residues per side chain were insoluble in water. This property may contribute to the increased immunogenicity of such conjugates. (The influence of the state of aggregation on the immunogenicity of a substance is discussed in Section 4.1.4.) As shown by inhibition experiments, the antibodies formed were directed against both the glycosyl-serine and the *N*-lauroyl-glucosaminyl-serine residues. In the latter case the fatty acid residue appeared to be an essential part of the determinant group.

Model antigens containing polysaccharides as "backbones" instead of linear poly-α-amino acids have been synthesized for further investigations. In particular, simple peptide side chains were to be introduced into polysaccharides to determine the minimum conditions under which a non-immunogenic polysaccharide becomes immunogenic. With this in mind, dextran and amylose, both of which are non-immunogenic for rabbits, have been aminoethylated with ethyleneimine (every 7th to 40th glucose residue was substituted) [see *(23)*]. As in the synthesis of branched polypeptides, side chains of 6–7 tyrosine residues each were polymerized onto the primary amine groups by means of *N*-carboxy-L-tyrosine anhydride to form *(24)* [63].

Following the immunization of rabbits with poly-L-tyrosyl-polysaccharides *(24)* having both low and high degrees of substitution, specific antibodies were detected in the serum. Thus even relatively few tyrosine chains are sufficient to confer immunogenicity. Aggregation and low solubility of these polymers containing tyrosine peptides may also contribute to their immunogenicity. The antibodies formed in the



case of the dextran derivative are directed *both against the tyrosine side chains and against dextran itself*, whereas those formed in the case of the amylose derivative are directed *only against the tyrosine side chains*. This may be due to a natural tolerance of the animals to glycogen, which in its basic structure of (1→4)-α-linked glucose units is closely related to amylose. Finally, treatment of rabbits with polymers in which tyrosine side chains were attached to a polyvinyl alcohol backbone also led to a very weak

[61] *H. Finger*, Klin. Wschr. *44*, 1105 (1966).

[62] *O. Lüderitz, K. Jann*, and *R. Wheat* in: Comprehensive Biochemistry. Elsevier, Amsterdam, 1968, Vol. 26A, p. 105.

[63] *C. Sorg*, Diplomarbeit, Universität Freiburg 1967.

antibody response directed against the tyrosine chains[64]. According to *Gill* and *Kunz*[86], several other vinyl polymers were also immunogenic when injected in doses of 1 to at most 100 μg (see Section 4.1.5).

4.1.4. Molecular Weight and State of Aggregation of the Immunogen

It has long been accepted that a high molecular weight is a necessity if a substance is to be immunogenic. No general values can be given for the minimum molecular weight, which can evidently differ considerably from substance to substance. In the case of dextran, *Kabat* and *Bezer* found a sharp decrease in immunogenicity (in humans) when the average molecular weight was decreased from 90000 to 50000[65]. On the other hand, in studies with polypeptide antigens it was found that the molecular weight is frequently of surprisingly little importance to immunogenicity. Linear copolymers of alanine, tyrosine, and glutamic acid having an average molecular weight of 4000, for example, were similar in immunogenicity to polymers of higher molecular weight[17,66]. Among the oligotyrosine peptides the hexapeptide and the tripeptide, and even *N*-acetyltyrosine, were found to be immunogenic when coupled with, on average, one arsanilic acid residue[67].

Oligolysines whose terminal α-amino groups were substituted with 2,4-dinitrophenyl residues showed a very remarkable dependence of immunogenicity on the number of lysine residues[68,69]. All the substituted oligomers up to the hexapeptide were non-immunogenic, whereas α-dinitrophenyl-heptalysine and all higher homologs could induce both antibody formation and delayed hypersensitivity in guinea pigs.

Another surprising observation was that α-dinitrophenyl-nonalysine lost its immunogenicity when an L-lysine residue in the middle of the peptide chain was replaced by a D-lysine residue[70]. It has also been shown particularly clearly by these experiments that delayed type skin reactions could be caused only by substances that were themselves immunogenic, and not by haptens[69].

In experiments with low molecular weight substances one cannot rule out the possibility that the immunogenicity of these compounds arises only through fixation to body proteins or cells, particularly since it is known (see Section 4.1.1) that the binding of a hapten to a carrier need not be covalent. Even if such complex formation does occur, however, it does not explain the very marked dependence of immunogenicity on the chain length in the case of the oligolysine peptides.

As was mentioned in connection with synthetic sugar-polypeptide conjugates containing fatty acids, the association of molecules to form large aggregates may also have a considerable influence on immunogenicity. This was demonstrated particularly well in studies on the immunogenicity of immune globulin G (IgG)[71]. Normal preparations of bovine IgG usually contain small quantities of aggregated material in addition to IgG monomers, and when injected into mice without an adjuvant, induce antibody formation. After separation of the aggregated fraction by centrifugation, the aggregate-free material is no longer immunogenic, but leads to partial tolerance to bovine IgG after injection.

These and other experiments corfirm the long-established empirical rule that particles such as viruses, bacterial flagellae, *etc.* are much more potent immunogens than soluble proteins[72,73]. Since particles are more readily taken up by phagocytic cells (macrophages) than soluble materials, these observations are often regarded as an argument in favor of the participation of macrophages in induction of an immune response[74].

4.1.5. Optical Configuration of the Amino Acid Residues

As was first shown by *Landsteiner* and *van der Scheer* with tartaric acid, antibodies are capable of differentiating between the enantiomeric forms of determinant groups[75]. For example, antisera directed against a peptide consisting of L-amino acids do not cross-react with the corresponding peptide from D-amino acids, and *vice versa*. In the present discussion, however, we are not so much interested in the serological specificity of a polypeptide synthesized from L- or D-amino acids as in its immunogenicity and the following results are important in this connection.

As described above, the immunogenicity of gelatin or of multichain poly-D,L-alanine *(5)* could be considerably enhanced by the attachment of short peptide chains composed of L-tyrosine. The same effect is found with the corresponding peptides from D-tyro-

[64] *C. Sorg*, Dissertation, Universität Freiburg 1969.

[65] *E. A. Kabat* and *A. E. Bezer*, Arch. Biochem. Biophysics *78*, 306 (1958).

[66] *P. H. Maurer*, J. Immunology *90*, 493 (1963).

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[68] *S. F. Schlossmann*, *A. Yaron*, *S. Ben Efraim*, and *H. A. Sober*, Biochemistry *4*, 1638 (1965).

[69] *S. F. Schlossman*, *S. Ben Efraim*, *A. Yaron*, and *H. A. Sober*, J. exp. Medicine *123*, 1083 (1966); *J. R. David* and *S. F. Schlossman*, J. exp. Medicine *128*, 1451 (1968).

[70] *A. Yaron* and *S. F. Schlossman*, Biochemistry *7*, 2673 (1968).

[71] *D. W. Dresser*, Nature (London) *191*, 1169 (1961); Immunology *5*, 378 (1962).

[72] *F. A. Anderer* and *H. D. Schlumberger*, Immunochemistry *6*, 1 (1969); *R. N. Pinckard*, *D. M. Weir*, and *W. H. McBride*, Clinical exp. Immunology *2*, 331 (1967); *R. Gallily* and *J. S. Garvey*, J. Immunology *101*, 924 (1968).

[73] *G. L. Ada*, *C. R. Parish*, *G. J. V. Nossal*, and *A. Abbot*, Cold Spring Harbor Sympos. quantitat. Biol. *32*, 382 (1967); *G. L. Ada*, *G. J. V. Nossal*, *J. Pye*, and *A. Abbot*, Nature (London) *199*, 1257 (1963); *C. R. Parish*, *P. G. Lang*, and *G. L. Ada*, Nature *215*, 1202 (1967); *G. L. Ada* and *C. R. Parish*, Proc. nat. Acad. Sci. USA *61*, 559 (1968).

[74] See, *e.g.*, *E. R. Unanue* and *B. A. Askonas*, Immunology *15*, 287 (1968); *E. Kölsch* and *N. A. Mitchison*, J. exp. Medicine *128*, 1059 (1968); *D. Rowley*, Experientia *22*, 1 (1966).

[75] *K. Landsteiner* and *J. van der Scheer*, J. exp. Medicine *50*, 407 (1929).

sine when polymerized onto these weakly immunogenic carriers, which themselves consist mainly of L-amino acids [76].

On the other hand, several authors found that polypeptides composed *exclusively* of D-amino acids were not immunogenic under the usual immunization conditions (about 1–10 mg of polypeptide per injection in the case of rabbits) [76–78]. However, the incorporation of 3% of L-amino acids into pure D-polymers was sufficient to convert the latter into weak immunogens, and the immunogenicity was further increased by a higher content of L-amino acids [79]. *Gill et al.* [80] then found – and this has since been confirmed [79,81] – that even polymers consisting entirely of D-amino acids are immunogenic when injected in very small quantities. Investigations on mice with D- and L-polymers of analogous composition gave the relation shown in Figure 5 for the antibody titer and the immunization dose [82].

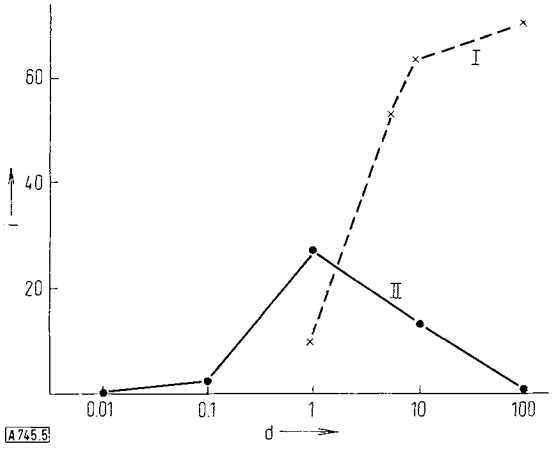


Fig. 5. Immunogenicity of copolymers of D- and L-amino acids having analogous composition, as a function of the dose used for immunization, according to *Janeway* and *Sela* [82]. I: L-polymer; II: D-polymer; *d*: dose in μg of polymer per mouse; i: antibody titer in % of 5 μg of radioactively labeled antigen bound to antibody per ml of serum.

Whereas the antibody titers increase with increasing dose for the L-polymer, reaching a plateau at 10 μg per mouse, the antibody titer obtained after immunization with the D-polymer passes through a maximum at about 1 μg per mouse, and falls off rapidly with larger doses. When injected without an adjuvant, the D-polymer, unlike the L-polymer, leads to immunological paralysis or tolerance even in very small doses. Similar experiments with rabbits also showed that polymers of D-amino acids produced no appreciable booster reaction [*] following secondary injection [81]. Polymers of D-amino acids thus behave in nearly all respects like certain polysaccharides (see Section 4.1.3). It seems reasonable to correlate this with the *very slow enzymatic degradation* observed for polymers of D-amino acids and for some polysaccharides [83–85].

Branched polymers having a linear poly-L-lysine backbone, poly-L-proline side chains, and short copolymers of D-tyrosine and D-glutamic acid attached to these side chains [cf. *(7)*] behaved like polymers that consist entirely of D-amino acids, despite their high content of L-amino acids (about 90%). Since no endopeptidases capable of cleaving the peptide linkage between L-proline residues have been yet detected, this becomes comprehensible because polymers of this type would behave as D-polymers insofar as their enzymatic degradation is concerned [18].

Even pure vinyl polymers such as polyvinylamine, polymethacrylic acid, and polyvinylpyrrolidone, which certainly show practically no susceptibility to enzymatic degradation, are, like polymers of D-amino acids, weakly immunogenic in rabbits when injected in very small quantities [86].

The possibility of enzymatic degradation thus appears to be of great importance for the immunological properties of a substance. Antigens that suffer little or no degradation and are eliminated from the organism only very slowly readily cause immunological paralysis, particularly when injected in fairly large doses. Paralyzed animals, like tolerant animals (see Section 1), appear to be incapable of producing circulating antibodies against the antigen in question, even after further injections of antigen with adjuvant.

Recent studies with polysaccharide antigens have shown that contrary to earlier observations, paralyzed mice have roughly the same number of cells forming antibody as do immunized animals, though no antibodies are detectable in their serum [58]. The antibody formation thus does not appear to be blocked as such. It is therefore proposed that the antibodies synthesized are immediately intercepted by the antigen and are then broken down enzymatically, while the antigen returns unchanged to the circulation. It is not yet certain whether this interpretation of the phenomenon of immunological paralysis is also generally valid for other antigens such as polymers of D-amino acids, or whether true blockage of antibody formation, and hence a state of tolerance, predominates.

[76] *M. Sela* and *S. Fuchs*: Proc. Sympos. on Molecular and Cellular Basis of Antibody Formation, Prague. Publishing House of the Czechoslovak Academy of Sciences 1965, p. 43.

[77] *T. J. Gill III, H. J. Gould*, and *P. Doty*, Nature (London) *197*, 746 (1963); *P. H. Maurer*, Proc. Soc. exp. Biol. Med. *113*, 553 (1963).

[78] *F. Borek, Y. Stupp, S. Fuchs*, and *M. Sela*, Biochem. J. *96*, 577 (1965).

[79] *Y. Stupp* and *M. Sela*, Biochim. biophysica Acta *140*, 349 (1967).

[80] *T. J. Gill III, H. W. Kunz, H. J. Gould*, and *P. Doty*, J. biol. Chemistry *239*, 1107 (1964).

[81] *T. J. Gill III, H. W. Kunz*, and *D. S. Papermaster*, J. biol. Chemistry *242*, 3308 (1967).

[82] *C. A. Janeway jr.* and *M. Sela*, Immunology *13*, 29 (1967).

[*] In comparison to the "primary response" this is the rapid and increased production of antibody upon secondary injection of an antigen (secondary response).

[83] *T. J. Gill III, D. S. Papermaster*, and *J. F. Mowbray*, J. Immunology *95*, 794 (1965); *C. B. Carpenter, T. J. Gill III*, and *L. T. Mann jr.*, J. Immunology *98*, 236 (1967); *G. Zubay*, Nature (London) *200*, 483 (1964).

[84] *C. A. Janeway jr.* and *J. H. Humphrey*, Immunology *14*, 225 (1968).

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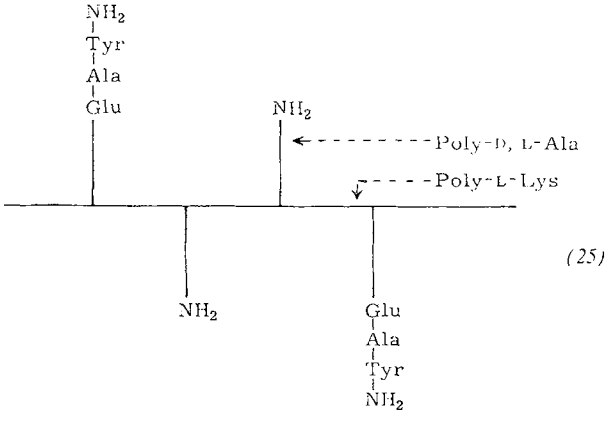
[86] *T. J. Gill III* and *H. W. Kunz*, Proc. nat. Acad. Sci. USA *61*, 490 (1968).

4.1.6. Secondary Structure and Serological Specificity

In addition to model antigens prepared by polymerization or copolymerization of various amino acids, increasing use has recently been made of polypeptide antigens having a specific amino acid sequence, which allow a more precise interpretation of the immunological results, particularly with regard to the specificity of the antibodies formed.

The structure of the determinant groups of native proteins, as was mentioned earlier, is often determined, not directly by the linear sequence of amino acids, but by the three-dimensional configuration of the peptide chains. Using a synthetic antigen *(13)* consisting of repeating tripeptide units (Tyr-Ala-Glu-)$_n$ (see Section 2.4), *Sela et al.* were able to demonstrate clearly the influence of the secondary structure on the serological specificity of a polypeptide chain [28]. The linear polymer *(13)* is in the form of an α helix under physiological conditions, and is immunogenic for rabbits. The precipitation of the resulting antibodies with the helical polymer is not inhibited by the tripeptide Tyr-Ala-Glu or by the hexapeptide (Tyr-Ala-Glu-)$_2$. Moreover, these antisera do not cross-react with a branched polymer *(25)* having the same sequence Tyr-Ala-Glu at the ends of the side chains.

Conversely, antibodies obtained by immunization with this branched polymer exhibited practically no reaction with the linear helical polymer *(13)*. The



(25)

specificity of the antibodies is thus determined by the conformation of the peptide chain (α helix) in the first case (conformational determinant), and not simply by the linear sequence of the amino acids (sequential determinant), as with the branched polymer.

A polymer having the repeating sequence (Pro-Gly-Pro-)$_n$, which was synthesized as a model for collagen, probably exists in solution, like collagen, as a three-stranded helix [28]. This similarity of secondary structure is probably the reason for the positive cross reaction of the antibodies formed in response to this polymer with collagen from various sources.

It follows as a necessary conclusion from these observations that the frequently discussed "processing" of an antigen [87,90] in the induction of antibody formation cannot consist in extensive enzymatic degradation into small fragments, or at least not before recognition of the specificity of the determinant groups. Degradation of this nature would lead to loss of the tertiary and secondary structures of proteins or polypeptides, *i.e.* destruction of those features against which the antibodies are directed in many cases [10]. The immunogenicity exhibited by vinyl polymers under certain conditions also leads to the conclusion that degradation of the antigen is not necessary for the specific stimulation of antibody formation itself. On the other hand, the results described in Section 4.1.5 appear to indicate that enzymatic degradation is very important for the removal of antigen that has been circulating in the organism for a long time, since this can otherwise lead to immunological paralysis or tolerance.

[87] *B. Benacerraf, A. Ojeda*, and *P. H. Maurer*, J. exp. Medicine *118*, 945 (1963).

4.2. Genetic Aspects

It is well known that individuals of the same species often exhibit considerable differences in antibody formation against certain substances. Studies with protein antigens showed that this characteristic can be transmitted from one generation to the next [88]. It was not possible at first to clarify the relations, since the proteins used contained a large number of determinant groups (mostly unknown), and the formation of antibodies against such complex molecules is presumably controlled by several genes. The situation was greatly simplified, however, by the use of synthetic antigens that have proved particularly useful for investigations of this type.

The studies on the genetic control of antibody formation against synthetic antigens were stimulated by the observation that only about 40% of Hartley strain guinea pigs formed antibodies against a linear copolymer of L-lysine and L-glutamic acid [66], and also against derivatives of poly-L-lysine, such as 2,4-dinitrophenyl-, *p*-toluenesulfonyl-, and benzylpenicilloyl-polylysines [45,89]. It was then shown that for individual animals, either all or none of these hapten-polylysine conjugates were immunogenic, and that the ability to recognize this group of macromolecules as immunogens is determined by a dominant autosomal gene [46].

The failure of the immune response to occur in the group of animals that lack this "polylysine gene" (nonresponders) is not, however, due to the inability of these animals to synthesize antibodies of appropriate specificity, since anti-hapten antibodies were readily formed if the haptenic groups were coupled to another carrier or if *e.g.* dinitrophenylpolylysine was injected in the form of an insoluble complex with egg albumin [38]. In this case, the egg albumin functioned as carrier for the macromolecular hapten (see Section 4.1.1), and the animals produced antibodies of the same specificity as those formed by

[88] *E. Carlinfanti*, J. Immunology *59*, 1 (1948); *J. H. Sang* and *W. R. Sobey*, J. Immunology *72*, 52 (1954).

[89] *B. B. Levine, A. Ojeda*, and *B. Benacerraf*, Nature (London) *200*, 544 (1963).

animals for which dinitrophenyl-polylysine was itself immunogenic (responders). It is thus fairly certain that the "polylysine gene" is not directly involved in the synthesis of the antibody combining site. The two groups of animals also do not appear to differ significantly in their ability to degrade polylysine derivatives enzymatically [90].

The delayed hypersensitivity reaction, which is not due to circulating antibodies but is directly mediated by cells, could be produced in sensitized animals by intradermal injection of dinitrophenyl-polylysine only if the animals belonged to the group for which dinitrophenyl-polylysine was immunogenic. It did not appear in animals that lacked the "polylysine gene" and in which dinitrophenyl-polylysine functioned only as a hapten [38]. Recently it could be shown that the ability to respond to dinitrophenyl-polylysine can be transferred with bone marrow, spleen, or lymph node cells from normal responder guinea pigs into lethally irradiated nonresponder animals [91a]. Upon immunization about 15 days after cell transfer the recipients were able to form specific antibodies and to give delayed hypersensitivity reactions towards dinitrophenyl-polylysine. For reasons not yet understood it was not possible, however, to elicit a delayed skin reaction in nonresponder animals which had received one hour before lymphoid cells from responders previously immunized with dinitrophenyl-polylysine, though a passive sensitization by transferred cells was successful with other antigens [91].

Genetic differences have also been observed on immunization of mice of various inbred strains with linear and branched polypeptides [92,93]. In the latter case there were differences in the quantities of antibodies formed (Table 1) [94]. The antigens used were synthesized from multichain poly-D,L-alanine *(5)*, the side chains of which were elongated either with short polymers of L-glutamic acid or with short copolymers of L-phenylalanine and L-glutamic acid, L-tyrosine, and L-glutamic acid [cf. *(7)*], or L-histidine and L-glutamic acid.

When the first two polymers were tested, mice of strain CBA and C 57 showed no difference in antibody response, *i.e.* the first polymer was non-immunogenic and the second was strongly immunogenic in both strains. However, the two strains showed a very different antibody response to the polymer *(7)* containing tyrosine. The antibody titers for mice of strain CBA were only about 10% of those found for animals of strain C 57. The results were reversed on injection of the polymer containing histidine; it was now the C 57 mice that produced only very small quantities of antibodies.

Table 1. Immunogenicity of branched poly-α-amino acids for two inbred strains of mice, according to *McDevitt* and *Sela* [94].

Synthetic polypeptide	Immunogenicity [a] for mice of strain	
	CBA	C 57
Poly-L-Glu-*(5)*	−	−
Poly-(L-Phe, L-Glu)-*(5)*	+	+
Poly-(L-Tyr, L-Glu)-*(5)* ≡ *(7)*	+	++
Poly-(L-His, L-Glu)-*(5)*	+	+

[a] − Non-immunogenic; + weakly immunogenic; ++ strongly immunogenic.

Thus, the genetic control of the immune response to this group of polypeptides is – similar to antibodies – highly specific for the amino acid composition of the antigenic determinants. Crossover experiments indicated, that the ability to form high levels of antibody is controlled in each case to a large extent by an autosomal dominant gene. When such immunization experiments were extended to other strains of mice similar results were obtained and it was discovered that the ability to respond to these multichain polypeptides is genetically linked to the H2-locus which in mice controls the formation of certain histocompatibility antigens [95].

The influence of genetic factors on the immunogenicity of natural antigens such as insulin [96], bovine serum albumin [97], and lactate dehydrogenase has recently been studied in some detail. The immunological properties of lactate dehydrogenase were in certain respects analogous to those of the complexes of dinitrophenyl-polylysine with egg albumin [98]. The enzyme exists in the form of isozymes which consist of combinations of four of the subunits A or B (A_4, A_3B, A_2B_2, AB_3, B_4). The subunit B corresponds in its action to dinitrophenyl-polylysine in the experiments with guinea pigs; it is itself (as the isozyme B_4) immunogenic only for some of the animals (rabbits), but not for others. In the latter group, B behaves as a hapten, and only when combined with A as a carrier (isozyme A_2B_2) does it induce the formation of B-specific antibodies in these animals.

Very little is known yet about the mechanism of the genetic control of the immune response. Experimental results suggest that the recognition of the antigen is involved, whereas the information required for the synthesis of the corresponding antibodies appears to be potentially available.

[90] *B. B. Levine* and *B. Benacerraf*, J. exp. Medicine *120*, 955 (1964).

[91] *I. Green, W. E. Paul*, and *B. Benacerraf*, J. exp. Medicine *126*, 959 (1967); *W. E. Paul, I. Green*, and *B. Benacerraf*, J. Reticuloendothelial Soc. *5*, 282 (1968).

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[93] *S. Ben Efraim, S. Fuchs*, and *M. Sela*, Immunology *12*, 573 (1967); *S. Ben Efraim*, Ann. Inst. Pasteur *112*, 476 (1967).

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[95] *H. O. McDevitt* and *M. L. Tyan*, J. exp. Medicine *128*, 1 (1968); *H. O. McDevitt* and *A. Chinitz*, Science (Washington) *163*, 1207 (1969).

[96] *E. R. Arquila* and *J. Finn*, J. exp. Medicine *122*, 771 (1965).

[97] *W. R. Sobey, J. M. Magrath*, and *A. H. Reisner*, Immunology *11*, 511 (1966); *D. Hardy* and *D. Rowley*, Immunology *14*, 401 (1968).

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5. Conclusion

The type of immune response induced in higher animals by an antigenic stimulus depends primarily on biological factors, of which only the genetic factors have been mentioned here. However, the chemical and physical nature of the antigen, as well as the dose and the method of administration, also play an important part. These factors, the combined effects of which are not yet clear, lead either to preferential formation of circulating antibodies and stimulation of cellular immunity or to specific tolerance. Selected examples have been presented to show that not only the investigation of the biological principles but also the study of the antigens themselves, particularly with the aid of synthetic antigens, can contribute to a better understanding of these processes. This discussion was restricted mainly to the aspect of antibody formation. However, mention should at least be made of the use of synthetic polypeptide antigens, and polypeptide derivatives of proteins for the study of immunological tolerance [99], the competition of determinant groups [26], and the localization of radioactively labeled antigens in lymphatic tissue [84, 100].

The wide use of *synthetic antigens* in the study of immunological problems is based primarily on their suitability as model substances. Our interest, however, is ultimately in the function of *natural antigens*. Only in rare cases have serological cross-reactions so far been observed between synthetic polypeptide antigens and natural antigens (see Section 4.1.6). With a more precise knowledge of the structure of natural antigens, however, it will become increasingly possible to synthesize antigens in such a way that they have certain determinants in common with the natural products. Whereas this aim was achieved by *Goebel* [54] as early as 1939 for polysaccharides, attempts to do the same with protein antigens have only recently been successful. Thus antigens containing the serologically important C-terminal hexapeptide sequence of the coat protein of tobacco mosaic virus [101] and a large polypeptide loop of lysozyme [102] have been prepared. Antigens of this type allow specific immunization against certain sub-units of natural antigens, and, consequently hold out hopes of useful practical applications.

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Detection of Hindered Rotation and Inversion by NMR Spectroscopy [1]

By Horst Kessler [*]

Rotations and inversions in organic molecules are readily recognizable from the temperature dependence of the NMR spectra. The study of the effects of substituents on the activation barriers of such processes permits the elucidation of reaction mechanisms, and the stability limits of isomers can also be determined. The knowledge of the stability limits is necessary for the specific synthesis of stable rotamers and invertomers.

1. Introduction

Modern organic stereochemistry has two aspects, one static and the other dynamic. The reactivity of a molecule is not determined purely by the predominant steric arrangement; the possibility of assuming other conformations that are more favorable to the reaction is often an important factor.

NMR spectroscopy provides the chemist with a means of studying intramolecular movements with activation energies of 5 to 25 kcal/mole [2–4]. Processes of this type are so fast that the resulting isomers cannot be separated at room temperature. On the other hand,

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[1] Part 13 of a series of reports on the detection of intramolecular mobility by NMR spectroscopy. For Part 12 see [109].

[2] *G. Binsch*: Topics in Stereochemistry, Interscience, New York 1968, Vol. 3, p. 97ff., and literature cited therein.

[3] Ring inversion processes: *J. E. Anderson*, Quart. Rev. (chem. Soc. London) *19*, 426 (1965); *F. G. Riddel, ibid. 21*, 364 (1967).

[4] Valence isomerizations: *G. Schröder* and *J. F. M. Oth*, Angew. Chem. *79*, 458 (1967); Angew. Chem. internat. Edit. *6*, 414 (1967); *E. Vogel* and *H. Günther*, Angew. Chem. *79*, 429 (1967); Angew. Chem. internat. Edit. *6*, 385 (1967).

they are too slow for investigation by IR and Raman spectroscopy or by dielectric constant measurements [5].

The present article describes the application of NMR spectroscopic methods to the study of rotations. In view of their close relationship with rotations, inversions are also briefly discussed. Processes in which parts of a molecule (*e.g.* in cycloolefins [6]) rotate by simultaneous rotation about two or more bonds are not considered, and rotation in σ [7] and π metal complexes [8] is also excluded.

2. Theory

2.1. General

In the rotation about a bond in a molecule, there are certain energetically favored positions of the substituents. For example, a *planar* arrangement is most favorable for the substituents on two carbon atoms joined by a (p-p)π double bond. The dependence of the energy on the angle of rotation about the double bond is shown in Figure 1.

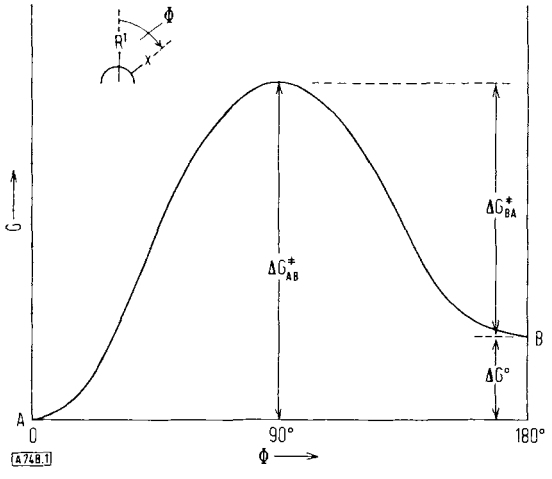


Fig. 1. Energy profile for rotation about a double bond. For A and B cf. *(1)*.

To convert the isomer A into the isomer B, it is necessary to supply the free enthalpy of activation $\Delta G^{\ddagger}_{AB}$. The energy $\Delta G^{\ddagger}_{BA}$ that must be supplied for the reverse isomerization differs by ΔG^0 from $\Delta G^{\ddagger}_{AB}$. The magnitude of the free enthalpy of activation determines the rate of the thermal isomerization. If $\Delta G^{\ddagger} \gtrapprox 23$ kcal/mole, the isomers are stable at room temperature; smaller $\Delta G^{\ddagger}$ values lead to more or less rapid thermal isomerization, the rate constant k_r of which is related to $\Delta G^{\ddagger}$ in accordance with the Eyring equation [eq. (1)] [9].

$$k_r = \frac{k_B T}{h} \exp\left(-\frac{\Delta G^{\ddagger}}{RT}\right) \qquad (1)$$

(k_B = Boltzmann's constant, h = Planck's constant, R = gas constant, T = absolute temperature).

$$\Delta G^{\ddagger} = 4.57\, T\,(10.32 + \log T/k_r \qquad (1a)$$

This situation is again illustrated in Figure 2, in which the rate constant k_r of an isomerization increases from left to right. The free enthalpies of activation $\Delta G^{\ddagger}$ at room temperature as calculated from eq. (1) are also shown. Separation of isomers is possible if the mean lifetime is of the order of a few hours or more. This corresponds to k_r values of less than 10^{-4} sec^{-1} or $\Delta G^{\ddagger}$ values greater than 23 kcal/mole (at 25 °C). The NMR method (see Section 2) covers a range extending downward from the vicinity of the separation limit, which is difficult to study by other methods.

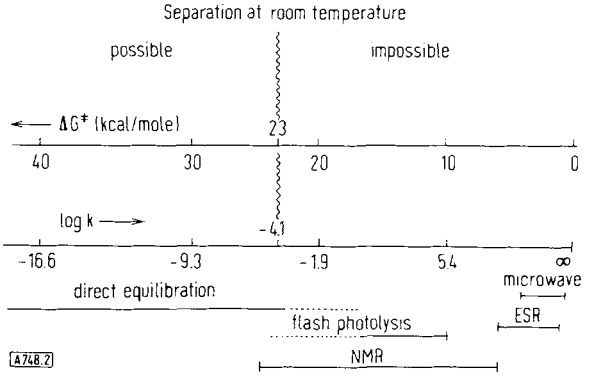


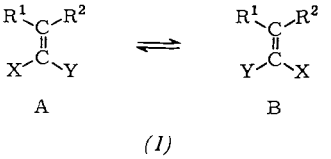
Fig. 2. Possibilities for the detection of intramolecular mobility.

Isomerization of this nature can be followed particularly readily by NMR spectroscopy when ΔG^0 is small, *i.e.* according to

$$\Delta G^0 = -RT \ln([A]/[B]) \qquad (2)$$

when the concentrations of the isomers are comparable.

The conditions for NMR spectroscopy are particularly favorable when $R^1 = R^2$ in *(1)*. A and B are then chemically identical [*]. In the NMR spectrum, how-



(1)

[5] *S. Mizushima*: Structure of Molecules and Internal Rotation. Academic Press, New York 1954; *H. Dreizler*, Fortschr. chem. Forsch. *10*, 59 (1968).

[6] *G. M. Whitsides, B. A. Pawson*, and *A. C. Cope*, J. Amer. chem. Soc. *90*, 639 (1968); *G. Binsch* and *J. D. Roberts, ibid. 87*, 5157 (1966); *S. Dev, J. E. Anderson, V. Cormier, N. P. Damodaran*, and *J. D. Roberts, ibid. 90*, 1246 (1968); *I. C. Calder, Y. Gaoni, P. J. Garratt*, and *F. Sondheimer, ibid. 90*, 4954 (1968); *G. Schröder* and *J. F. M. Oth*, Tetrahedron Letters *1966*, 4083.

[7] *G. M. Whitesides* and *J. S. Fleming*, J. Amer. chem. Soc. *89*, 2855 (1967).

[8] *R. Cramer*, J. Amer. chem. Soc. *86*, 217 (1964); *A. R. Brause, F. Kaplan*, and *M. Orchin, ibid. 89*, 2661 (1970).

[9] *A. Frost* and *R. Pearson*: Kinetik und Mechanismus homogener chemischer Reaktionen. Verlag Chemie, Weinheim/Bergstrasse 1967.

[*] A and B are "degenerate isomers", for which we propose the term "topomers". A and B differ by the exchange of diastereotopic [11d] groups, and are therefore diastereotopomers. The process of interconversion would then be called topomerization (diastereotopomerization). The exchange of prochiral [11d] groups then corresponds to an enantiotopomerization, which can be followed NMR spectroscopically because of the nonequivalence of the two X groups in CX_2Y substituents as prochiral groups. (*G. Binsch, E. L. Eliel*, and *H. Kessler*, unpublished).

ever, R^1 and R^2 are not equivalent if X and Y are different, and rotation about the double bond accordingly leads to "exchange" of the groups R^1 and R^2.

"Slow"[*] isomerization leads to two separate signals for R^1 and R^2 in the NMR spectrum, while "fast" rotation gives only one signal with an intermediate chemical shift (cf. Fig. 3).

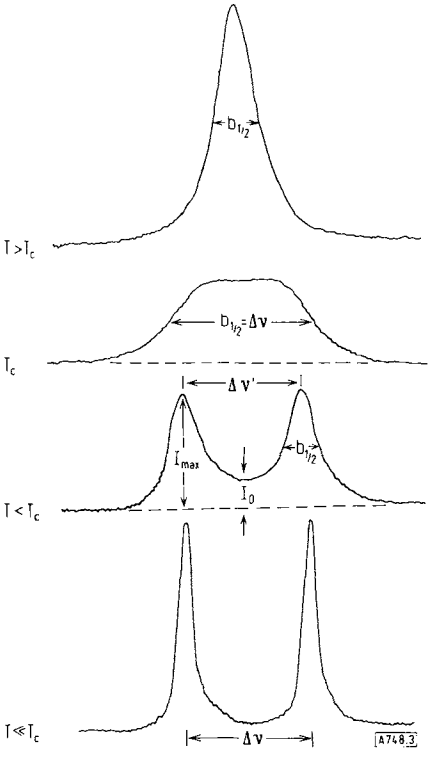
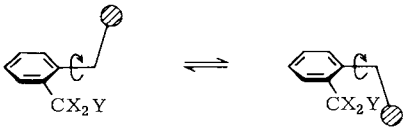


Fig. 3. Temperature dependence of the NMR spectrum as a result of chemical exchange (uncoupled AB case). For explanations see text.

For thermally induced rotations, the NMR spectra are temperature dependent in the transition region between "slow" and "fast" rotation, and can be used to determine the rate constants k_r. The activation parameters ($\Delta G^{\ddagger}$, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, E_a) can be found from k_r (see Section 2.2).

A different situation arises when rotation leads to racemization. The two X groups in CX_2Y substituents may be magnetically non-equivalent when the remainder of the molecule (viewed from the direction of the CX_2Y group) is chiral[10,11]. The intramolecular rotation can be detected with the aid of the temperature dependence of the magnetic non-equivalence. This is so *e.g.* in compounds of the type *(2)*[11c].



object mirror image

(2)

2.2. Kinetic Evaluation of NMR Spectra

As was mentioned above, the shape of the signal in the transition region can be used to determine the rate constants. The theory of line broadening is well developed and has been presented clearly[12], particularly for simple cases. Several methods of evaluation are available in practice:

1. By approximation equations.
2. By graphical evaluation of certain spectral parameters.
3. By computer matching of measured and calculated spectra.

A particularly simple situation occurs when two atoms (or groups) with initially sharp signals of equal intensity undergo chemical exchange (uncoupled AB case, see Fig. 3). For evaluation by approximation equations, parameters such as the line separation $\Delta\nu$[13], the line broadening $b_{1/2}$[14,21], and the intensity ratio I_0/I_{max}[15] in the low-temperature case, the line width $b_{1/2}$ in the high-temperature case[16], and the coalescence temperature[18] are found from the spectrum. The coalescence temperature is the temperature at which two signals just coincide (see Fig. 3). The validity of the equations is limited in most cases[17]. It is relatively easy to obtain the rate constant k_c of the chemical exchange at the coalescence temperature T_c. Ignoring the intrinsic width, we then have:

$$k_c = \pi\Delta\nu/\sqrt{2} \qquad (3)$$

($\Delta\nu$ = line separation without exchange)

for the uncoupled AB case[18][**].

---

[*] "Slow" on the NMR timescale means that the reaction rate constant $k_r \ll \pi\Delta\nu/\sqrt{2}$ ($\Delta\nu$ = signal splitting without exchange) [see eq. (3)]. "Slow" is to be regarded as a statistical-kinetic description in this context. A slow rotation is one in which only a small fraction of the molecules can overcome the energy barrier in unit time. The actual rotation of the individual molecule, however, is very fast owing to the small moment of inertia. "Infrequent" would therefore be a better term than "slow" and "frequent" would then have to be used instead of "fast".

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[16] *L. H. Piette* and *W. A. Anderson,* J. chem. Physics *30,* 899 (1959).

[17] *A. Allerhand, H. S. Gutowsky, J. Jonas,* and *R. A. Meinzer,* J. Amer. chem. Soc. *88,* 3185 (1966).

[18] *J. A. Pople, W. G. Schneider,* and *H. J. Bernstein*: High-Resolution Nuclear Magnetic Resonance. McGraw-Hill, New York 1959.

[**] The uncoupled AB case refers to the spectrum of two types of nuclei (A and B) that are not coupled to each other. In the normal AB case, on the other hand, four lines are observed because of coupling of A with B and *vice versa.*

For the coalescence of an AB-type spectrum (to A_2), we have [19] (disregarding the intrinsic width):

$$k_c = \pi (\Delta\nu^2 + 6 J^2)^{1/2} / \sqrt{2} \quad (4)$$

where J is the constant for the coupling between the nuclei A and B.

Graphical methods [20] are particularly suitable for the evaluation, since the intrinsic widths of the lines and the temperature dependence of the splitting without chemical exchange [17,21] can be taken into account more satisfactorily.

If the contributions of two rotamers to the equilibrium are no longer equal ($\Delta G^0 \neq 0$), the ratio of the intensities of the bands is not equal to unity (evaluation *e.g.* according to [14]). Computers are necessary for the evaluation in more complicated cases; the shapes of the curves can then be simulated and compared with the experimental spectra.

The free enthalpy of activation $\Delta G_T^{\neq}$ can be calculated from the rate constants k_r by means of the Eyring equation (1). The temperature-dependent $\Delta G^{\neq}$ value contains the activation entropy $\Delta S^{\neq}$. To find the Arrhenius activation energy E_a, log k_r is plotted against the reciprocal of the temperature (A = frequency factor):

$$k_r = A \exp(-E_a/RT) \quad (5)$$

$$\log k_r = \text{const} - E_a/4.56\,T \quad (5a)$$

The E_a values (or $\Delta H^{\neq} = E_a - RT$) should be used for the comparison of compounds, since it does not contain the temperature-dependent entropy term $T\Delta S^{\neq}$. It has been shown, however, that the E_a values are mostly very uncertain. Thus for dimethylformamide [*], which has probably been studied more often by NMR spectroscopy than any other compound, the literature contains E_a values ranging from 7 to 28 kcal/mole and log A values of from 7 to 17 [2,23]. On the other hand, the values found for the free enthalpy of activation $\Delta G_c^{\neq}$ from the coalescence temperature with the aid of equations (1) and (3) all differ by less than 1 kcal/mole from the average (21.5 kcal/mole) [13, 15, 23, 24].

The reason for this is to be found in the k_r values, the errors in which increase with increasing distance from the coalescence temperature. However, only a relatively small temperature range of from about 20 to at most 60 °C is available for the evaluation. The gradient of the Arrhenius line, which is a measure of the activation energy E_a, and hence also its intercept on the ordinate (log A) are very strongly influenced by small deviations of the k_r values; high E_a values go with high log A values and *vice versa*. In a plot of the E_a values for dimethylformamide from the literature against the corresponding log A values, all but one of the points lie on a straight line passing through the origin (Fig. 4).

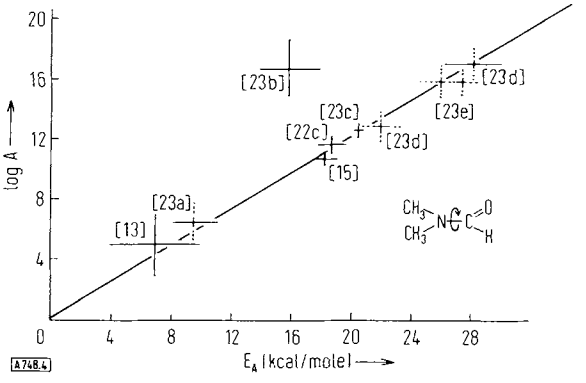


Fig. 4. Experimental kinetic data for the rotation about the C—N bond in solvent-free dimethylformamide. The numbers are literature references, and the lengths of the lines indicate the error limits. —E_a = Arrhenius activation energy, A = frequency factor [eq. (5)].

Where accurate measurements (such as *e.g.* in [21]) covering a fairly wide temperature range are not available, it is better to avoid a discussion of the physically accurate but numerically doubtful E_a values (or $\Delta H^{\neq} = E_a - RT$), and to use the $\Delta G_c^{\neq}$ values instead [17]. The temperature dependence of $\Delta G^{\neq}$ is then deliberately ignored, and normal frequency factors are postulated (low reaction entropies $\Delta S^{\neq}$). This procedure is not problematic above all in the comparison of similar types of substances. The stability of isomers at a given temperature is determined in any case by $\Delta G^{\neq}$.

If it is still desired to determine E_a and $\Delta H^{\neq}$, several methods should be used if possible in order to extend the temperature range. This can be done in suitable cases both by the measurement of k_r values by the spin echo method [25] and the double resonance method described by *Forsen* and *Hoffmann* [26] and by direct equilibration [24,27]. Since very few investigations of this nature and reliable line shape analyses have been carried out so far, the free enthalpies of activation at the coalescence temperature T_c are used for discussion in this article. The error in T_c (usually about ±2 to 5 °C) largely determines the error in the $\Delta G_c^{\neq}$ values (±0.5 to 4%). Owing to the temperature dependence of $\Delta G^{\neq}$, the coalescence temperature, which

[19] *R. J. Kurland, M. B. Rubin,* and *W. B. Wise,* J. chem. Physics *40,* 2426 (1964).

[20] *M. Takeda* and *E. O. Stejskal,* J. Amer. chem. Soc. *82,* 25 (1960); *H. G. Schmid, H. Friebolin, S. Kabuss,* and *R. Mecke,* Spectrochim. Acta *22,* 623 (1966).

[21] *F. A. L. Anet* and *A. J. R. Bourn,* J. Amer. chem. Soc. *89,* 760 (1967).

[*] Without solvent; for measurements in solution see [22].

[22] *J. V. Hatton* and *W. G. Schneider,* Canad. J. Chem. *40,* 1285 (1962); *M. L. Blanchard, A. Chevallier,* and *G. J. Martin,* Tetrahedron Letters *1967,* 5057; *R. C. Neumann, Jr.* and *L. B. Young,* J. physic. Chem. *69,* 2570 (1965).

[23] a) *G. Fraenkel* and *C. Franconi,* J. Amer. chem. Soc. *82,* 4478 (1960); b) *A. G. Wittaker* and *S. Siegel,* J. chem. Physics *42,* 3320 (1965); c) *M. Rabinowitz* and *A. Pines,* J. Amer. chem. Soc. *91,* 1585 (1969); *A. Pines* and *M. Rabinowitz,* Tetrahedron Letters *1968,* 3259; d) *F. Conti* and *W. v. Philipsborn,* Helv. chim. Acta *50,* 603 (1967); e) *C. W. Fryer, F. Conti,* and *C. Franconi,* Ric. sci., Parte II, Sez. A *35,* 788 (1965).

[24] *A. Mannschreck, A. Mattheus,* and *G. Rissmann,* J. molecular Spectroscopy *23,* 15 (1967).

[25] *K. H. Abramson, P. T. Inglefield, E. Krakower,* and *L. W. Reeves,* Canad. J. Chem. *44,* 1685 (1966); *P. T. Inglefield, E. Krakower, L. W. Reeves,* and *R. Stewart,* Molecular Physics *15,* 65 (1968); *A. Allerhand* and *H. S. Gutowsky,* J. Amer. chem. Soc. *87,* 4092 (1965), and literature cited therein.

[26] *S. Forsen* and *R. A. Hoffmann,* J. chem. Physics *40,* 1189 (1964); Acta chem. scand. *17,* 1787 (1963); J. chem. Physics *39,* 2892 (1963).

[27] *H. S. Gutowsky, J. Jonas,* and *T. H. Siddall,* J. Amer. chem. Soc. *89,* 4300 (1967).

can be varied within certain limits by the choice of the measuring frequency, is given whenever possible.

The rate of intramolecular rotations and inversions, like that of other reactions, also depends on the solvent and on the concentration of the solute. In series of measurements on various substances, therefore, only one solvent should be used if possible[*]. Comparative discussions become increasingly problematic with increasing dissimilarity of the structures of the compounds and solvents investigated and of the concentrations and coalescence temperatures.

Other methods besides NMR spectroscopy can be used for the detection of intramolecular rotations[5].

3. Applications

3.1. General

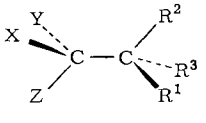
Free rotation about a bond in the molecule may be sterically and electronically hindered. Thus the stability of *cis-trans* isomers about the CC double bond is so great because of electronic effects that their rotamers are described as configurational isomers, though they are really mostly very stable conformers. Rotation about a CC single bond (the σ bond is rotationally symmetrical) may be sterically hindered, as in the well-known example of atropisomerism in biphenyl derivatives, but can also be restricted by resonance effects, which give the single bond partial double bond character.

3.2. Rotations about Single Bonds

3.2.1. Carbon-Carbon Single Bonds

3.2.1.1. sp^3-sp^3 Hybridization

In the rotation about single bonds between sp^3-hybridized carbon atoms as in *(3)*[28], the heights of the energy barriers are determined mainly by the steric hindrance in the eclipsed transition state. The types of spectrum to be expected for fast and slow rotation have been discussed by *Pople*[29].



(3)

With identical substituents R^1, R^2, and R^3, the conformations C, D, and E in Figure 5 have equal energy contents and there is only *one* activation energy. For methyl groups ($R^1 = R^2 = R^3 = H$), this has a value of $E_a \lesssim 3$ kcal/mole[30], and can no longer be detected

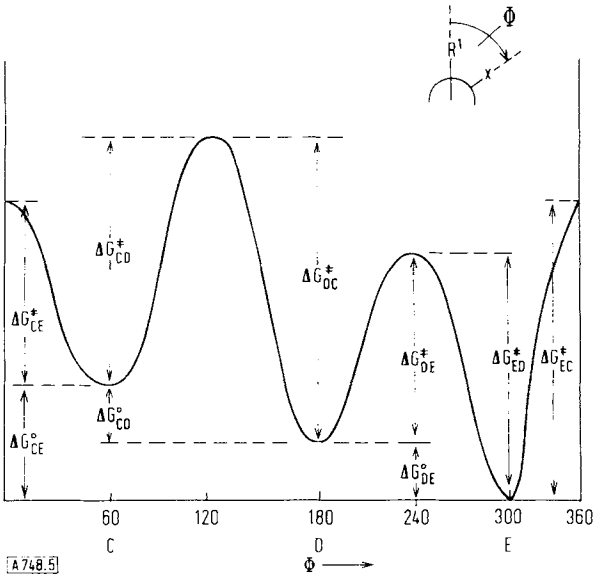
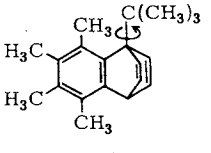


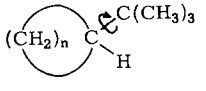
Fig. 5. Energy profile for rotation in an unsymmetrical ethane. C, D, and E are the stable staggered conformations at the indicated angles of rotation.

by NMR spectroscopy. Splitting due to hindered rotation about the CC single bond is however found for the *tert*-butyl group ($R^1 = R^2 = R^3 = CH_3$) (Table 1).

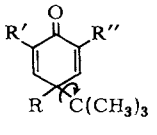
In the compounds *(7)* and *(9)*, one should expect splitting of the *tert*-butyl signal into three singlets having relative intensities of 1 : 1 : 1, and in the other compounds into two singlets having an intensity ratio of 2 : 1. The fundamental correctness of these considerations is shown by the low temperature spectrum of *(7a)*, in which all three methyl groups of the *tert*-butyl group are separated (Fig. 6)[33b].



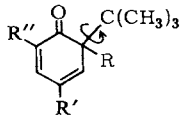
(4)



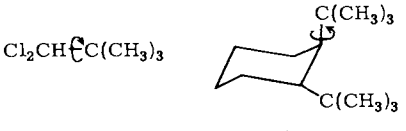
(5)



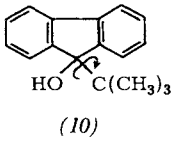
(6)



(7)



(8) *(9)*



(10)

[*] This is unfortunately not always possible, owing to the general properties of the solvents (b.p., m.p., solvent power) and possible absorptions in the measurement region.

[28] *E. L. Eliel*: Stereochemistry of Carbon Compounds. McGraw-Hill, New York 1962.

[29] *J. A. Pople*, Molecular Physics *1*, 3 (1958).

[30] *J. P. Lowe* and *R. G. Parr*, J. chem. Physics *44*, 3001 (1966); *O. J. Sovers* and *M. Karpens*, *ibid. 44*, 3033 (1966); *J. Dale*, Tetrahedron *22*, 3373 (1966).

Table 1. Hindered rotation of *tert*-butyl groups.

Cpd.	$\Delta G_c^{\neq}$ (kcal/mole)	Ref.	Cpd.	$\Delta G_c^{\neq}$ (kcal/mole)	Ref.
(4)	[a]	[31]	*(8)*	9.0	[34]
(5), n = 4–7	6–8	[32]	*(9)*	10.1	[35] [b]
(6), R = Br,OCH_3	9	[33]	*(10)*	9.4	[34]
(7), R = Br	9	[33]			

[a] No energy barrier data.

[b] The low temperature process described in this reference is better explained by hindered rotation of the *tert*-butyl group than by an equilibrium between a chair form and a twist form. Further investigations are in progress.

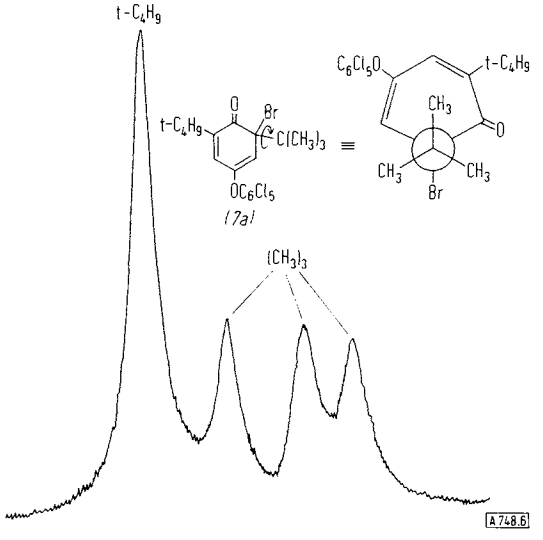


Fig. 6. Aliphatic region in the NMR spectrum of *(7a)* at −90 °C (220 MHz) [*].

The resolution is often not sufficient for complete separation of all the bands.

Many halogenated alkanes *(11)* have been studied mostly by fluorine resonance [36]. The energy differences ΔG^0 between the three rotamers are determined by the nature of the substitution.

$$F_mCl_nBr_oC-CF_pCl_qBr_r \qquad (11)$$
$$m \rightarrow r = 0 \rightarrow 3$$

The activation barriers generally increase with the size of the atoms [36a], and can be as high as 12 kcal/mole. Hindered rotation of a CF_3 group has recently been observed [37].

[31] *J. P. N. Brewer, H. Heaney*, and *B. A. Marples*, Chem. Commun. *1967*, 27.

[32] *F. A. L. Anet, M. S. Jaques*, and *G. N. Chmurny*, J. Amer. chem. Soc. *90*, 5243 (1968).

[33] a) *A. Rieker, N. Zeller*, and *H. Kessler*, J. Amer. chem. Soc. *90*, 6566 (1968); b) *A. Rieker* and *H. Kessler*, unpublished.

[34] *A. Rieker* and *H. Kessler*, Tetrahedron Letters *1969*, 1227.

[35] *H. Kessler, V. Gusowski*, and *M. Hanack*, Tetrahedron Letters *1968*, 4665.

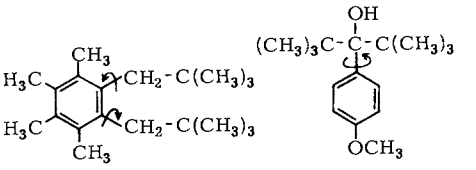
[*] We are grateful to Dr. *W. Brügel*, BASF, Ludwigshafen, for recording the spectrum.

[36] a) *R. A. Newmark* and *C. H. Sederholm*, J. chem. Physics *43*, 602 (1965); b) *J. D. Roberts*, Angew. Chem. *75*, 20 (1963); Angew. Chem. internat. Edit. *2*, 53 (1963); c) *H. S. Gutowsky*, Pure appl. Chem. *7*, 93 (1963); d) *R. L. Vold* and *H. S. Gutowsky*, J. chem. Physics *47*, 2495 (1967); e) *T. D. Alger, H. S. Gutowsky*, and *R. L. Vold, ibid. 47*, 3130 (1967).

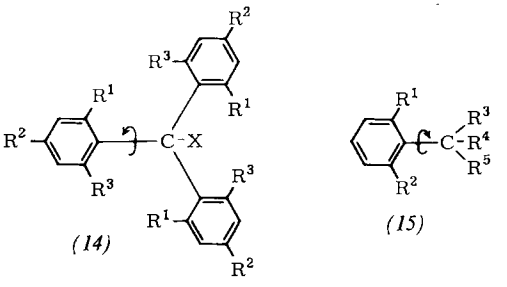
[37] *F. J. Weigert* and *J. D. Roberts*, J. Amer. chem. Soc. *90*, 3577 (1968).

3.2.1.2. sp^2-sp^3 Hybridization

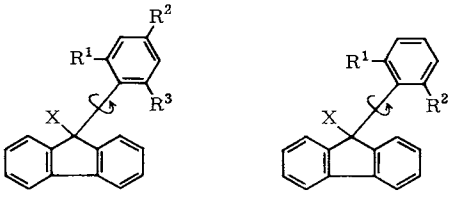
Rotation about the single bond between sp^2- and sp^3-hybridized carbon atoms can be hindered by bulky substituents. Hindered rotation attracted particular interest in two *tert*-butyl derivatives *(12)* [38] and *(13)* [39] of benzene, triarylmethanes *(14)* [40], *o*-disubstituted alkylbenzenes *(15)* [34,41], and 9-arylfluorenyl compounds *(16)* [34,42] and *(17)* [34].



(12) *(13)*



(14) *(15)*



(16), $R^1 = R^3 = CH_3$ *(17)*, $R^1 = R^2 = OCH_3$

The "chemical exchange" of the methyl and methoxy groups in *(16)* and *(17)* also proceeds in principle by dissociation of the group X. However, this is not possible in the derivatives with X=H (except in the presence of basic catalysts). The decrease in $\Delta G_c^{\neq}$ in the order H > OH > Cl appears to be connected with the bulk of X. The larger X is, the greater is the hindrance in the ground state, and the smaller the energy difference between the ground state and the transition state [34].

3.2.1.3. sp^2-sp^2 Hybridization

Rotation barriers in biphenyl derivatives have so far been measured in only a few cases (Table 2).

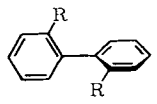
[38] *D. T. Dix, G. Fraenkel, H. A. Karnes*, and *M. S. Newman*, Tetrahedron Letters *1966*, 517.

[39] *G. P. Newsereff* and *S. Sternhell*, Tetrahedron Letters *1967*, 2539.

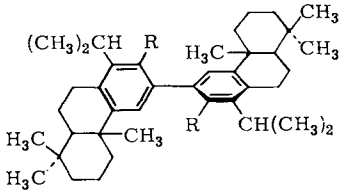
[40] *H. Kessler, A. Moosmayer*, and *A. Rieker*, Tetrahedron *25*, 287 (1969)

[41] a) *A. Mannschreck* and *L. Ernst*, Tetrahedron Letters *1968*, 5939; b) *C. A. Cupas, J. M. Bollinger*, and *M. Haslanger*, J. Amer. chem. Soc. *90*, 5502 (1968).

[42] *E. A. Chandross* and *C. F. Sheley, Jr.*, J. Amer. chem. Soc. *90*, 4345 (1968); *T. H. Siddall* and *W. E. Stewart*, Tetrahedron Letters *1968*, 5011; Chem. Commun. *1968*, 1116.



(18)



(19)

Table 2. Rotation in biphenyl derivatives.

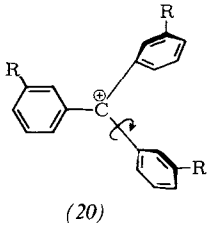
Cpd.	R	$\Delta G_c^{\neq}$ (kcal/mole)	T_c (°C)	Ref.
(18a)	CH_3	17.4	−35	[43] [a]
(18b)	CH_2OCOCH_3	20.2	127	[44] [b]
(18c)	$CH(CH_3)_2$	>26.1	>200	[45]
(18d)	$C(OH)(CH_3)_2$	>24.5	>190	[45]
(19a)	OCH_3	13.7	−25	[46]
(19b)	$OCOCH_3$	18.5	+46	[46]

[a] Measured by direct equilibration.
[b] Calculated from the literature data.

$\Delta G_c^{\neq}$ increases very rapidly with the size of the residue R, and can ultimately no longer be determined by NMR spectroscopy.

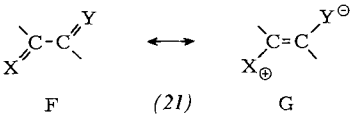
Steric hindrance of the rotation about the aryl-CO bond has been found in benzamides [47], benzophenones [48], and benzils [48]. It is so great in *tert*-butyl aryl ketones that the optical antipodes can be separated [49].

Rotation about C-aryl bonds is also sterically hindered in the propeller conformations of triarylmethyl cations *(20)* [50]. The geometry of the propeller (right-hand or left-hand screw) and the position of the substituents R lead to interesting isomerism phenomena.



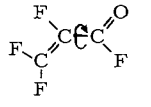
(20)

Steric hindrance of rotation is less common than "electronic hindrance". Owing to the participation of ionic limiting structures such as G in *(21)*, formal

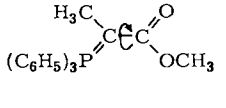


F (21) G

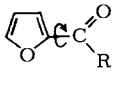
single bonds often possess partial double-bond character. In such cases, the energy is lowest in the planar conformations *s-cis* (cisoid) and *s-trans* (transoid) [50a]; however, the activation energy required for rotation about the central bond is generally not very high. Some examples are given in Table 3.



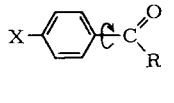
(22)



(23)

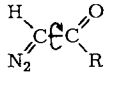


(24)



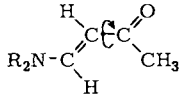
(25)

R = H, CH_3
X = $N(CH_3)_2$, OCH_3, H



(26)

R = Alkyl, Alkoxyl



(27)

R = H, CH_3

Table 3. Hindered rotation about partial CC double bonds

Cpd.	$\Delta G_c^{\neq}$ (kcal/mole)	T_c	Ref.	Cpd.	$\Delta G_c^{\neq}$ (kcal/mole)	T_c	Ref.
(22)	[a]	[a]	[51]	*(25)*	6—11	−142 to −56	[54]
(23)	17	55	[52]	*(26)*	12—16	−32 to +13	[55]
(24)	10—11	−57	[53]	*(27)*	[b]	—	[56]

[a] "Frozen in" at −105 °C. No barrier data.
[b] No barrier data.

$\Delta G_c^{\neq}$ increases with increasing difference between the electron donor and acceptor properties of X and Y. In compounds of the type *(25)*, therefore, rotation becomes increasingly difficult in the order X=H < OCH_3 < $N(CH_3)_2$. Hindrance of rotation about the aryl-C bond as a result of opposite polarization (aryl ring negative, substituent positive) has been found in ketene aminals [82, 112d].

[43] *W. Theilacker* and *H. Böhm*, Angew. Chem. *79*, 232 (1967); Angew. Chem. internat. Edit. *6*, 251 (1967).

[44] *W. L. Meyer* and *R. B. Meyer*, J. Amer. chem Soc. *85*, 2170 (1963).

[45] *H. Kessler*, unpublished.

[46] *L. D. Colebrook* and *J. A. Jahnke*, J. Amer. chem. Soc. *90*, 4687 (1968).

[47] *T. H. Siddall* and *R. H. Garner*, Tetrahedron Letters *1966*, 3513; *T. H. Siddall* and *W. E. Stewart*, Chem. Commun. *1967*, 393; *G. R. Bedford, D. Greatbanks*, and *D. B. Rogers, ibid. 1966*, 330; *T. H. Siddall* and *R. H. Garner*, Canad. J. Chem. *44*, 2387 (1966).

[48] *D. Lauer* and *H. A. Staab*, Tetrahedron Letters *1968*, 177.

[49] *A. G. Pinkus, J. I. Riggs, Jr.*, and *S. M. Broughton*, J. Amer. chem. Soc. *90*, 5043 (1968).

[50] *J. J. Schuster, A. K. Colter*, and *R. J. Kurland*, J. Amer. chem. Soc. *90*, 4679 (1968); *R. Breslow, L. Kaplan*, and *D. LaFollette, ibid. 90*, 4056 (1968).

[50a] *K. Mislow*: Einführung in die Stereochemie, Verlag Chemie, Weinheim/Bergstr. 1967, p. 70.

[51] *W. S. Brey, Jr.* and *K. C. Ramey*, J. chem. Physics *39*, 844 (1963).

[52] *H. J. Bestmann, G. Joachim, I. Lengyel, J. F. M. Oth, R. Merenyi*, and *H. Weitkamp*, Tetrahedron Letters *1966*, 3355; *F. J. Randall* and *A. W. Johnson*, Tetrahedron Letters *1968*, 2841.

[53] *K. I. Dahlquist* and *S. Forsen*, J. physic. Chem. *69*, 1760, 4062 (1965).

[54] *F. A. L. Anet* and *M. Ahmad*, J. Amer. chem. Soc. *86*, 119 (1964); *R. E. Klinck, D. H. Marr*, and *J. B. Stothers*, Chem. Commun. *1967*, 409.

[55] *F. Kaplan* and *G. K. Meloy*, J. Amer. chem. Soc. *88*, 950 (1966).

[56] *J. Dabrowsky* and *L. Kozerski*, Chem. Commun. *1968*, 586.

σ-π rearrangements or CC rotation are discussed for the isomerizations in π-allyl complexes [57].



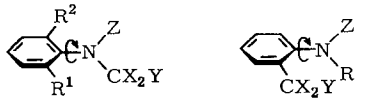
(28) *(29)*

In connection with rotations in anions *(28)* [58] and cations *(29)* [59] of the allyl type, the reader is referred to the literature.

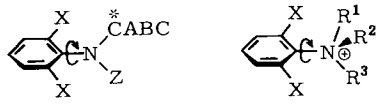
3.2.2. Carbon-Nitrogen Single Bonds

3.2.2.1. Steric Hindrance of Rotation

Steric hindrance of rotation about the aryl-N bond is the reason for the magnetic non-equivalence of the X atoms in substances of the types *(30)* to *(33)*. The rotation is less hindered in amines (Z = alkyl) [60,61] than in amides (Z = COR) [11c,60,62,63] and nitrosamines (Z = NO) [61,63]. The ammonium salts *(33)* are com-



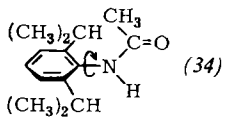
(30) *(31)*



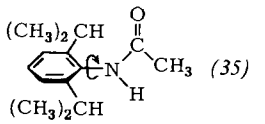
(32) *(33)*

parable to the alkylated benzenes *(15)*; the energy threshold is higher because of the shorter bond (C–N as compared with C–C) [41a]. Examples from the amides [11c] and nitrosamines [61] are *(34)/(35)* and *(36)/(37)* respectively (the figures give $\Delta G_c^{\ddagger}$ in kcal/mole).

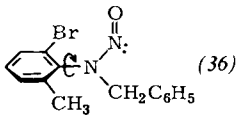
The degree of steric hindrance in the transition state of the rotation [*(34)* > *(35)*; *(36)* > *(37)*] determines the free enthalpy of activation $\Delta G_c^{\ddagger}$, which increases with the bulk of the substituents; the same is true of ring substitution [61].



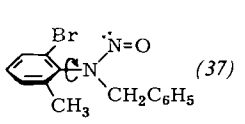
(34) 18.9[*]



(35) 11.8



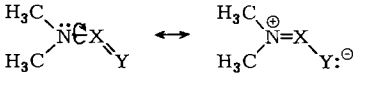
(36) 21.8



(37) 17.9

3.2.2.2. Hindered Rotation About Partial Double Bonds

C–N bonds with partial double-bond character occur in compounds of the type *(38)*.



(38)

X = CR, N

Y = CRR^1, NR, O, S, Se, $^{\oplus}$O-R, $^{\oplus}$S-R

The hindrance of rotation about the N–X bond is often used as proof of the planarity of the nitrogen atom. This is not evident because a partial double bond character can also result from overlap of the filled sp^3 orbitals on nitrogen with the empty p orbital on X. The nitrogen pyramid is flattened and the inversion rate on nitrogen increases by conjugation (see section 3.4.1).

The temperature dependence of the nuclear resonance has very often been used for the investigation of rotation about the partial double bond in amides. Since the discovery of the hindrance of rotation in dimethylformamide *(39a)* by *Phillips* [64], the first application of the NMR method to the study of kinetic processes, numerous articles dealing with the improvement of the measuring method and evaluation [2,13,15,23] as well as with the solvent and concentration dependence [2,22,65] of *(39a)* have been published. The substituents on the nitrogen and on the carbon have also been varied and their effects on the rate of rotation checked.

Let us first consider some examples that show the influence of the acyl component (substituent R) on the rotation barrier of *N,N*-dimethylamides *(39)* (Table 4). The $\Delta G_c^{\ddagger}$ values give a reliable indication at least of the direction (accelerating or retarding) in which the substituents affect the rotation rate.

The rotation about the amide bond (C–N) is hindered by the participation of the limiting structure I in the ground state. *Pauling* predicted an energy barrier of

[57] *K. C. Ramey, D. C. Lini,* and *W. B. Wise,* J. Amer. chem. Soc. *90,* 4275 (1968), and literature cited therein; *M. Tsutsui, M. Hancock, J. Ariyoshi,* and *M. N. Levy,* Angew. Chem. *81,* 453 (1969); Angew. Chem. internat. Edit. *8,* 410 (1969).

[58] *V. R. Sandel, S. V. McKinley,* and *H. H. Freedman,* J. Amer. chem. Soc. *90,* 495 (1968); *R. B. Bates, D. W. Gosselink,* and *J. A. Kaczinski,* Tetrahedron Letters *1967,* 205.

[59] *G. A. Olah* and *J. M. Bollinger,* J. Amer. chem. Soc. *90,* 6082 (1968).

[60] *B. J. Price, J. A. Eggleston,* and *I. O. Sutherland,* J. chem. Soc. (London) *B 1967,* 922.

[61] *A. Mannschreck* and *H. Muensch,* Tetrahedron Letters *1968,* 3227.

[62] *T. H. Siddall* and *C. A. Prohaska,* J. Amer. chem. Soc. *88,* 1172 (1966); *Y. Shvo, E. C. Taylor, K. Mislow,* and *M. Raban, ibid. 86,* 4910 (1967); *T. H. Siddall* and *W. E. Stewart,* Chem. Commun. *1968,* 617.

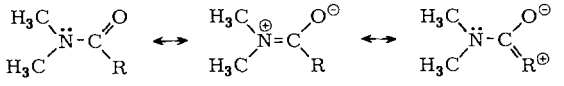
[63] *R. J. Seymour* and *R. C. Jones,* Tetrahedron Letters *1967,* 2021.

[*] This energy is comparable to that of a *cis-trans* isomerization about the amide bond. It is therefore possible that previous isomerization occurs into the *trans* form *(35)*, in which the rotation takes place more readily [11c].

[64] *W. D. Phillips,* J. chem. Physics *23,* 1363 (1955).

[65] *J. V. Hatton* and *W. G. Schneider,* Canad. J. Chem. *40,* 1285 (1962).

about 21 kcal/mole, corresponding to a double bond component of about 40% [74]; this is surprisingly close to the value found experimentally for dimethylformamide. Substituents influence the activation energy



H I J

(39)

both electronically and sterically [*]. A strong contribution of the limiting structure J to the resonance reduces the double-bond character of the amide bond, and hence also the rotation threshold. This effect is clearly recognizable in the low $\Delta G_c^{\ddagger}$ value of the urethane *(39g)* as compared with those of the amides *(39a)* and *(39b)*.

Table 4. Hindered rotation in amides *(39)*.

Cpd.	R	Solvent	$\Delta G_c^{\ddagger}$ (kcal/mole)	T_c (°C)	Ref.
(39a)	H	without	21.7	116	[23]
(39b)	CH_3	without	18.9	87	[66]
(39c)	C_2H_5 [a]	without	16.7 [b]	61	[15, 67]
(39d)	CCl_3	without	14.9	14	[15, 68]
(39e)	CF_3	without	17.6 [b]	95	[15]
(39f)	Cl	without	16.8 [b]	53	[15, 67, 69]
(39g)	OCH_3	$CHCl_3$	14.8 [c]	− 13	[70] [e]
(39h)	$CH=CH_2$	without	16.1 [b]		[15]
(39i)	C_6H_5	[d]	14.4	12	[24]
(39k)	$2,4,6\text{-}(CH_3)_3C_6H_2$	[d]	22.5	168	[24]
(39l)	$2,4,6\text{-}[(CH_3)_3C]_3C_6H_2$	[d]	≈30	>200	[71]

[a] For other alkyl groups, see [72]. [b] Based on 25 °C. [c] Calculated from the literature data. [d] 1-Chloronaphthalene/benzotrichloride (1 : 1). [e] Cf. also [73].

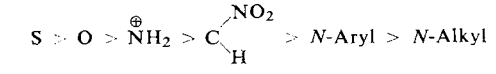
The bulkiness of the substituents can have various effects:

1. Large substituents on the nitrogen and in the acyl residue increase the energy content of the almost planar ground state because of their steric interaction (see also Section 3.4), with the result that the energy difference for the transition state ($\Delta G^{\ddagger}$) becomes smaller. This probably explains why the rotation barrier is lower for *N,N*-dimethyltrichloroacetamide [*(39d)*, $\Delta G_c^{\ddagger} \approx 15$ kcal/mole] than for *N,N*-dimethyltrifluoroacetamide [*(39e)*, $\Delta G_c^{\ddagger} \approx 18$ kcal/mole]. A similar effect is observed when the size of the residues on the nitrogen is increased [75].

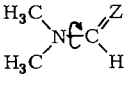
2. Large substituents on the phenyl ring of benzamides *(39k)*, *(39l)* lock the dialkylamino group, *i.e.* they destabilize the transition state of the rotation, and so give stable separable rotamers.

Replacement of the oxygen of the amide grouping by other elements yields the compounds listed in Table 5.

The height of the rotation barrier, and hence the double-bond character, decreases with variation of the substituent Z in the order



Electron-attracting substituents increase $\Delta G^{\ddagger}$ (cf. [82]). A similar picture is found for *N,N*-dimethylbenzamide



(40)

Table 5. Activation parameters for rotation in substances of the type *(40)*.

Cpd.	Z	Solvent	T_c (°C)	$\Delta G_c^{\ddagger}$ (kcal/mole)	E_a (kcal/mole)	log	Ref.
(40a)	S	without	193		27.9	13.6	[76]
(39a)	O	without	116	21.7 [a]	20.5	12.7	[23]
(40b)	$NH_2^{\oplus}$	formamide			19.6	12.7	[22] [b]
(40c)	$CH(NO_2)$	$CDBr_3$	52	16.5			[78] [c]
(40d)	$p\text{-}C_6H_4\text{—}CH_3$	$CDCl_3$		14.1			[80]
(40e)	*N-tert.*-C_4H_9	toluene		11.9	13.0		[81]

[a] Based on 25 °C. [b] Cf. also [77]. [c] Cf. also [79].

[*] Too few data are available at present for a quantitative breakdown of the measured effects into the two contributions [66b].

[66] a) *A. Mannschreck*, Tetrahedron Letters *1965*, 1341; b) *R. C. Neuman, Jr.* and *V. Jonas*, J. Amer. chem. Soc. *90*, 1970 (1968).

[67] *J. T. Woodbrey* and *M. T. Rogers*, J. Amer. chem. Soc. *84*, 13 (1962).

[68] *A. Allerhand* and *H. S. Gutowsky*, J. chem. Physics *41*, 2115 (1964).

[69] *R. C. Neuman, Jr., D. N. Roark*, and *V. Jonas*, J. Amer. chem. Soc. *89*, 3412 (1967).

[70] *E. Lustig, W. R. Benson*, and *N. Duy*, J. org. Chemistry *32*, 851 (1967).

[71] *H. A. Staab* and *D. Lauer*, Chem. Ber. *101*, 864 (1968).

[72] *G. Isaksson* and *J. Sandström*, Acta chem. scand. *21*, 1605 (1967).

[73] *B. J. Price, R. V. Smallman*, and *I. O. Sutherland*, Chem. Commun. *1966*, 319; *H. Günther* and *R. Wenzl*, Tetrahedron Letters *1967*, 4155; *C. H. Bushweller* and *M. A. Tobias, ibid. 1968*, 595; *S. van der Werf* and *J. B. F. N. Engberts, ibid. 1968*, 3311; *C. E. Holloway* and *M. H. Gitlitz*, Canad. J. Chem. *45*, 2659 (1967).

[74] *L. Pauling:* Die Natur der chemischen Bindung, 3rd Edit., Verlag Chemie, Weinheim/Bergstrasse, Germany 1968, p. 167.

[75] *R. M. Hammaker* and *B. A. Gugler*, J. molecular Spectroscopy *17*, 356 (1965).

[76] *A. Loewenstein, A. Melera, P. Rigny*, and *W. Walter*, J. physic. Chem. *68*, 1597 (1964).

[77] *G. S. Hammond* and *R. C. Neuman, Jr.*, J. Amer. chem. Soc. *67*, 1655 (1963).

[78] *A. Mannschreck* and *U. Koelle*, Tetrahedron Letters *1967*, 863.

[79] *H. E. A. Kramer* and *R. Gompper*, Z. physik. Chem. *43*, 292 (1964); *M. Martin* and *G. Martin*, C. R. hebd. Séances Acad. Sci. *256*, 403 (1963); *A. P. Downing, W. D. Ollis*, and *I. O. Sutherland*, Chem. Commun. *1967*, 143.

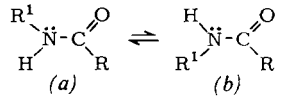
[80] *D. J. Bertelli* and *J. T. Gerig*, Tetrahedron Letters *1967*, 2481; *J. P. Marsh* and *L. Goodman, ibid. 1967*, 863.

[81] *D. L. Harris* and *K. M. Wellman*, Tetrahedron Letters *1968*, 5225.

[82] *H. Kessler*, Angew. Chem. *80*, 971 (1968); Angew. Chem. internat. Edit. *7*, 898 (1968); Chem. Ber. *103*, 973 (1970).

and its derivatives[84]. In enamines (C⟨) and *N*-aryl amidines (*N*-Aryl), the relationships are very strongly dependent on the substituents on the double bond and on the aromatic ring. Thus a very much smaller $\Delta G^{\neq}$ value is to be expected for Z = CH_2 than for $CHNO_2$.

The rotation barriers are particularly high in thioamides [cf. *(40)*, Z = S], so that some of these compounds can be resolved into rotational isomers[85]. This is due to the small tendency of sulfur to form double bonds, which leads to a particularly large contribution from the polar limiting structure [cf. I in *(39)*]. The energy thresholds for rotation in thioamides, so far as this can still be detected by NMR measurement, correlate well with the calculated π-bond orders[83].

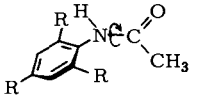


(a) *(b)*

(41)

In *N*-monosubstituted amides *(41)*, the rotamers have different energy contents and participate unequally in the thermal equilibrium. Numerous studies have been carried out on compounds of this type, since they are of particular interest in biochemistry (peptide linkage)[86]. Both rotamers can always be detected in formamides (R = H)[86,87], whereas in higher amides (R = Alkyl) only the form *(41a)*, in which the residues R^1 and R are *trans* to each other, are found[88]. ΔG^0 is usually greater than 2–3 kcal/mole; the concentration of the form *(41b)* is thus <5%, and can no longer be measured (but cf.[89]).

In the ring-substituted acetanilides *(42)*, on the other hand, the Z form and the E form[89a] have very similar energies, and both can be detected[90]. As in the (substituted) benzamides *(39i)–(39l)* (Table 4), the energy barrier for rotation increases with the bulk of R. The



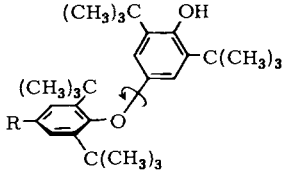
(42)

tert-butylated compound [R = *tert*-C_4H_9 in *(42)*] is the first *N*-monosubstituted amide for which both rotamers have been isolated as such[90].

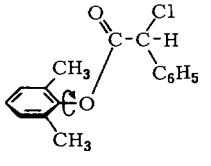
Of the many articles on hindered rotation about partial CN double bonds, we should like to draw the reader's attention to a few from the natural products field[91].

3.2.3. Carbon-Oxygen and Carbon-Sulfur Single Bonds

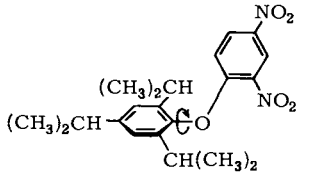
Sterically hindered rotations about the C–O bond have been detected in aromatic ethers and esters *(43)* to *(45)* (see Table 6).



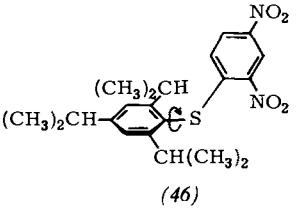
(43)



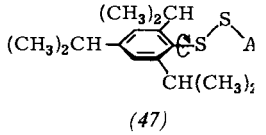
(44)



(45)



(46)



(47)

Table 6. Sterically hindered rotation about the aryl-O and aryl-S bond.

Compound	$\Delta G_c^{\neq}$ (kcal/mole)	T_c (°C)	Ref.
(43), R = OC_6H_5	[a]	[a]	[92]
(44)	12.4	−30	[93]
(45)	17.8	54	[94]
(46)	15.0	12	[94]
(47)	12.8	−27	[94, 95a]

[a] Broadening in the spectrum at room temperature; no data on the energy barrier.

[83] *J. Sandström*, J. physic. Chem. *71*, 2318 (1967).

[84] *G. Schwenker* and *H. Rosswag*, Tetrahedron Letters *1967*, 4237; *1968*, 2691.

[85] *W. Walter* and *G. Maerten*, Liebigs Ann. Chem. *715*, 35 (1968); *A. Mannschreck*, Angew. Chem. *77*, 1032 (1965); Angew. Chem. internat. Edit. *4*, 985 (1965); *W. Walter*, *E. Schaumann*, and *K. J. Reubke*, Angew. Chem. *80*, 448 (1968); Angew. Chem. internat. Edit. *7*, 467 (1968); *W. Walter* and *G. Maerten*, Liebigs Ann. Chem. *669*, 66 (1963).

[86] *C. Franconi*, Z. Elektrochem. *65*, 645 (1961); *L. A. LaPlanche* und *M. T. Rogers*, J. Amer. chem. Soc. *86*, 337 (1964).

[87] *A. J. R. Bourn*, *D. G. Gillies*, and *E. W. Randall*, Tetrahedron *22*, 1825 (1966); *H. Kessler*, Angew. Chem. *80*, 201 (1968); Angew. Chem. internat. Edit. *7*, 228 (1968).

[88] *L. A. LaPlanche* and *M. T. Rogers*, J. Amer. chem. Soc. *85*, 3728 (1963).

[89] *R. H. Barker* and *G. J. Boudreaux*, Spectrochim. Acta *23 A*, 727 (1967).

[89a] *J. E. Blackwood*, *C. L. Gladys*, *K. L. Loening*, *A. E. Petrarea*, and *J. E. Rush*, J. Amer. Chem. Soc. *90*, 509 (1968).

[90] *H. Kessler* and *A. Rieker*, Z. Naturforsch. *22b*, 456 (1967); Liebigs Ann. Chem. *708*, 57 (1967).

[91] *H. Paulsen* and *K. Todt*, Chem. Ber. *100*, 3397 (1967); *W. A. Szarek*, *S. Wolfe*, and *J. K. N. Jones*, Tetrahedron Letters *1964*, 2743; *R. J. Parry*, Chem. Commun. *1967*, 1294; *R. R. Shoup*, *H. T. Miles*, and *E. D. Becker*, J. Amer. chem. Soc. *89*, 6200 (1967); *D. M. G. Martin* and *C. B. Reese*, Chem. Commun. *1967*, 1275.

[92] *D. A. Bolon*, J. Amer. chem. Soc. *88*, 3148 (1966).

[93] *T. H. Siddall*, *W. E. Stewart*, and *M. L. Good*, Canad. J. Chem. *45*, 1290 (1967).

[94] *H. Kessler*, *A. Rieker*, and *W. Rundel*, Chem. Commun. *1968*, 475.

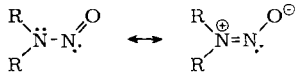
[95] a) *H. Kessler* and *W. Rundel*, Chem. Ber. *101*, 3350 (1968); b) *A. J. Gordon*, private communication.

The temperature dependence of the NMR spectra of aromatic sulfides *(46)* and disulfides *(47)* must be interpreted similarly. The hindered rotation about the aryl-hetero atom bond decreases with increasing size of the hetero atom (O→S), as is shown by a comparison of the compounds *(45)* and *(46)*.

This also gave a lower limit for the barrier for inversion at a dicoordinate oxygen atom. From the results of measurements on *(45)*, this barrier must be higher than 17.8 kcal/mole in diaryl ethers [94]. If we generalize the findings for the inversion at nitrogen (Sections 3.3.2 and 3.4.1), the inversion barriers at the oxygen in dialkyl ethers, alcohols, and water should be much higher. This agrees with SCF calculations, which gave a barrier of >34 kcal/mole for these compounds [95b].

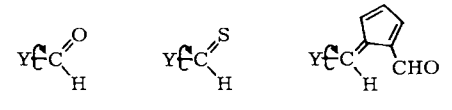
3.2.4. Nitrogen-Nitrogen and Nitrogen-Oxygen Single Bonds

The hindrance of rotation in nitrosamines *(48)* has been known for some time [2,96]. The high energy threshold (>20 kcal/mole) separating the preferred "planar" (cf. Section 3.2.2.2) conformations can be explained by the strong contribution of the polar limiting structure to the resonance. With suitable substitution on the amino nitrogen, the rotamers are so stable that they can be isolated as such [14,97].

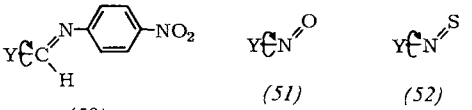


(48)

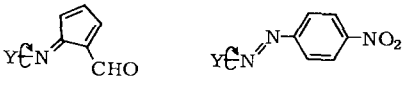
Examples of other classes of compounds with hindered rotation about the N–N bond are shown in Table 7. The rotation barriers of similar NN and CN compounds are comparable in their order of magnitude. Besides *rotation*, *inversion* consisting of folding in the plane of the double bond is also conceivable at the doubly bonded nitrogen atom in nitrogen compounds of the types *(51)–(54)*.



(39a) *(40a)* *(49)*



(50) *(51)* *(52)*



(53) *(54)*

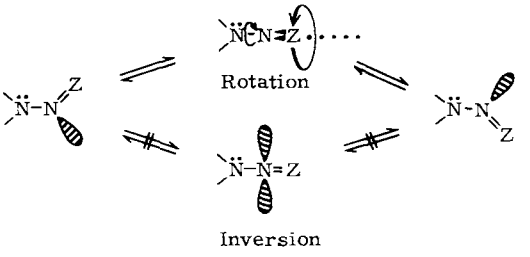
Y = $N(CH_3)_2$

[96] *R. K. Harris* and *R. A. Spragg*, Chem. Commun. *1967*, 362.

[97] *A. Mannschreck*, *H. Münsch*, and *A. Mattheus*, Angew. Chem. *78*, 751 (1966).

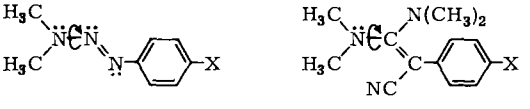
Table 7. Comparison of the $\Delta G_c^{\neq}$ and T_c values for rotations about partial CN and NN double bonds.

Cpd.	$\Delta G_c^{\neq}$ (kcal/mole)	T_c (°C)	Ref.
(39a)	21.7	116	[23]
(51)	23.3	183	[96]
(40a)	–	193	[76]
(52)	>17.2	> 70 (dec.)	[98]
(49)	17.0	49	[78]
(53)	11.8	– 39	[78]
(50)	15.9	≈ 17	[80]
(54)	15.7	35	[99]



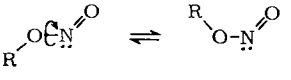
However, an inversion of this nature is hindered by the dialkylamino group (hetero effect, see Section 3.4) and is therefore less likely.

The barrier for rotation about the dimethylamino group in the substituted triazenes *(55)* has been correlated with the Hammett constant of X in the aryl residue (ρ = –2.0 to –2.1) [99]. The difficulty of rotation of the dimethylamino groups in the ketene aminals *(56)* also increases with the σ_p constant (ρ = –1.3) [82, 112d].



(55) *(56)*

Like the types of compounds mentioned so far, the alkyl nitrites *(57)* also exist as mixtures of cisoid and transoid rotamers [2]. The rotation barriers (approx. 10–14 kcal/mole) are lower than in the comparable nitrosamines.



(57)

Suitable hydrazine derivatives give complex temperature-dependent NMR spectra [100], which can only be explained by assuming hindered rotation about the NN single bond with simultaneous "slow" inversion at the nitrogen [101]. Calculations indicate that the energy required for rotation about NN single

[98] *W. J. Middleton*, J. Amer. chem. Soc. *88*, 3842 (1966).

[99] *M. H. Akhtar*, *R. S. McDaniel*, *M. Ferser*, and *A. C. Oehlschlager*, Tetrahedron *24*, 3899 (1968); *N. P. Marullo*, *C. B. Mayfield*, and *E. H. Wagener*, J. Amer. chem Soc. *90*, 510 (1968).

[100] *G. J. Bishop*, *B. J. Price*, and *I. O. Sutherland*, Chem. Commun. *1967*, 672; *B. H. Korsch* and *N. V. Riggs*, Tetrahedron Letters *1966*, 5897.

[101] *J. E. Anderson* and *J. M. Lehn*, Tetrahedron *24*, 123 (1968).

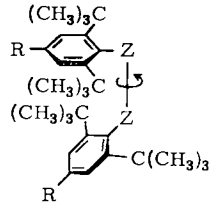
bonds (*ca.* 12 kcal/mole[102]) is significantly greater than for rotation about CC single bonds (approx. 3 kcal/mole).

3.2.5. Rotation About Other Single Bonds

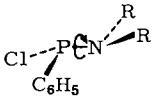
Hindrance of rotation about S–S and Se–Se bonds has been found in sterically hindered aromatic disulfides and diselenides *(58)*[95].

The rotation about the P–N bond in *(59)* can be "frozen in"[103]. The rotation barriers are lower in these compounds than in the hydrazine derivatives, since the greater distance between P and N leads to a decrease in hindrance. The repulsion of the lone pairs of electrons is undoubtedly partly responsible for the magnitude of the hindrance of rotation about N–O[103b], N–N, N–S[104], and N–P bonds.

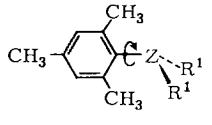
The trimesityl compounds of the elements of Group V [*(60a)–(60d)*; the values in parentheses are $\Delta G_c^{\neq}$ (kcal/mole) and T_c (°C)] are comparable to the triarylmethane derivatives *(14)*. The hindrance of rotation about the aryl-Z bond decreases as the size of the atom Z increases[34]. The observed temperature dependence of the NMR spectra is therefore not due to inversion at the Z atom (see Section 3.4).



(58), Z = S, Se



(59)



(60)

(60a) Z = P(12.4; -35)
(60b) Z = As (9.3; -91)
(60c) Z = Sb (<7.3; <-120)
(60d) Z = Bi (<7.3; <-120)

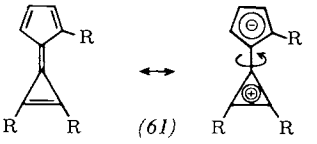
R^1 = Mesityl

3.3. Isomerizations at Double Bonds

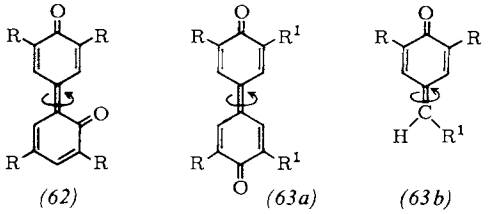
3.3.1. Carbon-Carbon Double Bond

The CC double bond has a very high configurational stability[*]. The rotation becomes detectable in the NMR spectrum only when the double-bond character is weakened, as in compounds of the types *(61)*[106] and *(62)*[107].

In the calicene derivatives *(61)*, strong participation of the polar limiting structure is to be expected. This greatly reduces the double-bond character and lowers the rotation barrier (cf.[108]). A polar limiting structure is also conceivable in *(62)*, though less likely. The



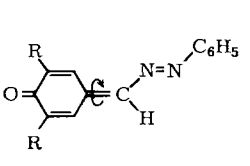
(61)



(62) *(63a)* *(63b)*

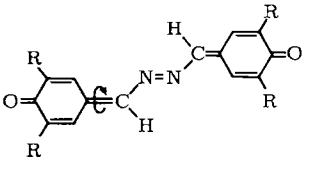
R = tert.-C_4H_9

investigation of suitable *p*-diphenoquinones *(63a)*[109] and quinonemethides *(63b)*[110] shows in fact that the symmetry plays an important part. Neither electron-attracting nor electron-repelling residues R^1 in quinonemethides *(63b)* are sufficient to lower the rotation barrier to such a degree that it can be determined by NMR spectroscopy. The rotation is sufficiently fast only in the symmetrical quinonemethide *(64b)*, whereas the barrier in the electronically comparable but unsymmetrical quinonemethide *(64a)* is considerably higher[110] (the figures indicate $\Delta G^{\neq}$ in kcal/mole).



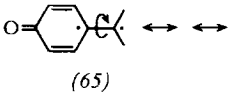
R = tert.-C_4H_9
>25.6

(64a)



R = tert.-C_4H_9
19.9

(64b)



(65)

This observation points to uncoupling of the π electrons in the transition state *(65)*. This cannot be the triplet state of the olefin because for the singlet-triplet-transition one would except a low transmission coefficient in the Eyring equation and also a low fre-

[102] *A. Veillard*, Theoret. chim. Acta *5*, 413 (1966).

[103] a) *D. Imbery* and *H. Friebolin*, Z. Naturforsch. *23b*, 759 (1968); *A. H. Cowley*, *M. J. S. Dewar*, and *W. R. Jackson*, J. Amer. chem. Soc. *90*, 4185 (1968); b) *M. Raban* and *G. W. Kenney*, Tetrahedron Letters *1969*, 1295.

[104] *J. M. Lehn* and *J. Wagner*, Chem. Commun. *1968*, 1298; *M. Raban*, *F. B. Jones*, and *G. W. J. Kenney*, Tetrahedron Letters *1968*, 5055; *M. Raban*, *G. W. Kenney*, and *F. R. Jones*, J. Amer. chem. Soc. *91*, 6677 (1969).

[*] The *cis-trans* isomerization in 1,2-dideuteroethylene requires 65 kcal/mole. It may proceed *via* the triplet or the excited singlet state; the latter possibility is more likely [105].

[105] *M. C. Lin* and *K. J. Laidler*, Canad. J. Chem. *46*, 973 (1968); *J. E. Douglas*, *B. S. Rabinovitch*, and *F. S. Looney*, J. chem. Physics *23*, 315 (1955).

[106] *A. S. Kende*, *P. T. Izzo*, and *W. Fulmor*, Tetrahedron Letters *1966*, 3697.

[107] *H. Kessler* and *A. Rieker*, Tetrahedron Letters *1966*, 5257.

[108] *J. H. Crabtree* and *D. J. Bertelli*, J. Amer. chem. Soc. *89*, 5384 (1967); *G. Seitz*, Tetrahedron Letters *1968*, 2305.

[109] *A. Rieker* and *H. Kessler*, Chem. Ber. *102*, 2147 (1969); *P. Boldt*, private communication.

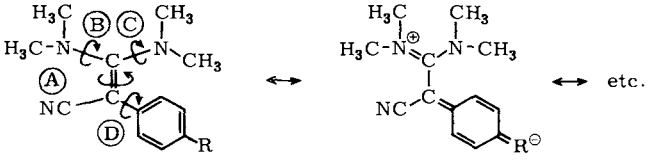
[110] *A. Rieker* and *H. Kessler*, Tetrahedron *24*, 5133 (1968).

quency factor A in the Arrhenius equation. The normal log A value (11.4) found for *(63a)* [109] gives evidence for the singlet biradical transition state of the rotation in these cases. The ease of rotation in hexapentaene can probably by explained in a similar manner [111].



(66) *(67)*

Substituents X and Z in *(66)* and *(67)* with strongly electron-repelling or electron-attracting effects [112] weaken the double bond sufficiently for the rotation to be measured by NMR spectroscopy. SR, OR, and NR_2 have been investigated as electron-repelling substituents, and NO_2, CN, COR, COOR, and aryl as electron-attracting substituents [82,112]. Up to four rotations can be detected simultaneously in 2-aryl-2-cyano-1,1-bis(dimethylamino)ethylenes *(68)* [82,112d]. A different coalescence temperature is found for each rotation.



(68)

The kinetic data found from the spectra for all four rotations can be correlated with the Hammett σ constants of the residues R in the benzene ring (Fig. 7).

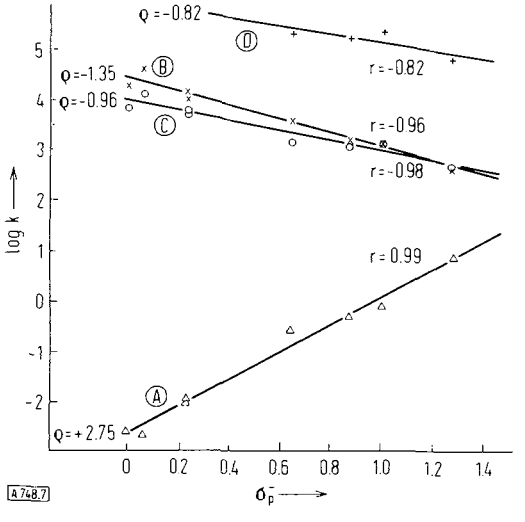


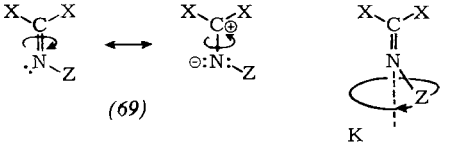
Fig. 7. Hammett correlation of the rotations in ketene aminals *(68)*.

It can be seen from the gradient of the log k/σ correlation lines that the rotations about both CN single bonds and about the C-aryl bond are hindered by electron-attracting substituents, while the rotation about the central CC double bond is greatly facilitated.

3.3.2. Carbon-Nitrogen Double Bond Rotation and Inversion

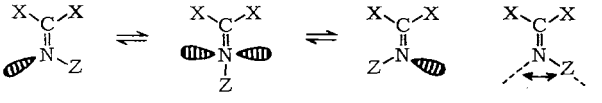
There are in principle two possibilities for the *syn-anti* isomerization in imines *(69)* (cf. Section 3.2.4).

a) Rotation. The substituent Z describes a circle about the axis of the C–N bond ("out of plane" isomerization, K). The process is favored by polarization of the CN double bond. The sp^2 hybridization of the nitrogen atom, and hence the bond angle (C–N–Z), is retained.



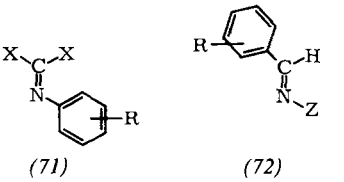
(69) K

b) Inversion. The N–Z bond swings in the bond plane of the imine system from the *syn* into the (identical) *anti* position ("in plane" isomerization, L). The bond angle (C–N–Z) increases to 180° in the transition state. The CN double bond is, to a first approximation, unaffected.



(70) L

The influence of *p* substituents R in the aryl residue of *N*-arylimines of the type *(71)* on the free enthalpy of activation of the *syn-anti* isomerization follows the Hammett relation [113–116]. Contrary to previous reports in the literature [123] we were also able to show such a correlation in imino esters [*]. Irrespective of the substituent X, the reaction constant is $\rho = 1.7$ [116]. A substituent R in benzylideneamines *(72)*, on the other hand, has a much smaller influence ($\rho = -0.4$) [117]. The difference in the effects of variation of substituents on the N and on the C atom has been taken as evidence of inversion [113].



(71) *(72)*

[111] *R. Kuhn, B. Schulz*, and *J. C. Jochims*, Angew. Chem. *78*, 449 (1966); Angew. Chem. internat. Edit. *5*, 420 (1966).

[112] a) *G. Isaksson, J. Sandström*, and *I. Wennerbeck*, Tetrahedron Letters *1967*, 2233; b) *Y. Shvo, E. C. Taylor*, and *J. Bartulin*, Tetrahedron Letters *1967*, 3259; *Y. Shvo, ibid. 1968*, 5939; c) *A. P. Downing, W. D. Ollis*, and *I. O. Sutherland*, J. chem. Soc. (London), *B 1969*, 111 and literature cited therein; d) *H. Kessler*, Chem. Ber. *103*, 973 (1970).

[113] *D. Y. Curtin, E. J. Grubbs*, and *C. G. McCarty*, J. Amer. chem. Soc. *88*, 2775 (1966).

[114] *A. Rieker* and *H. Kessler*, Tetrahedron *23*, 3723 (1967).

[115] *H. Kessler*, Tetrahedron Letters *1968*, 2041.

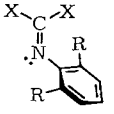
[*] *H. Kessler*, and *D. Leibfritz*, unpublished.

[116] a) *H. Kessler* and *D. Leibfritz*, Tetrahedron, in press; b) *ibid. 25*, 5127 (1969).

[117] *G. Wettermark, J. Weinstein, J. Sousa*, and *L. Dogliotti*, J. physic. Chem. *69*, 1584 (1965).

The small influence of the polarity of the solvent on the rate of isomerization of tetramethylphenylguanidine points to a similar conclusion[115,116b]. A polar solvent should facilitate isomerization by rotation, as has been found *e.g.* for ketene aminals[112d].

The influence of residues R in the *o*-position in arylimines *(73)* is particularly impressive. The activation threshold is lowered as the size of R increases[116, 118–120]. This can only be explained by inversion, in



(73)

which the steric hindrance is less in the extended transition state than in the ground state. Rotation would be hindered by the substituents R. Figure 8 shows a comparison of the $\Delta G_c^{\ddagger}$ values for the *inversion in guanidines (74)*[116] with those for *rotation* about the CN double bond *in the guanidinium salts (75)*[121][*], in which the lone pair of electrons is fixed and inversion is consequently impossible.

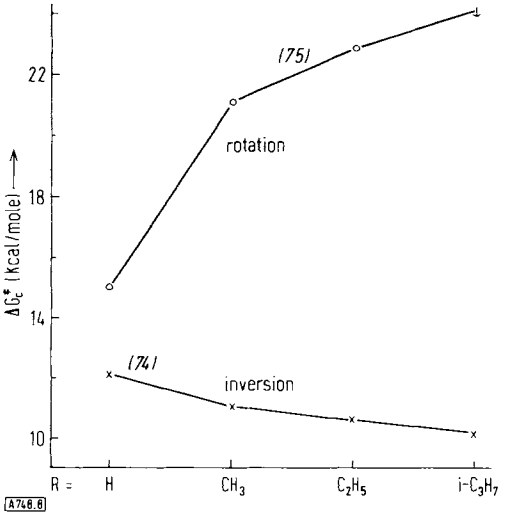
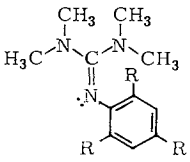


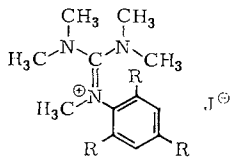
Fig. 8. Free enthalpies of activation for inversion [guanidines *(74)*] and rotation [guanidinium salts *(75)*] at doubly bonded nitrogen atoms.

The contrary substituent effects in the two series and the low energy barriers for the *syn-anti* isomerization of the guanidines *(74)* also indicate that the process involved is an inversion.

Another argument in favor of inversion is the similarity of the effect of the substituent Z on the *syn-anti* isomerization in imines ($X_2C{=}NZ$) and on the in-



(74)



(75)

version at tricoordinate nitrogen (*e.g.* in aziridines, see Section 3.4.1.1)[116]. The isomerization rate increases very rapidly as the substituent Z is varied in the order:

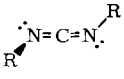
$$RO \approx R_2N < \text{halogen} < \text{alkyl} < \text{aryl} < \text{acyl}$$

Substituents X on the imino carbon atom also increase the inversion rate, the order being[115,116a]:

quinone ring < alkyl < acetyl < alkoxycarbonyl < aryl < methoxy [123, 124] < alkylthio [124] < dialkylamino

With the aid of these sequences, it is possible to predict the rate constants within wide limits.

The fast inversion at nitrogen also explains why carbodiimides *(76)*, unlike allenes, do not form stable isomers. As predicted from calculations[125], the diastereotopic geminal H and CH_3 groups in the residues R have been found to be NMR-spectroscopically equivalent even at −100 °C. The activation energy of the inversion is presumably smaller than ≈9 kcal/mole in these compounds[45].



(76)

R = C_2H_5, i-C_3H_7, $CH_2C_6H_5$

3.3.3. Isomerization at Other Double Bonds

Isomerizations of oxonium and sulfonium salts containing CO and CS double bonds, *e.g. (77)*, are closely related to the isomerizations just described.

In the protonated carbonyl compounds [*(77)*, Z = H] that have been the subjects of most of the investigations[**], isomerization by deprotonation/reprotonation is possible as well as the rotations and inversions discussed for the CN double bonds[126b]. Experiments with systematic variation of the substituents, which should make it possible to decide which course is in fact followed, have not yet been carried out.

In the series of sulfur compounds, investigations have been carried out on the thiuronium salts *(78)*[121].

The influence of the substituent Z on the isomerization rate in these compounds is comparable to that in

[118] *A. Rieker* and *H. Kessler*, Z. Naturforsch. *21b*, 939 (1966).

[119] *H. Kessler*, Angew. Chem. *79*, 997 (1967); Angew. Chem. internat. Edit. *6*, 977 (1967).

[120] *D. Wurmb-Gerlich*, *F. Vögtle*, *A. Mannschreck*, and *H. A. Staab*, Liebigs Ann. Chem. *708*, 36 (1967).

[121] *H. Kessler* and *D. Leibfritz*, Tetrahedron Letters *1969*, 427.

[*] Rotation about the CN double bond has also been observed in a nitrone [122].

[122] *R. W. Layer* and *C. J. Carman*, Tetrahedron Letters *1968*, 1285.

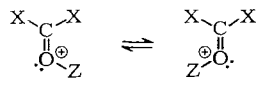
[123] *N. P. Marullo* and *E. H. Wagener*, J. Amer. chem. Soc. *88*, 5034 (1966).

[124] *F. Vögtle*, *A. Mannschreck*, and *H. A. Staab*, Liebigs Ann. Chem. *708*, 51 (1967).

[125] *M. S. Gordon* and *H. Fischer*, J. Amer. chem. Soc. *90*, 2471 (1968); *J. M. Lehn* and *B. Munsch*, Theoret. chim. Acta *12*, 91 (1968).

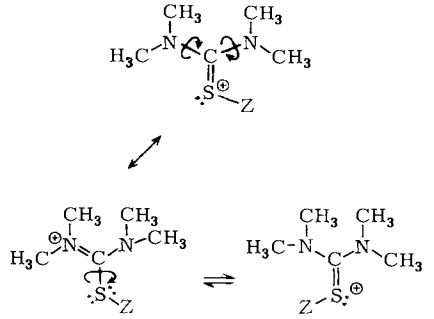
[**] In the literature the possibility of inversion is not usually taken into account.

[126] a) *D. M. Brouwer*, Recueil Trav. chim. Pays-Bas *86*, 879 (1967); b) *H. Hogeveen*, *ibid. 86*, 696 (1967).



(77)

Z = H; X = alkyl [126], aryl [127], OH [128], alkoxy [129]
Z = alkyl; X = alkyl, alkoxy [130], H [131], *p*-quinonoid ring [132]
Z = aryl; X = dialkylamino, alkoxy, alkylthio [132a]

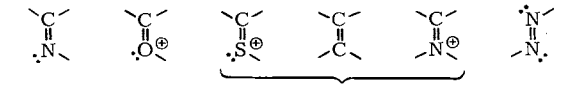


(78)

guanidinium salts *(75)* [45]. Thus large residues in the *o*-positions of *S*-arylthiuronium salts hinder the process, indicating that rotation is involved.

The inversion seems to have been conclusively verified in the imines. Some sulfonium salts appear to isomerize by rotation, but it is still too early to generalize.

Inversion is more likely in oxonium salts than in the sulfur analogs. However, no investigations on this point have been carried out as yet.

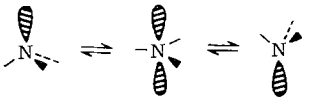


Rotation is the only possibility for *cis/trans* isomerization in olefins and immonium salts, apart from the protonated imines, in which inversion by deprotonation/reprotonation is also conceivable.

3.4. Inversions

3.4.1. Inversion at the Nitrogen Atom

The inversion of the nitrogen pyramid in amines has been known for a long time. It proceeds *via* a planar state by a change in the hybridization of the nitrogen atom from sp^3 to sp^2 [*].

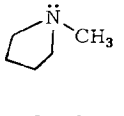


(79)

The barrier in ammonia and in many amines is so low ($\lesssim$6 kcal/mole) that it is difficult to detect by NMR spectroscopy, though the inversion rates can still be determined in such cases from the pH dependence of the spectra [135]. With suitable substituents, however, the pyramidal arrangement can be stabilized sufficiently to allow even the separation of invertomers ($\Delta G^{\neq} > 23$ kcal/mole).

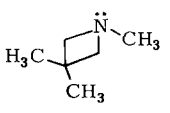
3.4.1.1. Influence of Ring Strain

The inversion barrier is much higher in the azetidines *(81)* and aziridines *(82)–(84)* than in the unstrained pyrrolidines *(80)*. ($\Delta G^{\neq}$ is given in kcal/mole under the formulas).



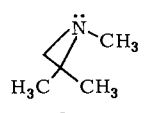
7 [136a]

(80)



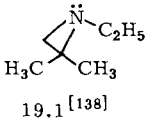
8.8 [136b]

(81)



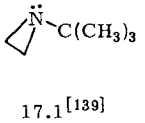
20.5 [136, 137]

(82)



19.1 [138]

(83)



17.1 [139]

(84)

An intuitive explanation of this phenomenon can be obtained by considering the transition state. In the planar state, the nitrogen is sp^2-hybridized, so that the bond angle must increase to 120 °C during the inversion. When the nitrogen is incorporated in a small ring, however, the necessary spreading is hindered, *i.e.* the activation energy increases.

On the other hand, the s-character of the lone electron pair on nitrogen is much higher in the three-membered ring than in acyclic amines. This is indicative of a ground state stabilization with respect to the inversion transition state.

[*] With H atoms on the nitrogen, inversion is also possible by the tunnel effect [134]. This process becomes increasingly unlikely as the mass of the substituents on the nitrogen increases.

[127] *R. van der Linde, J. W. Dornseiffen, J. U. Veenland,* and *T. J. de Boer*, Tetrahedron Letters *1968*, 525.

[128] *H. Hogeveen, A. F. Bickel, C. W. Hilbers, E. L. Mackor,* and *C. McLean*, Recueil Trav. chim. Pays-Bas *86*, 687 (1967).

[129] *G. A. Olah* and *A. M. White*, J. Amer. chem. Soc. *90*, 1884 (1968).

[130] *B. G. Ramsey* and *R. W. Taft*, J. Amer. chem. Soc. *88*, 3058 (1966).

[131] *R. F. Borch*, J. Amer. chem. Soc. *90*, 5303 (1968).

[132] *D. M. Brouwer, E. L. Mackor,* and *C. McLean*, Recueil Trav. chim. Pays-Bas *85*, 114 (1966).

[132a] *H. Kessler* and *H. O. Kalinowski*, unpublished.

[133] *E. R. Talaty* and *J. C. Fargo*, Chem. Commun. *1967*, 65; *I. G. Murgulesen* and *Z. Simon*, Rev. Roumaine Chim. *11*, 21 (1966).

[134] *H. A. Stuart*: Molekülstruktur, Springer-Verlag, Berlin 1967, p. 475.

[135] *J. J. Delpueck* and *M. N. Deschamps*, Chem. Commun. *1967*, 1188; *J. L. Sudmeier* and *G. Occupati*, J. Amer. chem. Soc. *90*, 154 (1968).

[136] a) *J. B. Lambert* and *W. L. Oliver*, J. Amer. chem. Soc. *91*, 7774 (1969); b) *J. M. Lehn* and *J. Wagner*, Chem. Commun. *1968*, 148.

[137] *A. Loewenstein, J. F. Neumer,* and *J. D. Roberts*, J. Amer. chem. Soc. *82*, 3599 (1960).

[138] *A. T. Bottini* and *J. D. Roberts*, J. Amer. chem. Soc. *80*, 5203 (1968).

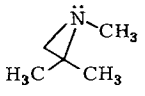
[139] *S. J. Brois*, J. Amer. chem. Soc. *89*, 4242 (1967).

3.4.1.2. Steric Effect

The $\Delta G^{\neq}$ value decreases with increasing size of the residues on the nitrogen [cf. the series *(82)*–*(83)*→*(84)*]. This effect, which is not very large, is due to the fact that the steric hindrance is less in the planar transition state than in the pyramidal ground state.

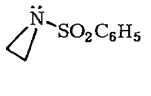
3.4.1.3. Electronic Effects

Electron-attracting substituents strongly depress the inversion barrier [cf. the series *(82)*→*(85)*→*(86)*→*(87)*, with indicated $\Delta G^{\neq}$ values].



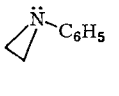
20.5[136, 137]

(82)



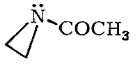
12.4[140]

(85)



11.7[141]

(86)



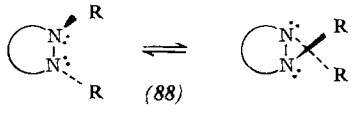
<6[141]

(87)

This effect, which stabilizes the planar transition state, is also the reason for the very fast nitrogen inversion in amides, which cannot be detected by NMR spectroscopy.

Electronegative substituents Z (halogen, oxygen, nitrogen) stabilize the pyramidal ground state of the nitrogen atom ("hetero effect"). Thus the inversion barrier has been measured in hydroxylamines[103, 142b] and hydrazine derivatives[100, 143] by NMR spectroscopy, though the inversion is to fast for measurement in this way in other acyclic amines.

Many articles have appeared on compounds *(88)*, in which two nitrogen atoms are built into adjacent positions in ring systems[144, 145].



(88)

R = Alkyl, Acyl, Carboxyl, $(CH_2)_n$ *etc.*

The inversion in systems of this type is easy to follow by NMR spectroscopy. The inversions of the two N atoms do not occur simultaneously[145].

The hetero effect, which is also found in imines (cf. Section 3.3.2), could have two causes. 1. As the electronegativity of the substituents increases, so also does the s character of the lone pair of electrons on the nitrogen[146], with the result that the energy difference for the transition state (p character of the lone pair of electrons) increases. 2. The transition state is destabilized by the mutual repulsion of the lone pairs of electrons on the nitrogen and on the hetero atom. It is not yet possible to say which of these two effects predominates.

The configuration-stabilizing effect of halogen atoms shows that (p-d)π interaction cannot play any decisive part in the transition state. Sulfur substituents, on the other hand, appear to accelerate the inversion[104]. This is contrary to findings in some earlier investigations, in which a "slow" inversion is assumed for sulfenamines[147]. However, the temperature effect observed in these investigations can be better explained by hindered rotation about the SN bond.

Appreciable stabilities of the nitrogen pyramid are achieved by combination of the effects of ring strain and of hetero substitution.



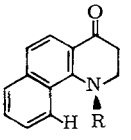
(89a), Z = Halogen[148]

(89b), Z = NR_2[149]



(90a), Z = O[150]

(90b), Z = NR[151]



(91)

Stable nitrogen invertomers were first separated by *Felix* and *Eschenmoser* and by *Brois* in the halogenoaziridine series *(89a)*[148]. Invertomeric oxaziridines [*(90a)*, Z = O][150a] and diaziridines [*(90b)*, Z = NR][150b] are also stable at room temperature.

If the nitrogen atom is substituted with two hetero atoms, the pyramid is stable to inversion even in rings with more than three members. This was recently demonstrated in the case of an *N*-methoxy-1,2-oxazolidine[151].

Hindrance of the inversion by steric effects has been observed in dihydroquinolone systems *(91)*[152].

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[140] *F. A. L. Anet, R. D. Trepka*, and *D. J. Cram*, J. Amer. chem. Soc. *88*, 357 (1967).

[141] *F. A. L. Anet* and *J. M. Osyany*, J. Amer. chem. Soc. *89*, 2072 (1967).

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[143] *R. M. Moriarty, sen., M. R. Murphy, S. J. Druck*, and *L. May*, Tetrahedron Letters *1967*, 1603.

[144] *E. L. Allred, C. L. Anderson, R. L. Miller*, and *A. L. Johnson*, Tetrahedron Letters *1967*, 525; *E. Fahr, W. Fischer, A. Jung, L. Sauer*, and *A. Mannschreck*, *ibid. 1967*, 161; *B. Junge* and *H. A. Staab*, *ibid. 1967*, 709; *J. Wagner, W. Nojnarowski, J. E. Anderson*, and *J. M. Lehn*, Tetrahedron *25*, 657 (1969), and literature cited therein; *J. M. Lehn* and *J. Wagner*, *ibid. 25*, 677 (1969).

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[146] *H. A. Bent*, Chem. Reviews *61*, 275 (1961).

[147] *K. Murayama* and *T. Yoshioka*, Tetrahedron Letters *1968*, 1363; *M. Raban, G. W. J. Kenney, J. M. Moldowan*, and *F. B. Jones*, J. Amer. chem. Soc. *90*, 2985 (1968); *H. J. Jakobson* and *A. Senning*, Chem. Commun. *1967*, 617; *M. Raban*, Chem. Commun. *1967*, 1017.

[148] *S. J. Brois*, J. Amer. chem. Soc. *90*, 506, 508 (1968); *D. Felix* and *A. Eschenmoser*, Angew. Chem. *80*, 197 (1968); Angew. Chem. internat. Edit. *7*, 224 (1968); *R. G. Kostyanovsky, Z. E. Samojlova*, and *J. J. Tchervin*, Tetrahedron Letters *1969*, 719.

[149] *R. S. Atkinson*, Chem. Commun. *1968*, 676; *S. J. Brois*, Tetrahedron Letters *1968*, 5997.

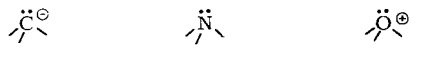
[150] a) *F. Montanari, I. Moretti*, and *G. Torre*, Chem. Commun. *1968*, 1694; *D. R. Boyd*, Tetrahedron Letters *1968*, 4561; *A. Mannschreck, J. Linss*, and *W. Seitz*, Liebigs Ann. Chem. *727*, 224 (1969); b) *A. Mannschreck, R. Radeglia, E. Gründermann*, and *R. Ohme*, Chem. Ber. *100*, 1778 (1967); *A. Mannschreck* and *W. Seitz*, Angew. Chem. *81*, 224 (1969); Angew. Chem. internat. Edit. *8*, 212 (1969).

[151] *K. Müller* and *A. Eschenmoser*, Helv. chim. Acta *52*, 1823 (1969).

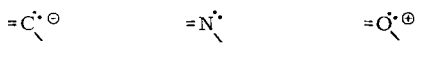
[152] *W. N. Speckamp, U. K. Pandit, P. K. Korver, P. J. van der Haak*, and *H. O. Huismann*, Tetrahedron *22*, 2413 (1966).

3.4.2. Other Inversions

Inversions can also occur at other atoms [152, 153].



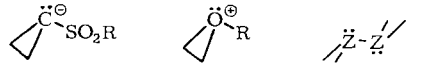
(92) *(93)* *(94)*



(95) *(96)* *(97)*

The pyramids of carbanions *(92)* and oxonium salts *(94)* are isosteric with those of amines *(93)*. The inverting central atoms can also be replaced by other elements from the same group of the periodic system. The number of possible inversions is considerably increased by the inversion processes in the systems *(95)* to *(97)* containing doubly bonded atoms. NMR studies have so far been carried out on only a few inversions at atoms other than nitrogen [*].

Thus *Anet et al.* studied the inversion in cyclic carbanions *(98)* [155], and *Lambert et al.* analysed the same process in the oxonium salts *(99)* [156] (the figures are the $\Delta G^{\ddagger}$ values for inversion in kcal/mole).



17-18 *(98)* ≈10 *(99)* *(100)*

Z = P, As

Surprisingly low values of 26 kcal/mole were found for the inversion barriers for phosphorus and arsenic in compounds *(100)* [157]. The inversion of Grignard compounds has also been investigated [158]. Organometallic compounds of the type *(92)* usually exhibit complete racemization in chemical reactions [28]. Stereospecific reactions are possible only when the inversion barrier is increased by ring strain, as in the aziridines [28]. The inversion therefore becomes increasingly easy in the order *(92)*→*(93)*→*(94)*. If this observation is generalized, one should expect very small inversion barriers (<5 kcal/mole) in acyclic oxonium salts of the type *(94)*.

Similar results can be deduced for the species *(95)*→*(96)*→*(97)*. Whereas vinyllithium compounds of the type *(95)* react stereospecifically (or stereoselectively) [28], the inversion rates for imines lie in the NMR measurement range, and the ketonium salts *(97)* appear from preliminary results [45] to invert faster than comparable imines.

In species with the same central atom [*e.g. (92)* and *(95)* or *(93)* and *(96)*], types *(95)* and *(96)* have a distinctly higher barrier than types *(92)* and *(93)*. These cautious generalizations require further experimental confirmation.

The inversions of comparable pyramidal compounds should also become increasingly difficult with decreasing electronegativity of the central atom, *i.e.* in the order *e.g.* N→P→As, since the s character of the lone pair of electrons increases in this order [146], and the stronger the s character in the ground state, the more difficult is the inversion *via* a state in which the lone pair of electrons has pure p character.

Care is necessary in the interpretation of inversion barriers, since the mirror-image invertomer can be formed not only by direct intramolecular inversion but also by dissociation and recombination of the fragments. Isomerization by rotation must also be considered in the case of doubly bonded atoms (see Section 3.3.2).

NMR spectroscopy is a good method for the study of the substituent effects and the influence of the central atom on the inversion rates. The current interest in this topic is obvious from the number of publications that have appeared in recent years.

The investigations by our research group that are mentioned here were carried out with the support of the Deutsche Forschungsgemeinschaft, for which I am grateful. I also thank Prof. Dr. Eugen Müller for his interest in the work. Thanks are also due to Doz. Dr. A. Rieker for perusal of the manuscript and for numerous discussions, as well as to Dipl.-Chem. D. Leibfritz and Fräulein C. Burk for their assistance.

Received: March 28, 1969 [A 748 IE]
German version: Angew. Chem. *82*, 237 (1970)
Translated by Express Translation Service, London

[153] *G. W. Koeppl, D. S. Sagatys, G. S. Krishnamurthy,* and *S. I. Miller,* J. Amer. chem. Soc. *89*, 3396 (1967).

[*] In this connection, mention should be made of the pseudorotation at pentacoordinate phosphorus [154]. This process involves a rearrangement of the ligands that requires a change in the hybridization of the central atom in the transition state. Inversions at bivalent atoms (*e.g.* at oxygen in ethers, alcohols, and water) with linear transition states are briefly discussed in Section 3.2.3 for interconversions of C—O bond rotamers.

[154] *G. M. Whitesides* and *W. M. Bunting,* J. Amer. chem. Soc. *89*, 6802 (1967); *D. Hellwinkel,* Angew. Chem. *78*, 749 (1966); Angew. Chem. internat. Edit. *5*, 725 (1966).

[155] *A. Ratajczak, F. A. L. Anet,* and *D. J. Cram,* J. Amer. chem. Soc. *89*, 2072 (1967).

[156] *J. B. Lambert* and *D. H. Johnson,* J. Amer. chem. Soc. *90*, 1349 (1968).

[157] *J. B. Lambert, G. F. Jackson* III, and *D. C. Mueller,* J. Amer. chem. Soc. *90*, 6401 (1968).

[158] *G. Fraenkel, D. T. Dix,* and *M. Carlson,* Tetrahedron Letters *1968*, 579, and literature cited therein.

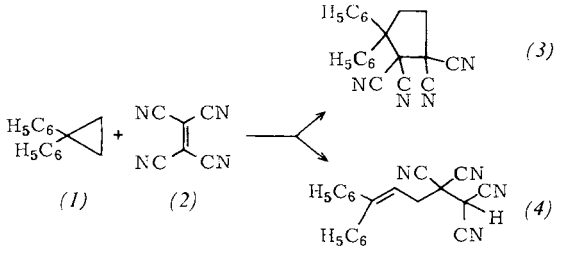
Reaction of 1,1-Diphenylcyclopropane with Tetracyanoethylene[**]

By *Th. Martini* and *J. A. Kampmeier*[*]

Thermal reactions between electron-deficient π-systems and C—C σ bonds have previously been encountered only with highly strained cyclopropane compounds[1] such as bicyclo-[2.1.0]pentanes, bicyclo[1.1.0]butanes, and quadricyclene[2,3]. A 1 : 1 cycloadduct of dispiro[2.4.2.0]decane and tetracyanoethylene was recently reported[4], but the structure was not clearly elucidated. We now report on the reaction of 1,1-diphenylcyclopropane *(1)*[5] with tetracyanoethylene *(2)*.

When compound *(1)* (4.4 g, 0.023 mole) and compound *(2)* (6.0 g, 0.047 mole) are heated together in benzene (100 ml) in an ampoule at 125 °C for 5 days, the color of the solution changes from blood-red to brown. After removal of the solvent, the residue is heated to boiling in CCl_4 (150 ml) and the hot solution filtered to remove undissolved *(2)*. The filtrate is kept at 0 °C for several hours and then reheated and refiltered to remove a final portion of *(2)*.

A 10 ml portion of $CHCl_3$ is added to the filtrate which is then allowed to stand at 0 °C for 2 days to give a brown crystalline product (4.5 g, 65 % calculated for a 1 : 1 adduct). The NMR spectrum of the product shows it to consist of *(3)* and *(4)* in the ratio 1 : 1.3. Careful NMR examination of all work-up fractions failed to give evidence for other products.



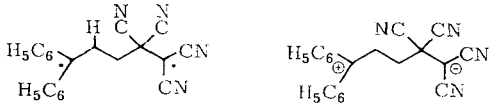
(1) *(2)* *(3)* *(4)*

The mixture could be separated by crystallization from absolute alcohol. The initial precipitate from alcohol is recrystallized from alcohol to give *(3)*, m.p. 202—203 °C. The alcoholic mother liquor from the original separation is evaporated to dryness and the residue taken up in cyclohexane. The crystalline product, obtained after the solution has been allowed to stand for a day, is recrystallized from cyclohexane to give *(4)*, m.p. 123—125 °C. Separation of 1.0 g of crude reaction product gives 0.35 g of *(3)* and 0.3 g of *(4)*. Both compounds give the expected C, H, N analyses and molecular weight (mass spectrometry).

The NMR spectrum of *(3)* [in $CDCl_3$ at 60 and 100 MHz: τ = 2.70 (10 aromatic H/s); 6.88 (4 aliphatic H/s)] and the UV spectrum [in CH_3OH (λ_{max} = 259 nm, ε = 665)] support structure *(3)*. The symmetrical structure, 1,1,2,2-tetracyano-4,4-diphenylcyclopentane, is ruled out by the NMR spectrum [in C_6D_6 (60 MHz); τ = 3.15 (10 aromatic H/m); 7.97 (4 aliphatic H/m[6])].

The NMR spectrum of *(4)* [in $CDCl_3$ (60 MHz): τ = 2.80 (10 aromatic H/m); 4.02 (1 olefinic H/t), J = 7.1 Hz; 5.80 (1 aliphatic H/s)[7]; 6.92 (2 allylic H/d), J = 7.1 Hz] shows an unusually large solvent shift[8] [in C_6D_6 (60 MHz): τ = 8.17 (1 aliphatic H/s) and 7.65 (2 allylic H/d)]. The UV spectrum [in cyclohexane (λ_{max} = 234 nm (sh), 259 nm, ε = 13600, 15500)][9] further supports structure *(4)*. Reaction of 1,1-diphenyl-3-propene[10] with *(2)* in an ene reaction[7,11], under the conditions described above, gave an independent synthesis of *(4)* in 9 % yield (pure product, based on reacted olefin). Neither the cycloadduct *(3)* nor rearrangement of the olefin to 1,1-diphenyl-1-propene is observed.

Cyclopropane does not react with *(2)* under the conditions described above. Heating compound *(1)* in benzene solution for four days with maleic anhydride (at 140 °C), fumaronitrile (at 175 °C), or 1,1-dichloro-2,2-difluoroethylene (at 130 °C) gave only unreacted starting materials. *(2)* is thermally stable at 130 °C. The formation of *(3)* and *(4)* is most simply explained in terms of a common, open-chain intermediate[2,11,12] *(5)* or *(6)*: cyclization leads to *(3)* and a 1,4 shift gives *(4)*.



(5) *(6)*

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[1] *R. B. Turner, P. Goebel, B. J. Mallon, W. v. E. Doering, J. F. Coburn, Jr.*, and *M. Pomerantz*, J. Amer. chem. Soc. *90*, 4315 (1968).

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[3] *A. B. Evnin* and *D. R. Arnold*, J. Amer. chem. Soc., *90*, 5330 (1968).

[4] *D. S. Magrill, J. Altman*, and *D. Ginsburg*, Israel J. Chem. *7*, 479 (1969).

[5] *C. L. Bumgardner*, J. Amer. chem. Soc. *83*, 4420 (1961).

[6] Symmetrical 12 line spectrum having AA'BB' character, cf. *F. A. Bovey*: Nuclear Magnetic Resonance Spectroscopy. Academic Press, New York 1969, p. 119.

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[8] *L. M. Jackman* and *S. Sternhell*: Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry. Pergamon, Oxford 1969, 2nd Edition, p. 105.

[9] UV spectrum of 1,1-diphenylethylene (*n*-heptane): λ = 235.4 (sh), 248 nm, ε = 13730; *H. Suzuki*, Bull. chem. Soc. Japan *33*, 619 (1960).

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[11] For ene reactions with compound *(2)*, see *H. M. R. Hoffmann*, Angew. Chem. *81*, 597 (1969); Angew. Chem. internat. Edit. *8*, 556 (1969).

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β-Substituted *N*-Formyl-*S*-benzylcysteines[11]

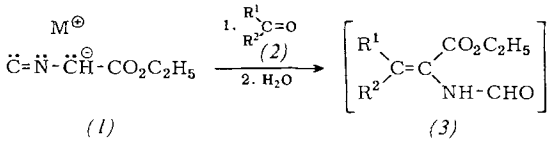
By *Ulrich Schöllkopf* and *Dieter Hoppe*[*]

β-Substituted *N*-formyl-*S*-benzylcysteines *(4)* warrant attention as cysteine precursors on account of the ease with which benzyl and formyl groups can be removed[2,3] and because they appear amenable to optical resolution[3].

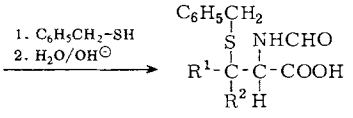
We have now found that these compounds can be prepared in a "single-vessel" process by treating metalated ethyl isocyanoacetate *(1)* (prepared from ethyl isocyanoacetate and *e.g.* butyllithium, potassium *tert*-butoxide, or sodium hydride in tetrahydrofuran) with carbonyl compounds *(2)*, then adding phenylmethanethiol, evaporating off the solvent, adding water and potassium hydroxide to the residue, and finally warming for a short period.

The synthesis probably proceeds *via* β-substituted ethyl α-formylaminoacrylates *(3)*[4] which add the thiol after the

manner of a Michael reaction to give ethyl *N*-formyl-*S*-benzylcysteinates. Support for this reaction course comes from the fact that *N*-formyl-*S*-benzyl-β-phenylcysteine is formed in 85% yield on reaction of ethyl α-formylaminocinnamate[4] with phenylmethanethiol in ethanol containing sodium ethoxide and subsequent hydrolysis.



(1) *(3)*



(4)

M = alkali metal

(4)	R^1	R^2	metalated with [a]	at (°C)	yield (%)
(a)	H	H	KOtBu	15	9
(b)	CH_3	CH_3	KOtBu	10	33
			BuLi	−70	61
			NaH	35	30
(c)	$(CH_3)_2HC$	H	BuLi	−70	21
(d)		$(CH_2)_5$	BuLi	−70	3 [b]
(e)	C_6H_5	H	BuLi	−70	67
			KOtBu	15	70
(f)	*p*-$CH_3OC_6H_4$	H	KOtBu	30	54
(g)	*p*-$(CH_3)_2NC_6H_4$	H	NaH	35	32
(h)	*m,p*-$(CH_3O)_2C_6H_3$	H	KOtBu	30	59
(i)	2-Thienyl	H	KOtBu	30	39

[a] In tetrahydrofuran. KOtBu = K *tert*-butoxide; BuLi = butyllithium. [b] The ester is only partially hydrolyzed.

N-Formyl-S-benzylpenicillamine (4b)

Butyllithium (0.04 mole as a 2.0 N solution in pentane) is added dropwise to a vigorously stirred solution of ethyl isocyanoacetate[5] (4.53 g, 0.04 mole) in tetrahydrofuran (30 ml) at −70 °C in such a way that the drops fall directly into the reaction mixture. A solution of acetone (2.35 g, 0.04 mole) in tetrahydrofuran (10 ml) is then also added dropwise, the mixture allowed to warm up to room temperature, and phenylmethanethiol added (5.0 g, 0.04 mole). After removal of solvent under vacuum, water (25 ml) is added to the residue and the mixture is stirred for 5 min before addition of potassium hydroxide (2.5 g, 0.045 mole). Stirring is continued until a homogeneous solution is obtained (*ca.* 15 min) which is then cooled to room temperature before addition of concentrated hydrochloric acid and subsequent ice-cooling. When crystallization starts, ether is added and the mixture is stirred for a short time. After 12 h (*ca.* −5 °C), 6.56 g (61%) of *(4b)* precipitated, m.p. 157 °C (from ethanol/water, 1 : 2).

N-Formyl-S-benzyl-β-phenylcysteine (4e)

A solution of ethyl isocyanoacetate (4.52 g, 0.04 mole) and benzaldehyde (4.26 g, 0.04 mole) in tetrahydrofuran (10 ml) is added dropwise to a vigorously stirred suspension of 80% potassium *tert*-butoxide (*tert*-butanol as crystal solvent) in tetrahydrofuran (30 ml) at 150 °C. After 15 min, phenylmethanethiol (5.0 g, 0.04 mole) is added and the mixture is treated as described above. *(4e)* (8.9 g, 70%) is obtained as a mixture of diastereomers. Recrystallization from ethanol affords a diastereomer having m.p. 170 °C.

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[1] Syntheses with α-Metalated Isocyanides, Part 4. – Part 3: Ref. [4].

[2] Cf. *Th. Wieland, R. Müller, E. Niemann, L. Birkofer, A. Schöberl, A. Wagner*, and *H. Söll* in: Houben-Weyl-Müller, Vol. 11/2. Thieme, Stuttgart 1958, p. 269, particularly pp.452ff.

[3] See, *e.g.*, for penicillamine *H. T. Clarke, J. R. Johnson*, and *R. Robinson*: The Chemistry of Penicillin. Princeton University Press, Princeton 1949, pp. 455ff.

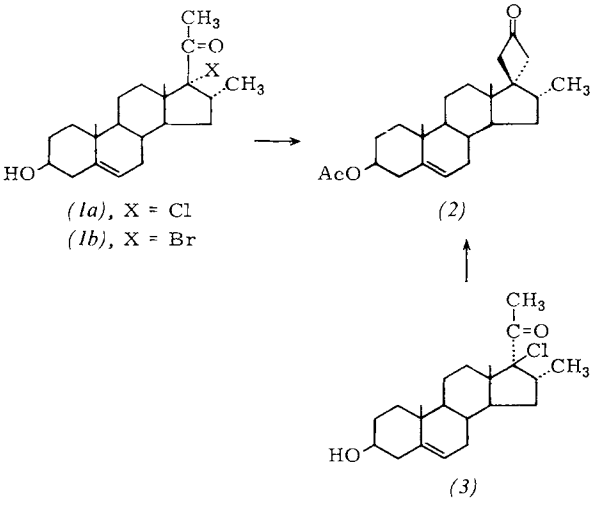
[4] Cf. *U. Schöllkopf, F. Gerhart*, and *R. Schröder*, Angew. Chem. *81*, 701 (1969); Angew. Chem. internat. Edit. *8*, 672 (1969).

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A New Spirocyclobutanone Synthesis in the Steroid Series[**]

By *Rudolf Wiechert*[*]

Reaction of 17-halogeno-16α-methyl-20-oxasteroids *(1a)*, *(1b)*, and *(3)*[1] with a 2.4-fold excess of dimethyloxosulfonium methylide[2] over a period of 90 minutes at 40 °C leads to formation of a product, which, after working-up, acetylation, and separation by column chromatography, affords the symmetrical spirocyclobutanone *(2)* [m.p. 190 to 192 °C (isopropyl ether), $[\alpha]_D^{24} = -126°$ ($CHCl_3$, $c = 0.5$)] in yields of 35–55%.



(1a), X = Cl
(1b), X = Br

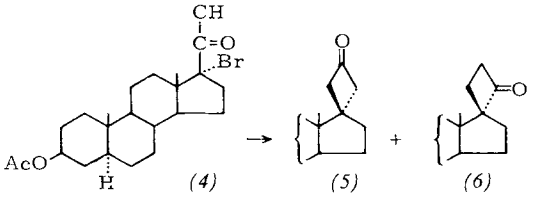
(2)

(3)

The νC=O band of the four-ring ketone *(2)* appears at 1790 cm^{-1}. A multiplet occurring at δ = 2.75 ppm in the NMR spectrum ($CDCl_3$, Varian A 60) can be assigned to the two CH_2 groups of the four-membered ring. On measuring the circular dichroism in dioxane a weak, negative Cotton effect can be detected (λ_{max} = 297 nm, $\Delta\varepsilon = -0.43$). The molecular weight (measured mass spectrometrically) is 384.

The analogous reaction of ketone *(4)*[3] (without methyl group on C-16) leads to formation of the symmetrical cyclobutanone *(5)* [yield 8%, m.p. 200.5–201.5 °C (isopropyl ether); IR: νCO = 1790 cm^{-1}; NMR: δ = 2.2–3.25 ppm (4H); CD: λ_{max} = 296 nm, $\Delta\varepsilon = -0.41$] and the ketone *(6)* (yield 17%, m.p. 162–164 °C).

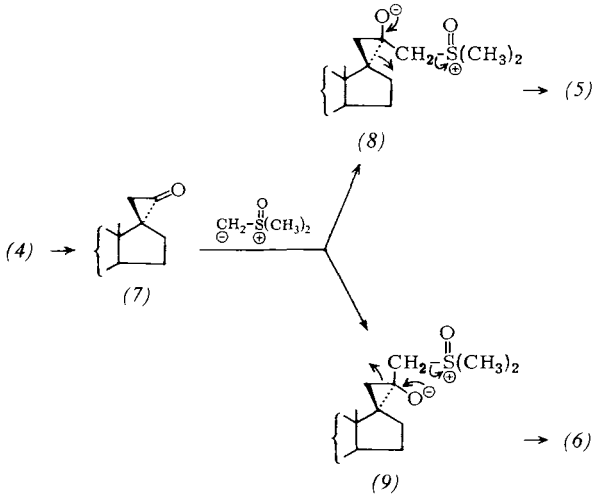
Signals due to the two protons adjacent to the keto group give rise to a triplet in the NMR spectrum of *(6)* [A_2 part of



(4) *(5)* *(6)*

an A_2B_2 system, J = 8 Hz at δ = 2.78 ppm]. It can be concluded from the negative Cotton effect obtained in the CD curve (λ_{max} = 308 nm, $\Delta\varepsilon$ = −0.43) that the keto group lies on the backside of the molecule.

The formation of *(5)* and *(6)* [as well as *(2)*] under strongly basic reaction conditions can be assumed to proceed *via* an intermediate, a spirocyclopropanone *(7)*, as has been discussed in the case of the Faworskii rearrangement[4]. The adducts *(8)* and *(9)* expected from *(7)* can, for example, be stabilized by elimination of dimethyl sulfoxide and ring expansion in a concerted process to give *(5)* and *(6)*.



3β-Acetoxy-16α-methylspiro[androst-5-ene-17,1′-cyclobutan]-3′-one (2)

A mixture of trimethyloxosulfonium iodide (21.05 g, 96 mmole) in dimethyl sulfoxide (363 ml) and sodium hydroxide (3.83 g, 96 mmoles) is stirred at room temperature for 45 minutes. Compound *(1a)* (14.55 g, 40 mmole) is then added to the mixture, which is stirred for a further 1 1/2 hours at 40 °C and finally transferred with stirring to an acetic acid/ice-water mixture. The precipitate that forms is filtered off under suction, dried, and acetylated in pyridine/acetic anhydride for 16 hours at room temperature. The acetylated product is purified by chromatographic separation on silica gel [yield 8.45 g (55%)].

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[**] We thank Dr. *G. Schulz* and Dr. *G. Cleve* for the spectroscopic investigations and *D. Bittler* for assistance with the preparative work.

[1] *J. C. Hielscher*, German Pat.-Appl. P 1793114.5 and P 1793374.3 (1968), Schering AG.

[2] *E. J. Corey* and *M. Chaykovsky*, J. Amer. chem. Soc. *84*, 867 (1962); *87*, 1353 (1965)

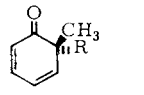
[3] *R. E. Marker, H. M. Crooks jr., R. B. Wagner*, and *E. L. Wittbecker*, J. Amer. chem. Soc. *64*, 2089 (1942).

[4] *D. N. Kirk* and *M. P. Hartshorn*: Steroid-Reaction Mechanisms. Elsevier, Amsterdam 1968, p. 206.

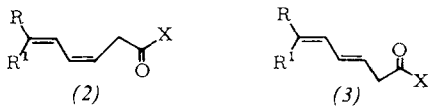
Photoacid Derivatives of an Achiral and a Chiral 2,4-Cyclohexadienone[1]

By *Gerhard Quinkert, Manfred Hintzmann, Peter Michaelis*, and *Peter Jürges*[*]

Light-induced cyclo/seco-isomerization of 2,4-cyclohexadienones affords dienylketenes that are converted into substituted hexadienoic acid derivatives by addition of protonic nucleophiles[2]. For instance, irradiation of 6,6-dimethyl-2,4-cyclohexadienone *(1a)*[3] by 365- or 313-nm light in the presence of water gives (3*Z*)-6-methyl-3,5-heptadienoic acid *(2a)*[2], whereas the cyclohexylamide *(2b)* thereof is formed in the presence of cyclohexylamine.



(1a), R = CH_3
(1b), R = C_6H_5 (rac.)



(2) *(3)*

(a), R = R^1 = CH_3; X = OH
(b), R = R^1 = CH_3; X = NH–C_6H_{11}
(c), R = C_6H_5; R^1 = CH_3; X = NH–C_6H_{11}
(d), R = CH_3; R^1 = C_6H_5; X = NH–C_6H_{11}

Cpd.	M.p. (°C)	UV (nm) (ε) [a]	IR (cm^{-1}) [b]	NMR (τ) [c]
(2b)	85	240 (24500)	3240, 1640	8.23 8.19
(3b)	100.5–101.5	240 (25300)	3280, 1640, 960	8.26 (ψ s)
(2c)	120–122	279 (23000)	3320, 1640	7.82
(2d)	100–100.5	255 (17000)	3320, 1640	7.89
(3c)	137–138	279 (27000)	3320, 1640 960	7.87

[a] In ether. [b] In KBr; all bands very strong. [c] Singlets of allylic methyl protons; HA 100; in $CDCl_3$; ψ s = pseudosinglet.

Monitoring the reaction UV-spectroscopically proves the transformation to occur in a *simple reaction* (*a series of straight lines* passes through the origin of the coordinates of an extinction difference diagram[4]). The 5,6-position of one double bond follows for *(2a)* from the results of ozonolysis[2], and for *(2a)* and *(2b)* from the NMR singlets of allylic methyl protons. Conjugation of the two CC double bonds can be deduced from the wavelength region of the electronic absorption spectrum, and absence of an IR band at 960 cm^{-1} requires the *Z*-configuration[5] for the 3,4-double bond[6]; the configurational isomer *(3b)* obtained by isomerization of *(2b)* with iodine, on the other hand, shows the CH wagging vibration characteristic of a doubly substituted ethylenic linkage with *E*-configuration[5].

The constitution of the photoproduct obtained from racemic 6-methyl-6-phenyl-2,4-cyclohexadienone *(1b)*[3] depends on the wavelength of the exciting light. In the presence of cyclohexylamine, 313-nm light *does not cause a simple reaction* (*a series of curves*, representing two linearly independent partial reactions, intersects the origin of the coordinates of an extinction difference diagram[4]); the amide *(2d)* is formed together with traces of *(2c)* and *(3c)*. Experiments with the individual amides *(2c)*, *(2d)*, and *(3c)* show that *(2c)* and *(3c)* are practically completely photoisomerized to *(2d)* under the irradiation conditions.

Under otherwise identical conditions, 365-nm light converts *(1b)* into a mixture of the (3*Z*, 5*Z*)- *(2d)* and the (3*Z*, 5*E*)-isomer *(2c)*. According to the extinction difference diagram this transformation occurs in a simple reaction. *(2c)* and *(2d)* are not isomerized either by direct irradiation with 365-nm light or by sensitization caused by electronically excited *(1b)*[8]. The constitution and configuration of *(2c)*, *(2d)*, and *(3c)* follow from the spectroscopic properties of the isomers and can be derived unambiguously from the straightforward relations to their synthetic precursors and derived products[9].

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[1] This work was supported by Farbwerke Hoechst AG, the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie.

[2] *D. H. R. Barton* and *G. Quinkert*, J. chem. Soc. (London) *1960*, 1.

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[4] *H. Mauser*, Z. Naturforsch. *23b*, 1025 (1968).

[5] For an unambiguous specification of stereoisomerism about a double bond see *J. E. Blackwood*, *C. L. Gladys*, *K. L. Loening*, *A. E. Petrarca*, and *J. E. Rush*, J. Amer. chem. Soc. *90*, 509 (1968).

[6] Because of the very strong absorption the *E*-configuration originally [2] was assigned to this double bond. Comparison of the UV data for the pairs of configurational isomers *(2b)/(3b)* and *(2c)/(3c)* shows this criterion to be invalid; cf. [7].

[7] *P. M. Collins* and *H. Hart*, J. chem. Soc. (London) *C 1967*, 1197.

[8] The absence of sensitized photoisomerization was proved by irradiation of mixtures of the individual amides with *(1b)* in ethanol by 365-nm light.

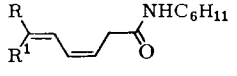
[9] *G. Quinkert*, *M. Hintzmann*, *P. Michaelis*, *P. Jürges*, and *U. Krüger*, Angew. Chem. *82*, 220 (1970); Angew. Chem. internat. Edit. *9*, 239 (1970).

Synthesis and Determination of Configuration of (3*Z*, 5*E*)-, (3*Z*, 5*Z*)-, and (3*E*, 5*E*)-*N*-Cyclohexyl-6-phenyl-3,5-heptadienamide[1]

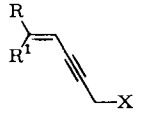
By *Gerhard Quinkert*, *Manfred Hintzmann*, *Peter Michaelis*, *Peter Jürges*, and *Uwe Krüger*[*]

Under conditions that exclude subsequent isomerization of the amide constituting the primary product, irradiation of 6,6-dimethyl-2,4-cyclohexadienone[2] by 365-nm light in the presence of cyclohexylamine leads to formation of *N*-cyclohexyl-6-methyl-3,5-heptadienamide, whereas under the same conditions racemic 6-methyl-6-phenyl-2,4-cyclohexadienone is converted into the (3*Z*, 5*E*)- and (3*Z*, 5*Z*)-configurations of *N*-cyclohexyl-6-phenyl-3,5-heptadienamide *(1a)* and *(1b)*[2]. Conversion of the enynes *(2a)* and *(2b)* into *(1a)* and *(1b)*, respectively, by partial hydrogenation on a Lindlar catalyst in methanol has shifted the problem of determination of the constitution and configuration from the dienes to the enynes. The pair of isomers *(2a)* and *(2b)* is readily accessible by synthesis (see below) and can be assigned structures with certainty by means of the nuclear Overhauser effect[3].

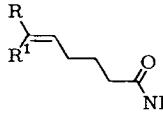
The amide *(3a)* is furnished by selective hydrogenation (Pt in glacial acetic acid) of the (3*Z*, 5*E*)-isomer *(1a)* or of the (3*E*, 5*E*)-isomer *(1b)* obtained from *(1a)* by isomerization with iodine; *(3b)* results from the (3*Z*, 5*Z*)-isomer *(1b)* under the same conditions.



(1a), R = C_6H_5; R^1 = CH_3
(1b), R = CH_3; R^1 = C_6H_5



(2a), R = C_6H_5; R^1 = CH_3; X = $CO\text{-}NHC_6H_{11}$
(2b), R = CH_3; R^1 = C_6H_5; X = $CO\text{-}NHC_6H_{11}$
(2c), R = C_6H_5; R^1 = CH_3; X = CH_2OH
(2d), R = CH_3; R^1 = C_6H_5; X = CH_2OH
(2e), R = C_6H_5; R^1 = CH_3; X = CO_2H
(2f), R = CH_3; R^1 = C_6H_5; X = CO_2H



(3a), R = C_6H_5; R^1 = CH_3
(3b), R = CH_3; R^1 = C_6H_5

Cpd.	M.p. (°C)	UV (nm) (ε) [a]	IR (cm^{-1}) [b]	NMR (τ) [c]
(2a)	101.5–102	274 (17000)	3425s, 1670s [d]	7.69 s
(2b)	110–111	269 (12900)	3330s, 1647s [d]	7.80 s
(2c)	49–50	275 (21900)	3560s, 3420s, 2200w	7.70 d; *J* 1.5 Hz
(2d)	oily	271 (11500)	3640–3125s, 2217w [e]	7.88 s
(2e)	120–121	274 (20900)	3570–2740s, 1724s, 2220w	7.70 s
(2f)	74–75	270 (11800)	3450–2780s, 1718s, 2227w	7.84 s
(3a)	78–79	245 (12000)	3320s, 1640s [d]	7.98 s
(3b)	95–96	232 (6170)	3320s, 1640s [d]	7.98 s

[a] In ether. [b] Unless otherwise stated, in $CHCl_3$; s = strong; w = weak. [c] Signals of allylic methyl protons; HA 100; in $CDCl_3$; s = singlet; d = doublet. [d] In KBr. [e] Measured as film.

(2a) and *(2b)* were prepared conventionally: Dehydration of 2-phenyl-4-pentyn-2-ol[4] by $POCl_3$ and pyridine gives a mixture of the configurational isomers of 4-phenyl-3-penten-1-yne; treatment of the derived Li compounds with ethylene oxide affords mainly *(2c)* with some *(2d)*, which can be separated by chromatography; Jones' reagent[5] converts *(2c)* and *(2d)* into *(2e)* and *(2f)*, respectively; and when treated with dicyclohexylcarbodiimide and cyclohexylamine, *(2e)* and *(2f)* give the amides *(2a)* and *(2b)*, respectively. Transfer from the 5*E*- to the 5*Z*-series can be effected for *(2c)* as well as for *(2a)*; both compounds photoisomerize on direct irradiation with light of the wavelength region above 300 nm (the 5*Z*-isomers preponderate in the photostationary state).

Additional radiation	Rel. intensity [a] of vinyl-H of *(2a)*	of *(2b)*
without	19.0 (m)	18.0 (m)
in CH_3 on *(2a)*	18.5 (t)	—
in CH_3 on *(2b)*	—	22.5 (t)

[a] Based on phenyl-H = 100; m = multiplet; t = triplet.

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[1] This work was supported by Farbwerke Hoechst AG, the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie.

[2] *G. Quinkert*, *M. Hintzmann*, *P. Michaelis*, and *P. Jürges*, Angew. Chem. *82*, 219 (1970); Angew. Chem. internat. Edit. *9*, 238 (1970).

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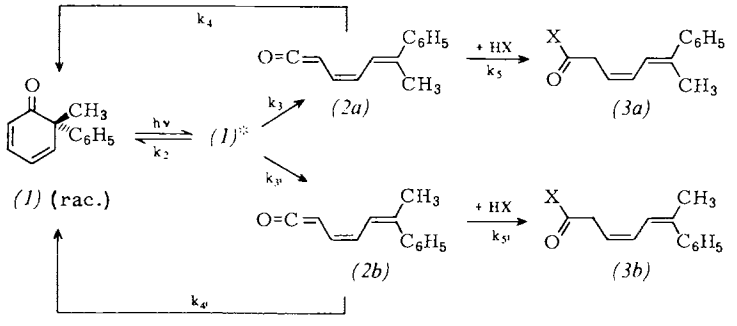
[4] *P. Läuger*, *M. Prost*, and *R. Charlier*, Helv. chim. Acta *42*, 2379 (1959).

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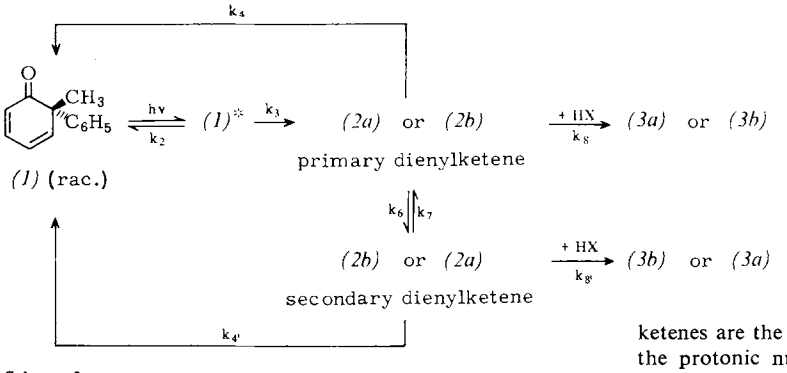
Evidence of Two Configurational Isomers of Dienylketenes from 6-Methyl-6-phenyl-2,4-cyclohexadienone by Low Temperature Spectroscopy[1]

By *Gerhard Quinkert, Bernd Bronstert, Peter Michaelis,* and *Uwe Krüger*[*]

Stereochemical statements about the light-induced cyclo/seco-isomerization (originally postulated by intuition[2]) of racemic 2,4-cyclohexadienones containing a chiral center at C-6 to yield dienylketenes have hitherto been based on the number[3] and configuration[4] of the 6,6-disubstituted 3,5-hexadienoic acid derivatives that were considered to be derived from the ketenes. Low-temperature UV[5,6] and IR[5–7] spectroscopy permit unambiguous demonstration of the existence of the seco-isomers which are kinetically unstable at room temperature. We have found that irradiation of 6-methyl-6-phenyl-2,4-cyclohexadienone *(1)* with 365-nm light in the presence of cyclohexylamine affords the (3*Z*, 5*E*)-*(3a)* and the (3*Z*, 5*Z*)-configuration *(3b)*[9] of *N*-cyclohexyl-6-phenyl-3,5-heptadienamide[8] in the ratio 1 : 1.8. This raises the question whether two configurations of the dienyl-



Scheme 1



Scheme 2

ketenes are the primary products which pass by addition of the protonic nucleophile present into the acid derivatives actually isolated.

As reported previously[5a] for another case, measuring the UV spectrum of a solution of *(1)* in methylcyclohexane/isopentane (1 : 4) after its irradiation at —185 °C by 365-nm light (Fig. 1) allows formation of a photoproduct to be detected that regenerates *(1)* in a dark reaction when the temperature is raised [$t_{1/2}$ = 48 (—8.5), 95 (—15.4), 135 (—18.8), and 345 min (—26.3 °C)]. IR spectra (Fig. 2) measured in

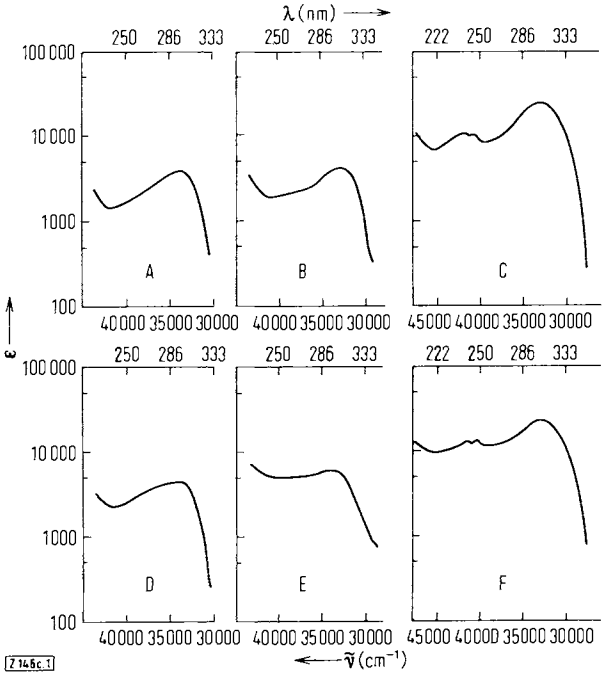


Fig. 1. UV spectra at various stages of cyclo/seco-isomerization. A, *(1)* in methylcyclohexane/isopentane (1 : 4) at room temperature; B, at —185 °C; C, after complete reaction with 365-nm light; D, after re-warming to room temperature; E, at —185 °C; F, after renewed irradiation with 365-nm light (94% reconversion of the photoproduct).

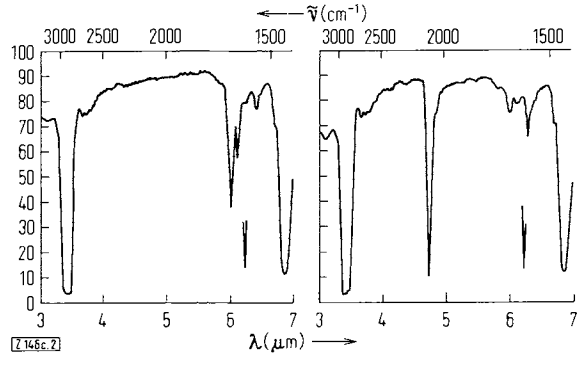


Fig. 2. Part of the IR spectra before (left) and after (right) irradiation of *(1)* in paraffin at —155 °C by 365-nm light.

paraffin before and after irradiation at —155 °C demonstrate the ketenic nature of the photoproduct and establish the ring opening that was previously assumed[2]. NMR spectra of the photoproduct (see Table) measured at —70 °C under various conditions[9] show that in this case the two ketenes *(2a)* and *(2b)* occur side by side. Rapid increase in temperature re-

NMR spectra of the photoproduct.

Condition \ Type of proton	Ketene-H [a] τ; J(Hz)	Methyl-H τ
HA 100; $CDCl_3$	5.56 (d/J = 10.8), 5.59 (d/J = 10.8)	7.85
HA 100; $CDCl_3/C_6D_6$ (3 : 1)	5.83 (d/J = 10.1), 5.85 (d/J = 10.1)	7.90 and 7.93
A 60; $CDCl_3$	5.45 (d/J = 11), 5.42 (d/J = 11)	7.76

[a] Typical for a series of dienylaldoketenes investigated, absent for dienylketoketenes. J for the dienylketene derived from 6,6-dimethyl-2,4-cyclohexadienone amounts to 10.8 Hz.

converts them completely into *(1)*, but addition of cyclohexylamine (HX) causes formation of *(3a)* and *(3b)*. The above qualitative findings can be reconciled with either of the reaction schemes 1 and 2.

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[1] This work was supported by Farbwerke Hoechst AG, the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie.

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[7] *O. L. Chapman* and *J. D. Lassila*, J. Amer. chem. Soc. *90*, 2449 (1968); *J. Griffiths* and *H. Hart*, *ibid.* *90*, 3297 (1968).

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[9] NMR spectra of aldoketenes at −80 °C have been reported recently by *O. L. Chapman, M. Kane, J. D. Lassila, R. L. Loeschen*, and *H. E. Wright*, J. Amer. chem. Soc. *91*, 6856 (1969).

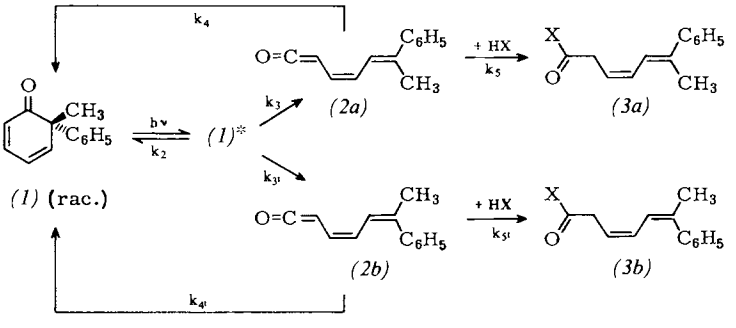
The Two Configurational Isomers of Dienylketenes Obtained as Primary Photoproducts from n,π*-Excited 6-Methyl-6-phenyl-2,4-cyclohexadienone[1]

By *Heinz-Helmuth Perkampus, Günter Prescher, Bernd Bronstert*, and *Gerhard Quinkert*[*]

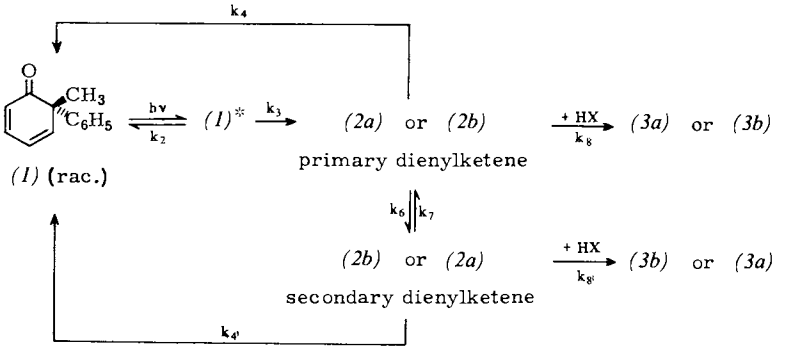
The light-induced reaction of 6-methyl-6-phenyl-2,4-cyclohexadienone *(1)* in presence of cyclohexylamine (HX) leads to the configurational isomers *(3a)* and *(3b)* of *N*-cyclohexyl-6-phenyl-3,5-heptadienamide. Two configurational isomers *(2a)* and *(2b)* of the dienylketene formed as intermediates can be detected by low-temperature spectroscopy. The reaction may be construed as occurring by Scheme 1 or Scheme 2[2].

Schemes 1 and 2 differ in the nature and/or number of linearly independent reactions; and in such cases extinction difference diagrams afford a ready means for their differentiation[3]. These diagrams may relate, in the present instance, to the complete process of photochemical formation of the acid derivatives[4] or may be restricted to the light-induced cyclo/seco-isomerization[2] studied at low temperatures.

Linear extinction difference diagrams are obtained for ring fission of *(1)*, caused by light of wavelength 365 nm, in ether/isopentane/ethanol (5 : 5 : 2) at −185 °C or in methylcyclohexane/isopentane (1 : 4) at −70 °C. This finding accords with Scheme 1, but can be reconciled with Scheme 2 only if, in accord with the conditions of Bodenstein's hypothesis, the



Scheme 1



Scheme 2

concentration of either the primary or the secondary dienylketene is very small. However, NMR spectroscopy at −70 °C proves that the two ketenes are produced in comparable concentrations[2], so that Scheme 2 is excluded. 365-nm light converts *(1)* at room temperature or at −70 °C in the presence of protonic nucleophiles into derivatives of the two 6-phenyl-3,5-heptadienoic acids with configurations (3*Z*, 5*E*) *(3a)* and (3*Z*, 5*Z*) *(3b)*, *i.e.* under conditions where the products prove kinetically stable[4].

Photochemical formation of the acid derivatives is also characterized by linear extinction difference diagrams if carried out under these conditions in ether/isopentane (1 : 1)[4]. When the nucleophile concentration is about 0.1 mole/l, the slope of the line for the case of ethanol depends on its momentary concentration, but the slope is independent of concentration of the stronger nucleophile cyclohexylamine. These findings are to be expected from the relation[5] valid for Scheme 1:

$$\frac{\Delta E_1}{\Delta E_2} = \frac{(\varepsilon_{(3a)}-\varepsilon_{(1)})_1 + b\,(\varepsilon_{(3b)}-\varepsilon_{(1)})_1}{(\varepsilon_{(3a)}-\varepsilon_{(1)})_2 + b\,(\varepsilon_{(3b)}-\varepsilon_{(1)})_2};\quad b = \frac{k_3'}{k_3}\cdot\frac{(1+k_4/k_5\cdot c(\mathrm{HX}))}{(1+k_4'/k_5'\cdot c(\mathrm{HX}))}$$

which defines the slope of the straight lines in the extinction difference diagrams for wavelengths 1 and 2. For ethanol the quotients $k_4/k_5 \cdot c(\mathrm{HX})$ and $k_4'/k_5' \cdot c(\mathrm{HX})$ are not negligible in comparison with unity in the concentration region used, but for cyclohexylamine the limiting condition $b = k_3'/k_3$ has already been reached[6,7].

Since the primary ketene photoproducts recyclize and/or add nucleophiles, the quantum yield for disappearance of *(1)* depends on the strength and concentration of the protonic nucleophile. Under limiting conditions[5], which are reached at much lower concentration of cyclohexylamine than of ethanol, the numerical value ($\varphi = 0.55$) of the quantum yield is independent of the wavelength used (365 or 313 nm[8]) and of the addition of piperylene and presence of oxygen. These observations are immediately reconcilable with a n,π*-excited cyclohexadienone[9] of singlet character, from which the two dienylketenes *(2a)* and *(2b)* are formed side by side.

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[1] This work was supported by Farbwerke Hoechst AG, the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie.

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[4] *G. Quinkert, M. Hintzmann, P. Michaelis,* and *P. Jürges,* Angew. Chem. *82*, 219 (1970); Angew. Chem. internat. Edit. *9*, 238 (1970).

[5] *G. Prescher,* Dissertation, Technische Universität Braunschweig 1970.

[6] *b* applies and is constant during an addition reaction; 1, Bodenstein's hypothesis being applicable for *(1)*, (2a),* and *(2b)*; 2, for *c*(HX) (≈ 0.1 mol/l) ≪ *c*(1) (≈ 10^{-4} mole/l).

[7] Concentration invariance at sufficiently high *c*(HX) could occur with scheme 2 only if $k_8 \cdot c(\mathrm{HX}) \gg k_6$, *i.e.* on formation of an addition product.

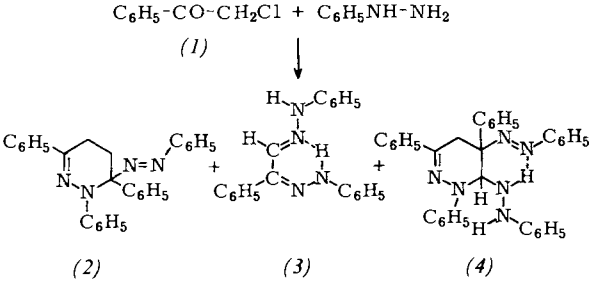
[8] 313-nm light subsequently converts the first portions of *(3a)* into *(3b)*. The quantum yield of this isomerization can, however, be separately determined as $\varphi = 0.47$.

[9] Independently of whether irradiation is undertaken in the π,π* or n,π* absorption region, the lower-energy n,π* state is obtained. Extreme external conditions may reverse the order of the two singlets [see *J. Griffiths* and *H. Hart,* J. Amer. chem. Soc. *90*, 5296 (1968)].

Osazone Formation from α-Haloketones. A Novel 1,4-Cycloaddition

By *William C. Stickler* and *William C. Hoffman*[*]

α-Haloketones are expected to give bis-phenylhydrazones (osazones) upon reaction with phenylhydrazine[1]. The reaction of the latter with phenacyl chloride *(1)* in cold alcoholic solution was first described by *Hess*[2]; neither the phenylhydrazone nor the osazone but the yellow crystalline 6-benzeneazo-1,3,6-triphenyl-1,4,5,6-tetrahydropyridazine *(2)* was isolated[3]. Our research group[4] was able to isolate from *(1)* in glacial acetic acid the long sought after osazone *(3)*, and also an unidentified pale-yellow crystalline product.

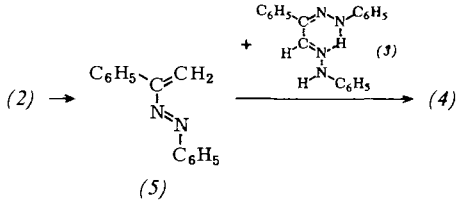


(1) *(2)* *(3)* *(4)*

Reinvestigation with the powerful aid of thin-layer chromatography revealed that in the reaction between phenacyl chloride *(1)* (0.01 mole) and phenylhydrazine (0.03 mole) in glacial acetic acid solution (40 ml), *(2)* is formed rapidly, reaching its maximum concentration in about 30 minutes and thereafter decreasing to a constant, very low concentration in about one hour. The osazone *(3)* gradually forms, reaching its maximum concentration after about 24 hours. After about 30 minutes from the start of the reaction, a third yellow substance *(4)*, m.p. 194—196 °C, makes its appearance, slowly increasing in concentration during several days; it proved to be identical with the above mentioned pale yellow compound.

NMR data[5], which we were able to confirm, and our own IR data[6] support the geometry given for the osazone *(3)*.

The structure *(4)* was derived from molecular weight determinations (*e.g.*, 522 from a mass spectrum), elemental analysis values, the IR spectrum [which resembles that of the osazone *(3)*: 3350 (N—H); a broad, low-intensity band centered at 3200 (N—H · · · N); 2930 and 2860 cm^{-1} (CH_2)], the NMR spectrum [in $CDCl_3$ δ = 13.03 (one N—H · · · N); 8.32 (C—H); 7.31 (25 aromatic C—H protons and one N—H proton (at δ = 7.53 ppm/m); 5.14 ppm (CH_2); the two N—H protons are readily "washed out" by D_2O], and the UV spectrum [in cyclohexane, λ_{max} = 405 nm (log ε = 2.158), which is considered characteristic of alkyl azo compounds[7]].



(2) *(5)* *(3)* *(4)*

Curtin and *Tristram*[3] rationalize formation of *(2)* as involving phenylhydrazone formation, followed by 1,4-elimination of HCl and subsequent dimerization of the resulting ene-azo intermediate *(5)*. They describe this dimerization as "suggestive of the Diels-Alder reaction".

We propose to extend their line of reasoning to explain the formation of *(4)*. The pyridazine *(2)* undergoes a retro-Diels-Alder type reaction to yield fragment *(5)*, which serves as the diene to the osazone *(3)*, acting here as the dienophile[8] in a novel 1,4-cycloaddition.

The phenacyl bromide behaves in an analogous fashion, but the iodide yields *(2)* in low concentration and leads to acetophenone phenylhydrazone as the main product.

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[1] See, *e.g.*, *E. Votoček*, Coll. czechoslov. chem. Comm. *2*, 681 (1930); Chem. Abstr. *25*, 1488 (1931).

[2] *O. Hess*, Liebigs Ann. Chem. *232*, 234 (1886).

[3] For the structure of *(2)* see: *D. Y. Curtin* and *E. W. Tristram*, J. Amer. chem. Soc. *72*, 5238 (1950). (Their review of previous work contains, however, some historical and factual errors.)

[4] *H. D. Hart*, M.S. Thesis, University of Denver, 1952; *W. C. Stickler*, *H. D. Hart*, and *P. Yin*, J. Colo.-Wyo. Acad. Sci. *1952*, 34; *W. C. Stickler*, *W. Epstein*, and *L. Gachic*, *ibid.* *1953*, 24.

[5] Cf. *O. L. Chapman et al.*, J. Amer. chem. Soc. *86*, 4968 (1964).

[6] We are indebted to Prof. *J. J. Schmidt-Collérus* and his staff, University of Denver Research Institute, and Mr. *R. H. Williams*, Univ. of Illinois, for obtaining the spectra and aiding us in their interpretation.

[7] *A. Burawoy*, J. chem. Soc. (London) *1937*, 1865; *e.g.*, $CH_3-N=N-C_6H_5$ absorbs at 403 nm.

[8] The dienophilic structure involving C=C can be arrived at by considering either limiting resonance structures or tautomeric forms.

α-Olefins from Ethylene[1]

By *Gisela Henrici-Olivé* and *Salvador Olivé*[*]

Ethylene is rapidly converted into solid polyethylene by the two-component catalyst $Cp_2TiRCl/RAlCl_2$ (Cp = cyclopentadienyl, R = alkyl) in toluene at 0 °C[2, 3]. *Bestian et al.*, however, have shown that the major products are liquid oligoethylenes — mainly 2-ethyl-1-olefins *(1)* having vinylidene terminal groups — when $Cl_2TiRCl/RAlCl_2$ is used as catalyst in CH_2Cl_2 as solvent at −70 °C[4, 5].

By systematically changing the reaction conditions and the ligands on titanium we have now been able to prepare C_6—C_{40} olefins *(2)* having predominantly vinylic end groups. The best results were obtained by using the following procedure:

$(C_2H_5O)_3TiCl$ (2 mmoles) is dissolved in toluene (100 ml) and treated with $C_2H_5AlCl_2$ (10 mmoles) under an atmosphere of argon. The homogeneous solution is then transferred to an autoclave and cooled to −20 °C. Ethylene is introduced into the autoclave at 12 atm and both pressure and temperature are kept constant during the time of reaction (1 hour). After withdrawal of the ethylene at the reaction temperature the conversion can be determined by weighing (increase in weight minus the solubility of the ethylene in the reaction solution): 34.6 g, corresponding to a conversion of 13.0 moles of ethylene per liter of reaction solution per hour.

The reaction solution was washed with water to remove catalyst; some solid polymer (0.9%) was precipitated. The organic phase was fractionated by vacuum distillation (see Table 1).

$H_2C=C(-H)-R$ (*1*) $H_2C=C(-H)-R$ (*2*)

Table 1. Fractionation of oligoethylene.

Fraction No.	Parts by weight (%)	M_n [a]	Vinyl *(2)* (%) [b]	Vinylidene *(1)* (%) [b]
1	2.3	56 [c]	≈ 100	—
2	13.7	84 [c]	≥95	≤ 5
3	16.0	112 [c]	≥95	≤ 5
4	2.0	150	≥90	≤10
5	12.0	175	≥90	≤10
6	6.7	195	≥90	≤10
7	8.0	215	≥90	≤10
8	9.5	225	≥80	≤15
9	13.4	292	≥70	≤20
10	15.5	465	≥70	≤20
11	0.9	solid	—	—

[a] Number average molecular weight, M_n, determined by vapor-pressure osmometry. [b] Percentage of molecules with vinyl- and vinylidene end groups calculated from the absorption at 910 and 890 cm^{-1} resp. [c] The first three fractions distilled together with the toluene and were identified gas-chromatographically as 1-butene, 1-hexene, and 1-octene.

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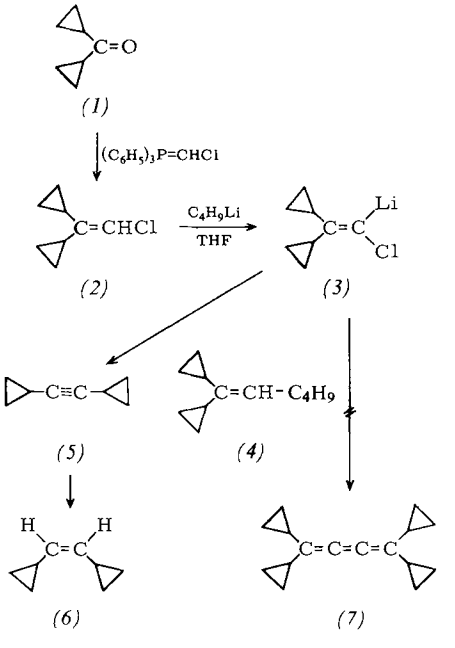
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Dicyclopropylacetylene by Fritsch-Buttenberg-Wiechell Rearrangement

By *Gert Köbrich* and *Dieter Merkel*[*][**]

Reaction of 1-chloro-2,2-dicyclopropylethylene *(2)*, prepared from dicyclopropyl ketone *(1)* by chloroolefination[1], with *n*-butyllithium in THF between −110 and +20 °C afforded the hitherto unknown dicyclopropylacetylene *(5)* as a stable, colorless liquid, beside 1,1-dicyclopropyl-1-hexene *(4)*. Hydrogenation of the acetylene *(5)* over a Lindlar catalyst proceeded almost quantitatively and stereospecifically to give *cis*-1,2-dicyclopropylethylene *(6)*[2].

The supposed carbenoid intermediate *(3)* has not been detected so far probably because the electron-repelling and bulky cyclopropyl groups slow down metalation of *(2)*, on the one hand, and accelerate decomposition of *(3)*[3] on the other.



Cpd.	Yield (%)	B.p. (°C/torr)	n_D^{20}	IR (cm^{-1}) [a]	NMR [b]
(2)	71	70/13	1.5028	3080 and 3005 (C—H); 1620 (C=C)	4.24 (1 =C—H/s); 7.7–8.3 (1 *cis*-allyl-H/m); 8.8–9.7 (9 H/m)
(4)	10 [c]	95/13	1.4725	3075, 3000, and 2955 to 2855 (C—H); 1650 (C=C)	4.95 (1 =C—H/t); 7.7–9.8 (19 H/m)
(5)	83 [c]	151/760	1.4900	3080 and 3000 (C—H); 2200 (C≡C), Raman band	8.6–9.3 (2 H/m); 9.3–9.6 (8 H/m)
(6)	97 [d]	140/760	1.4803	3070 and 3000 (C—H); 1690 and 1660 (C=C); 1043, 1015, 949, and 886	5.38 (2 =C—H) and 8.41 (2 allyl—H) as A_2B_2 system; 9.05 to 9.9 (8 H/m)

[a] Measured on capillary film. [b] τ scale; measured in CCl_4 with TMS as internal standard. [c] Based on *(2)*. [d] Based on *(5)*.

Interestingly, *(3)* does not undergo a dimerizing α-elimination to give butatriene *(7)*, as has been observed for analogous β,β-dialkyl derivatives under similar conditions[3a], but owing to the "olefinic behavior" of the three-membered rings[4] enters into a Fritsch-Buttenberg-Wiechell rearrangement that is characteristic of unsaturated β substituents (aryl[5], alkenyl, and alkynyl groups[3b]).

Experimental:

A solution of *(2)* (100 mmoles), prepared according to the general procedure given in ref.[6] and purified by distillation (spinning band column), in THF (200 ml) or THF/ether/light petroleum (50–70 °C) (4 : 1 : 1) (Trapp mixture[3a]) (200 ml) is treated with a solution of butyllithium (120 mmoles) in light petroleum at 20 °C under an inert gas and the reaction mixture stirred overnight. The crude product obtained after hydrolysis and the usual working up procedure contained *(5)* and *(4)* in 83 and 10% yield, respectively, (based on *(2)*, determined by gas chromatography) which were obtained about 97% pure on fractional distillation over a spinning band column, and free from impurities by preparative gas chromatography (6 m column, SE 30). Hydrogenation of *(5)* (10 mmoles) with Lindlar catalyst (0.5 g) and quinoline[7] (0.2 g) in a shaking apparatus (70 min at 20 °C) gave a 97% yield of *(6)* along with 3% of lower boiling products which were removed by preparative gas chromatography.

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N,N'-Sulfonylbis(sulfur difluoride diimide)[1]

By *Herbert W. Roesky* and *Horst H. Giere* [*]

Sulfamide reacts with sulfur tetrafluoride at room temperature in the presence of sodium fluoride as HF acceptor to give *N,N'*-sulfonylbis(sulfur difluoride diimide) *(1)* in 22% yield.

$$H_2NSO_2NH_2 + 2\ SF_4 \rightarrow F_2S{=}NSO_2N{=}SF_2 + 4\ HF$$
(1)

At higher temperatures, however, this reaction leads exclusively to formation of *N*-fluorosulfonylsulfur difluoride imide $FSO_2N{=}SF_2$[2].

Compound *(1)* is a yellow evil-smelling liquid which loses HF on reaction with water. Its composition follow sfrom the results of elemental analysis and from the mass spectrum, which shows, in addition to the molecular ion *m/e* 232 (8.7%), the following characteristic fragments: *m/e* = 167 (FSO_2NSF_2; 12.3%), 148 (SO_2NSF_2; 61.8%), 84 (NSF_2; 19.7%), 83 (SO_2F; 18.5%), 70 (SF_2; 39.4%), 67 (SOF; 17.0%), 65 (NSF; 16.5%), 64 (SO_2; 13.4%), 51 (SF; 10.7%), 48 (SO; 25.7%), 46 (NS; 100.0%), 32 (S; 6.8%).

The bands in the IR spectrum (capillary) have not, as yet, been completely identified because of the difficulties due to coupling and superpositions. In the region of the (S=O) and (N=S) stretching vibrations, bands occur at 1430 w, 1385 s, 1270 m, 1215 vs, and 1180 vs (cm^{-1}). The absorptions at 820 s, 790 s, and 660 s (cm^{-1}) have been tentatively assigned to the (SN) and/or (SF) vibrations. The symmetry of the molecule is confirmed by the ^{19}F-NMR spectrum: a singlet is observed with δ_F = −41.5 ppm (CCl_3F, external) which compares with δ_F = −40.0 ppm for FSO_2NSF_2.

Experimental:

Sulfur tetrafluoride (108 g, 1 mole) is condensed into a 300 ml monel cylinder cooled with liquid nitrogen and containing a mixture of sulfamide (48 g, 0.5 mole) and sodium fluoride (84 g, 2 moles). The cylinder is then allowed to warm to room temperature and shaken for 20 hours. After removal of gaseous components — a little SF_4 and SOF_2 — the reaction products are washed portionwise from the cylinder with 300 ml CCl_4 and separated from NaF · HF by filtration under dry nitrogen. Concentration of the filtrate followed by distillation under vacuum affords compound *(1)* [b.p. 49 to 51 °C/0.01 torr; yield 26 g (22.4%)].

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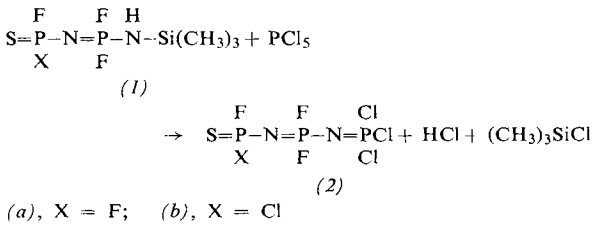
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Method for Preparation of Compounds of the Type $R{-}(N{=}PX_2)_x{-}N{=}PCl_3$[1]

By *Herbert W. Roesky* and *Ludwig F. Grimm* [*]

N-Trimethylsilylaminodifluorophosphoranylidenedihalothiophosphorylamines *(1)*, prepared from the corresponding *N*-trifluorophosphoranylidenedihalothiophosphorylamine and hexamethyldisilazane[2], react with phosphorus penta-

chloride to give the linear phosphazene compounds *(2)*, hydrogen chloride and trimethyl chlorosilane being eliminated in the process.



(a), X = F; *(b)*, X = Cl

This method of forming P—N=P linkages can be extended: thus compound *(2)* has also been found to undergo a corresponding reaction with hexamethyldisilazane and PCl_5. The products are colorless and react vigorously with water; they can be vacuum distilled without decomposition. Their composition is established by elemental analysis and by mass spectrometry. The mass spectrum of *(2a)* contains characteristic fragments in addition to the molecular ion at *m/e* 334; in the case of *(2b)*, the molecular ion at *m/e* 350 (28.9%) is accompanied by the fragment ions observed at *m/e* = 315 ($SPFClNPF_2NPCl_2$; 97.2%), 283 ($PFClNPF_2NPCl_2$; 33.9), 245 ($SPFNPF_2NPCl$; 13.3), 213 ($PFNPF_2NPCl$; 17.2), 200 ($SPFClNPF_2$; 8.3), 184 (PF_2NPCl_2; 3.3), 168 ($PFClNPF_2$; 8.9), 133 ($PFNPF_2$; 7.2), 114 ($PFNPF$; 9.4), 101 (PCl_2; 3.3), 85 (PFCl; 8.9), 69 (PF_2; 27.2), 66 (PCl; 2.8), 63 (SP; 4.4), 50 (PF; 5.6), 45 (PN; 2.8), 36 (HCl; 17.8), 35 (Cl; 5.0), 32 (S; 2.2), 31 (P; 1.7).

The IR spectra exhibit characteristic absorption bands, which, however, cannot be assigned unequivocally owing to superposition. — *(2a)*: ν(P=N) 1400—1300 vs; ν(PF), ν(P—N), ν(P=S) 960—940 vs, 900—860 vs, 780 s, 735 vs; ν(PCl) 650 vs, 615 vs, and 560 m, 500 vs cm^{-1}. — *(2b)*: ν(P=N) 1340—1300 vs; ν(PF), ν(P—N), ν(P=S) 960—940 vs, 865 vs, 730 vs; ν(PCl) 645 vs, 610 vs, and 495 vs cm^{-1}.

The ^{19}F-NMR spectra are of higher order owing to ^{31}P coupling. *(2a)* : SPF_2 part, $\delta_F = +35.1$; PF_2 part, $\delta_F = +67.3$ ppm. *(2b)*: SPFCl part, $\delta_F = +3.7$; PF_2 part, $\delta_F = +66.9$ ppm (CCl_3F as external reference). In comparison, $SPF_2NPF_2NHSi(CH_3)_3$ [2] gives $\delta_F = +36.4$ ppm for the SPF_2 part, and $\delta_F = +66.5$ ppm for the PF_2 part.

Procedure:

Compound *(1a)* (0.2 mole) or *(1b)* [2] (0.2 mole) is added dropwise to PCl_5 (41.6 g, 0.2 mole). The reaction mixture is stirred and heated to 60—80 °C during the addition and then refluxed until all solids have dissolved. The residue remaining on removal of trimethylchlorosilane under vacuum is subjected to fractional distillation. *(2a)*, b.p. 65 °C/≈ 0.01 torr, yield 16.7 g (25%); *(2b)*, b.p. 96 °C/≈ 0.01 torr, yield 31.7 g (45%).

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Conformational Analysis of 1,1'-Bisaziridyl by Vibrational Spectroscopy

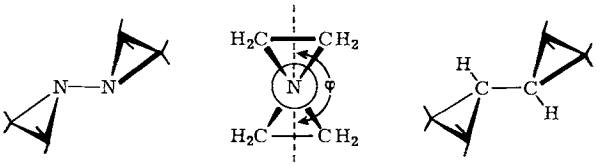
By *Paul Rademacher* and *Wolfgang Lüttke* [*]

Dedicated to Professor Walter Hückel on the occasion of his 75th birthday

An unbiased consideration of the internal rotation of hydrazine and its derivatives initially suggests that the torsional potential curve is mainly determined by the repulsion of the lone pair electrons at the nitrogen atom; accordingly, the s-*trans* conformation should be the most stable form.

In contrast to this assumption, and in agreement with *ab initio* LCAO-MO-SCF calculations for hydrazine [5], it is found that in the case of hydrazine [1] and its simple derivatives so far investigated (*e.g.* tetramethylhydrazine [2], tetrafluorohydrazine [3], and tetrakistrifluoromethylhydrazine [4]) the most stable and sole existing conformation is a *gauche* form having a dihedral angle of ≈ 90 °. Consequently, hydrazines behave in a manner fundamentally different from their isoelectronic hydrocarbons in which an s-*trans*/*gauche* equilibrium is always observed in the gaseous and liquid states and generally only the s-*trans* form in the crystalline state [6].

Since aziridine differs in many respects from amines having an open C—N—C chain, it appeared to be of interest to us, in our investigations of the structure and conformation of compounds having two small rings coupled by a central single bond [7,8], to examine the internal rotation of 1,1'-bisaziridyl [9] *(1)* and to determine whether it undergoes inversion like other amines.



(1) *(1a)* *(2)*

With this aim in mind we recorded the IR spectra of *(1)* in the gaseous liquid, and crystalline states and its Raman spectrum in the liquid state. The following observations were made:

1. Although 36 normal vibrations are to be expected for compound *(1)* as a 14-atom molecule, its IR spectrum and Raman spectrum show relatively few bands.

2. The rule of mutual exclusion applies to the IR and Raman spectra of liquid *(1)*: apart from three bands no frequency coincidences occur.

3. There is no change in the number of IR bands of *(1)* during transition from the crystalline to the liquid and the gaseous states.

These observations can only be explained on the basis of a centrosymmetric C_{2h} structure; therefore, of all the possible conformers *only* the s-*trans* form is present, within the limits of experimental error, in *each of the three* different states. Thus compound *(1)* differs significantly not only from all the previously investigated hydrazines [1–4] but also from the isoelectronic hydrocarbon, bicyclopropyl *(2)*, which occurs as the pure s-*trans* conformer in the crystalline state only but as a mixture of the *gauche* and s-*trans* forms in the liquid and gaseous states [7].

The s-*trans* form of *(1)* can give rise to non-centrosymmetric conformers either by internal rotation about the N—N bond or by inversion at one of the nitrogen atoms. Since we observed only the s-*trans* form spectroscopically and since the inversion barrier is particularly high in aziridines [10–13] (*e.g.* > 22 kcal/mole for *N*-aminoaziridine [13,14]), the internal rotation must also be strongly hindered in this case; both factors are probably due to the particular electronic arrangement in the aziridine [15].

In order to determine the structural parameters of *(1)* accurately we are at present carrying out an electron diffraction investigation, a complete analysis of the vibrational spectrum, and NMR measurements.

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Bis(trimethylstannyl) Selenide and Bis(trimethylstannyl) Telluride as Ligands in Carbonyl Complexes of Transition Metals[**]

By *Herbert Schumann* and *Robert Weis*[*]

We recently reported the first synthesis of pentacarbonylchromium(0), -molybdenum(0), and -tungsten(0) complexes with organo-silyl, -germyl, -stannyl, and -plumbyl sulfides as the sixth ligand[1]. The sulfur atom of these organometal sulfides is therefore sufficiently basic to act as σ donor and π acceptor toward the transition metal carbonyls which are to be regarded as Lewis acids.

Extension of these studies to organometal selenides and tellurides has shown that bis(trimethylstannyl) selenide[2] and bis(trimethylstannyl) telluride[3] react with hexacarbonylchromium, hexacarbonylmolybdenum, or hexacarbonyltungsten in tetrahydrofuran (THF) at room temperature and under UV irradiation[4] with displacement of one CO group.

The products *(1)*, *(2)*, and *(3)* are obtained almost quantitatively on irradiation of a mixture of the reactants; in the synthesis of *(4)* and *(5)*, however, owing to the high light-sensitivity of bis(trimethylstannyl) telluride complete formation of the highly reactive pentacarbonylmetal-THF complex must first be attained by UV irradiation of $Cr(CO)_6$ or $W(CO)_6$ in THF; in the dark, the complex exchanges THF for the new ligand bis(trimethylstannyl) telluride.

$$[(CH_3)_3Sn]_2X + M(CO)_6 \xrightarrow{h\nu} \begin{matrix}(CH_3)_3Sn\\ \\ (CH_3)_3Sn\end{matrix}\!\!>\!X\!-\!M(CO)_5 + CO$$

(1), X = Se, M = Cr; *(4)*, X = Te, M = Cr
(2), X = Se, M = Mo;
(3), X = Se, M = W; *(5)*, X = Te, M = W

Cpd.	X	M	Decomp. (°C)	νCO (cm^{-1})	$\nu_{as}Sn_2X$ [a] (cm^{-1})	$\nu_{s}Sn_2X$ [a] (cm^{-1})	δCH_3 [b] (Hz)
(1)	Se	Cr	84	2060 1984 1936 1914	218	185	−14
(2)	Se	Mo	86	2080 1998 1970 1925	207	164	−11
(3)	Se	W	107	2070 1986 1934 1914	218	183	−10.5
(4)	Te	Cr	73	2085 1970 1944 1935	162	125	+ 7
(5)	Te	W	71	2069 1984 1934 1919	164	122	+ 7.5

[a] Raman spectrum; we are grateful to Dr. *E. Lindner*, Erlangen, for recording the spectra.

[b] 5% solution in benzene; TMS as external reference.

All the compounds prepared are brilliant yellow and sensitive to atmospheric oxygen and water; their thermal stability is similar to that of the analogous organometal sulfide complexes. The IR spectra of the compounds in solution in cyclohexane show four CO stretching vibrations. This finding agrees neither with local C_{4v} symmetry for the $(CO)_5MX$ group (3νCO), nor with overall C_s symmetry for the $(CO)_5MXSn_2$ system (5νCO). On the other hand an sp^2 hybridization at X can certainly be ruled out. As illustrated by the frequencies of the CO stretching vibrations, the influence of the chalcogenide ligands on the band positions of these vibrations is so very slight that it is perfectly reasonable to assume C_{4v} symmetry for the group $(CO)_5MX$; in the presence of symmetry-lowering ligands the degeneracy of the E_1 vibration will, however, be lifted[5].

The remarkable stability of compounds *(1)* to *(5)* demonstrates that, in spite of their low basicity, organotin selenides and organotin tellurides can form σ-donor-π-acceptor complexes in the same way as diorganyl selenides or tellurides. Blocking one of the two lone pairs of the chalcogen atom by no means causes bond weakening such as would lead to cleavage of the tin-chalcogen bond.

Procedure:

Hexacarbonylchromium, hexacarbonylmolybdenum, or hexacarbonyltungsten (10 mmoles) and bis(trimethylstannyl) selenide (10 mmoles) are dissolved in THF (50 ml), which has been dried over CaH_2, in an irradiation apparatus (quartz immersion tube, argon countercurrent). The mixture is stirred and irradiated with a high-pressure mercury vapor lamp[4]. A pressure slightly lower than atmospheric in a gasometer that was fitted to check the evolution of CO is found to favor the reaction, which is complete after irradiation for 3 h when the solution has become orange yellow. In the synthesis of *(4)* and *(5)*, addition of bis(trimethylstannyl) telluride (10 mmoles) is carried out *after* irradiation of hexacarbonylchromium or hexacarbonyltungsten (10 mmoles) in the manner described above, and the reaction mixture is then stirred in the dark at room temperature for another two hours. After removal of the solvent under reduced pressure,

the products (light yellow powder in each case; yield 80 to 90%) can be recrystallized from pentane at −40 °C.

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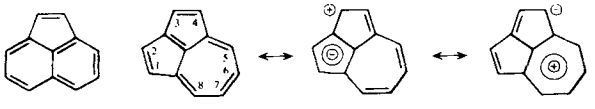
[4] Quartz lamp Q 81, Hanau.

[5] *E. O. Fischer* and *R. Aumann*, Angew. Chem. *79*, 900 (1967); Angew. Chem. internat. Edit. *6*, 879 (1967); *S. O. Grim, D. A. Wheatland*, and *W. McFarlane*, J. Amer. chem. Soc. *89*, 5573 (1967).

New Synthesis of Aceheptylene

By *Klaus Hafner* and *Rolf Fleischer* [*]

Like acenaphthylene *(1)*, the isomeric compound cyclopent[*cd*]azulene *(2)* can also undergo 1,2-cycloadditions at the double bond of the five-membered ring. In contrast to *(1)*,



(1) *(2)* A B

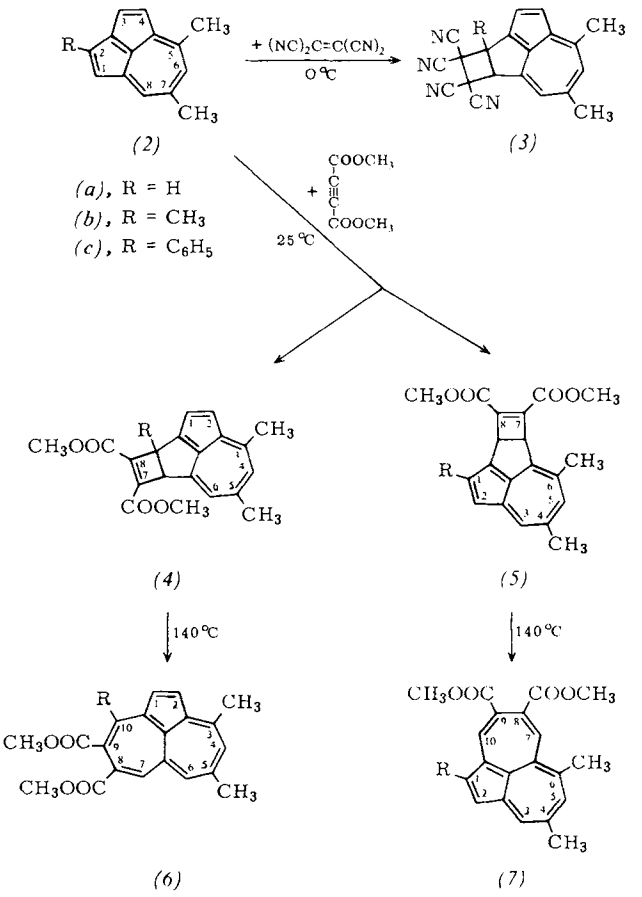
however, *(2)* — like other derivatives of pentalene [1] — combines with multiple-bond systems at 0 °C or at room temperature. The thermally labile 12π-electron system *(2)* is thus converted into stable azulene derivatives.

Reaction of *(2a)* with tetracyanoethylene at 0 °C affords the cyclobutane derivative *(3)* in 60% yield as the sole adduct [2]. Dimethyl acetylenedicarboxylate, however, adds to *(2a)* at 25 °C in methylene chloride (+1% of triethylamine, 15 h) both in the 1,2- and in the 3,4-position to form dimethyl 3,5-dimethyl-6b,8a-dihydrocyclobuta[*a*]cyclopent[*cd*]azulene-7,8-dicarboxylate *(4a)* (m.p. 112 °C, yield 40%) and the corresponding 4,6-dimethyl derivative *(5a)* (m.p. 143—144 °C, yield 10%) [3].

(2b) and *(2c)* [4] combine with dimethyl acetylenedicarboxylate only in the 1,2-position to give *(4b)* (m.p. 141 °C, yield 71%) and a mixture of *(4c)* (m.p. 103—104 °C, yield 53%) and the aceheptylene derivative *(6c)* (m.p. 152 °C, yield 8%), respectively.

X-ray structure analysis [5] and SCF calculations [5,6] indicate a high bond order for the 1,2- and 3,4-linkage in *(2)* and polarization consistent with participation of the resonance structures (2A) and (2B). These findings suggest that reactions of *(2)* with electron-deficient alkenes and alkynes are two-step cycloadditions proceeding *via* resonance-stabilized dipolar intermediates.

Thermal valence isomerization of the adducts *(4a)*, *(4b)*, *(4c)*, and *(5a)* in boiling xylene (1 h) leads to the aceheptylenes *(6a)* (m.p. 150 °C), *(6b)* (m.p. 147 °C), *(6c)* (152 °C), and *(7a)* (m.p. 119—120 °C), respectively, in yields of about 90%. The preparation of *(6)* and *(7)* from the readily accessible cyclopent[*cd*]azulenes supplements the previous syntheses [2,7] of the tricyclic 14π-electron system. The structures



of compounds *(4)*—*(7)* were established by elemental analysis, molecular-weight determination, and UV and NMR spectra.

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German version: Angew. Chem. *82*, 217 (1970)

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[1] 1,3-Bis(dimethylamino)pentalene [*K. Hafner, K. F. Bangert*, and *V. Orfanos*, Angew. Chem. *79*, 414 (1967); Angew. Chem. internat. Edit. *6*, 451 (1967)] reacts with dimethyl acetylenedicarboxylate at 0 °C to give dimethyl 4,8-bis(dimethylamino)azulene-5,6-dicarboxylate [*V. Orfanos*, Dissertation, Technische Hochschule Darmstadt 1968]. In this case, two-step cycloaddition of the enamine system to alkyne giving a cyclobutene derivative is probably followed by valence isomerization of the product to the substituted azulene. A concerted [2 + 8] cycloaddition has been suggested by *R. B. Woodward* [Special Publication No. 21, Chem. Soc. (London) *1967*, 217] as initial step in the formation of diethyl 1,2,3,4,5,8-hexaphenylazulene-6,7-dicarboxylate from hexaphenylpentalene and diethyl acetylenedicarboxylate at 160 °C [*E. LeGoff*, J. Amer. chem. Soc. *84*, 3975 (1962)].

[2] *K. Hafner* and *J. Schneider*, Liebigs Ann. Chem. *624*, 37 (1959).

[3] In addition to *(4a)* and *(5a)*, a 4% yield of dimethyl dimethylaceheptylenedicarboxylate is formed, presumably by addition of the acetylene ester to *(2a)* in the 2,2a- or 2a,3-position.

[4] *K. Hafner* and *K. F. Bangert*, Liebigs Ann. Chem. *650*, 98 (1961).

[5] *H. J. Lindner*, J. chem. Soc. (London), in press.

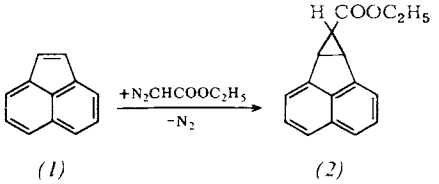
[6] *U. Müller-Westerhoff*, unpublished; *N. K. DasGupta* and *M. A. Ali*, Theoret. chim. Acta *4*, 101 (1966); *P. Hochmann, R. Zahradník*, and *V. Kvasnička*, Collect. czechoslov. chem. Commun. *33*, 3478 (1968).

[7] *K. Hafner, H. Pelster*, and *H. Patzelt*, Liebigs Ann. Chem. *650*, 80 (1961); *K. Hafner* and *G. Schneider*, *ibid. 672*, 194 (1964).

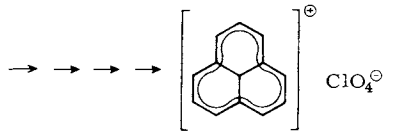
New Synthesis of 2*H*-Benzazulenes

By *Klaus Hafner* and *Wolfgang Rieper*[*]

Acenaphthylene *(1)* combines with ethoxycarbonylcarbene, generated by thermolysis of ethyl diazoacetate, to give the stable cyclopropane derivative *(2)*, which can be converted into phenalenium perchlorate *(3)* *via* a multi-step synthesis[1].



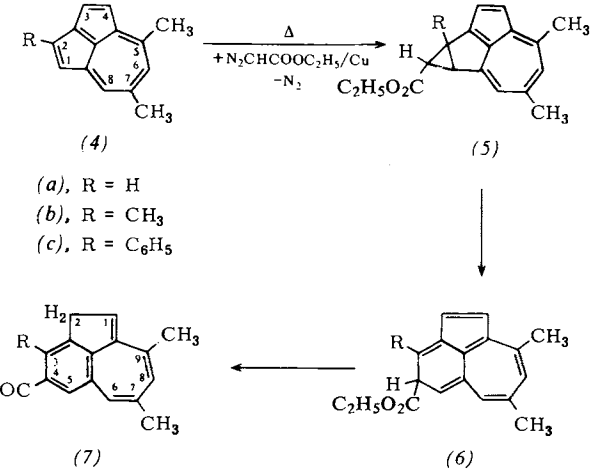
(1) *(2)*



(3)

The derivatives *(4a)*—*(4c)* of cyclopent[*cd*]azulene, an isomer of *(1)*, react similarly with carbenes (carbenoids) to yield 1,2-cycloaddition products. Unlike *(2)*, however, these products isomerize under the reaction conditions to the hitherto rather inaccessible 2*H*-benz[*cd*]azulene system *(7)*[2] which warrants interest as an isomer of phenalene.

The copper-catalyzed decomposition of ethyl diazoacetate in the presence of *(4a)*[3] in methyl cyclohexane at 90—100 °C leads directly to ethyl 7,9-dimethyl-2*H*-benz[*cd*]azulene-4-carboxylate *(7a)* (m.p. 93—94 °C) in 55—60% yield. Cycloaddition to the 1,2 bond of *(4a)* giving *(5a)* is probably followed by valence isomerization of the latter to the cross-conjugated tricyclic compound *(6a)*, which undergoes a hydrogen shift to give the stable molecules *(7a)*.



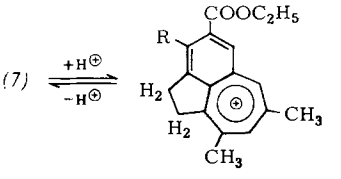
(4) *(5)*

(a), R = H
(b), R = CH_3
(c), R = C_6H_5

(7) *(6)*

Cycloaddition to the 3,4-bond of *(4a)*, which is also characterized by a high bond order, was not observed. In the case of *(4b)* and also *(4c)*[4], cycloaddition occurs exclusively at the 1,2-bond to give *(7b)* (m.p. 79—81 °C, 64%) and *(7c)* (m.p. 106—108 °C, 59%) (cf. ref.[5]).

In contrast to 2*H*-benz[*cd*]azulene[2b] and its 7,9-dimethyl derivative[6], compounds *(7a)*, *(7b)*, and *(7c)* can be isolated at room temperature and can be stored below 0 °C in the absence of atmospheric oxygen. Like 3,4,7,9-tetramethyl-2*H*-benz[*cd*]azulene[2a] they form trinitrobenzene adducts, and the heptafulvene system is reversibly protonated in position 1 to the bridged benzotropylium cation *(8)* by 70% perchloric acid. The structures of compounds *(7)* were established by elemental analysis, molecular-weight determination, and UV and NMR spectra.



(8)

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[1] *R. Pettit*, J. Amer. chem. Soc. *82*, 1972 (1960).

[2] a) *K. Hafner* and *H. Schaum*, Angew. Chem. *75*, 90 (1963); Angew. Chem. internat. Edit. *2*, 95 (1963); b) *V. Boekelheide* and *C. D. Smith*, J. Amer. chem. Soc. *88*, 3950 (1966).

[3] *K. Hafner* and *J. Schneider*, Liebigs Ann. Chem. *624*, 37 (1959).

[4] *K. Hafner* and *K. F. Bangert*, Liebigs Ann. Chem. *650*, 98 (1961).

[5] *K. Hafner* and *R. Fleischer*, Angew. Chem. *82*, 217 (1970); Angew. Chem. internat. Edit. *9*, 247 (1970).

[6] *W. Rieper*, Dissertation, Technische Hochschule Darmstadt 1968. 7,9-Dimethyl-2*H*-benz[*cd*]azulene was prepared by thermolysis of 4-(3,3-diethoxypropyl)-6,8-dimethylazulene at 150—180 °C/10^{-5} torr and isolated as the trinitrobenzene adduct [m.p. 170—171 °C (decomp.)].

CONFERENCE REPORTS

Biochemical and Genetic Aspects of Ribosome Specificity in Protein Synthesis

By *Orio Ciferri*[*]

70 S type of ribosomes, prepared from prokaryotic organisms or cell organelles (mitochondria and chloroplasts) of eukaryotic organisms, catalyze the reactions for protein synthesis *in vitro* only in the presence of polymerizing enzymes obtained from prokaryotes or organelles. No activity is evident when such ribosomes are tested in the presence of preparations of polymerizing enzymes extracted from the cytoplasm of the eukaryotic organisms. Ribosomes of the 80 S type, like those present in the cytoplasm of eukaryotes, are active *in vitro* only in the presence of preparations of polymerizing enzymes from the cytoplasm of such organisms.

Transfer factors T and G, which may be separated from the preparations of polymerizing enzymes, appear to be strictly ribosome specific. Indeed only one transfer factor T and one transfer factor G, specific for 70 S ribosomes, are present in the extract from cells of *E. coli*. In contrast, two transfer factors G and two transfer factors T, each specific for just one type of ribosome, may be detected in the non-photosynthetic eukaryotic alga *Prototheca zopfii*. Two ribosome specific transfer factors G have been demonstrated also in the case of the yeast *Saccharomyces cerevisiae*.

Extracts prepared from dark-grown cells of the photosynthetic flagellate *Euglena gracilis* display polymerizing activity only

on ribosomes of the 80 S type. On exposure to light, which induces the synthesis of the photosynthetic apparatus, a polymerizing activity specific for 70 S ribosomes becomes evident.

Ribosome specificity is not limited to the factors responsible for peptide chain elongation. Indeed the initiation factors, prepared from *E. coli*, catalyze the reactions for peptide chain initiation also on *Bacillus subtilis* ribosomes and on the ribosomes prepared from the mitochondria of the fungus *Neurospora crassa*.

The development of such studies at the genetic and biochemical levels may provide some interesting clues on the evolutionary relations that may exist between prokaryotic and eukaryotic organisms. In addition, within the latter group of organisms such studies may give some information on the genetic and metabolic autonomy of cellular organelles.

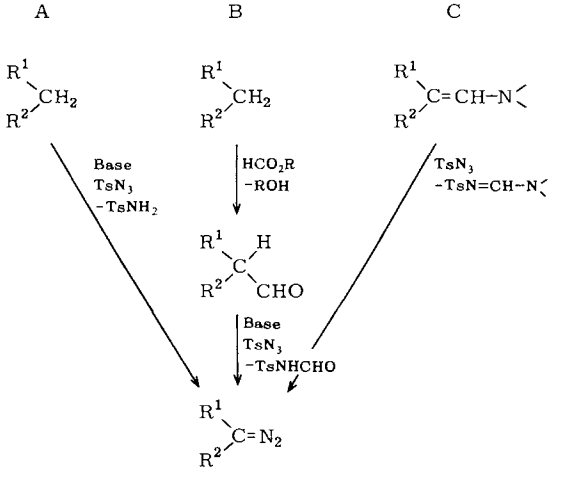
Lecture at Göttingen on November 13, 1969 [VB 222 IE]
German version: Angew. Chem. *82*, 259 (1970)

[*] Prof. Dr. O. Ciferri
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Università di Pavia
Pavia (Italy)

Recent Investigations on the Synthesis and Reactivity of Diazo Compounds

By *Manfred Regitz* [*]

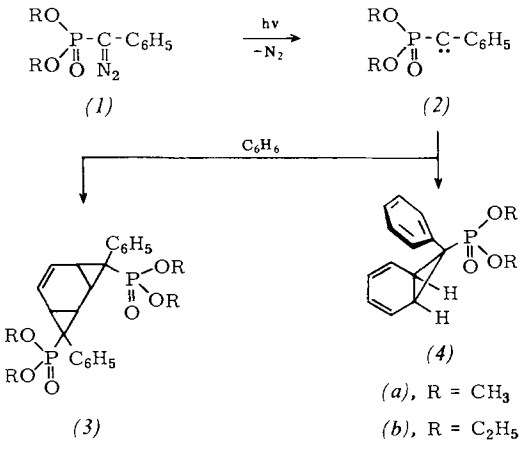
Aliphatic diazo compounds can be prepared *via* three different but complementary routes by diazo group transfer with tosyl azide. Diacylmethanes react directly with the diazo-transfer agent (Route A)[1], whereas monoacylmethanes react only after previous formylation[1] (Route B). Diazomethane and non-acylated derivatives are accessible only *via* enamines of suitable structure (Route C).



Route A: R^1 and R^2 = acyl
Route B: R^1 or R^2 = acyl
Route C: R^1 and R^2 = H or alkyl

The synthesis of phenyldiethylphosphonodiazomethane *(1b)*[2] and diphenylphosphinyldiazomethanes *(5)*[3] and of 2-oxo-1-diazocycloalkanes[4] serve as model examples for routes A and B respectively. The carbenes *(2)* obtained photolytically from *(1)* add to benzene to give the 2 : 1 adducts *(3)* and the stable norcaradienes *(4)*; the NMR spectrum largely rules out an isomeric cycloheptatriene structure for *(4)* ($CDCl_3$, δ = 5.7—6.3 ppm, 4 olefinic protons; δ = 3.5—4.0 ppm, 2 cyclopropane protons).

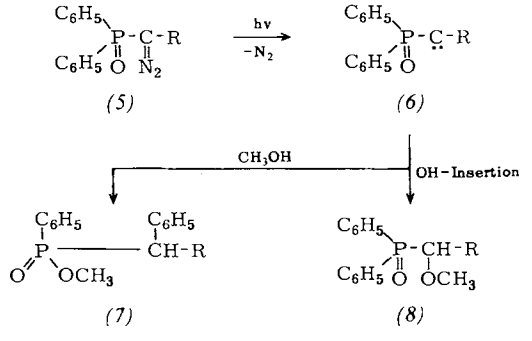
Diphenylphosphinylcarbenes *(6)* have been investigated, particularly with regard to their rearrangeability. Thus photolysis of *(5a)* and *(5b)* in methanol leads *via* a Wolff



(1) *(2)* *(3)* *(4)*

(a), R = CH_3
(b), R = C_2H_5

rearrangement to the formation of the phosphinic esters *(7a)* and *(7b)* [61 and 71% resp.; NMR ($CDCl_3$): δ (OCH_3) = 3.6—3.7 ppm, doublet, $J_{POCH} \approx 11$ Hz].



(5) *(6)* *(7)* *(8)*

(a), R = H; *(b)*, R = COC_6H_5; *(c)*, R = $CO_2C_2H_5$;
(d), R = C_6H_5; *(e)*, R = $CONH_2$

The analogously generated carbenes *(6d)* and *(6e)*, on the other hand, undergo OH insertion to give the phosphine oxides *(8d)* and *(8e)* [100 and 81% resp.; NMR ($CDCl_3$): δ (OCH_3) = 3.4—3.5 ppm, singlet], while *(6c)* follows both routes [61% *(7c)* and 22% *(8c)*].

Depending on the size of the ring the photolysis and thermolysis of 2-oxo-1-diazocycloalkanes proceed either *via* ring contraction and hydride shift (2-cycloalken-1-ones) or transannular carbene insertion (bicyclic ketones)[5].

Lectures at Leverkusen on December 11, 1969,
and at Karlsruhe on December 13, 1969 [VB 227 IE]
German version: Angew. Chem. *82*, 224 (1970)

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[1] *M. Regitz*, Angew. Chem. *79*, 786 (1967); Angew. Chem. internat. Edit. *6*, 733 (1967).

[2] *M. Regitz, W. Anschütz*, and *A. Liedhegener*, Chem. Ber. *101*, 3734 (1968).

[3] *M. Regitz* and *W. Anschütz*, Chem. Ber. *102*, 2216 (1969).

[4] *M. Regitz* and *J. Rüter*, Chem. Ber. *101*, 1265 (1968).

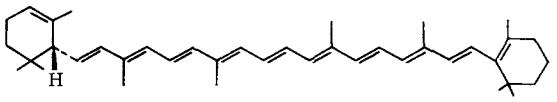
[5] *M. Regitz* and *J. Rüter*, Chem. Ber. *102*, 3877 (1969).

Recent Investigations of Plant Pigments

By *Conrad H. Eugster* [*]

1. *Carotenoids.* Most of the almost 180 carotenoids known to date have chiralic character. Until quite recently nothing was known about their absolute configuration (with the exception of capsanthin). Chemical correlation of the enantio-

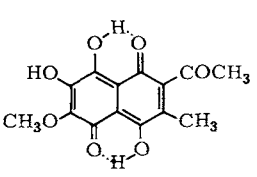
mers of α-cyclogeranic acids with α- and γ-ionones and with α- and ε-carotenes has now been achieved. Thus natural α-carotene was found to have the following structure *(1)* [1]:



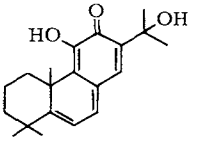
(1)

Xanthophyll (lutein), which is one of the main carotenoids found in green leaves, has the same configuration at C-6 [2].

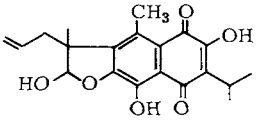
2. *Pigments from leaf glands.* Several East African Labiatae and Leguminosae possess colored leaf glands from which new quinonoid pigments have been isolated, *e.g.*: cordeauxione *(2)* from *Cordeauxia edulis*; fuerstione *(3)* from *Fuerstia africana*; coleone A *(4)* and coleone B *(5)* from *Coleus igniarius*; coleone *(6)* from *C. aquaticus*.



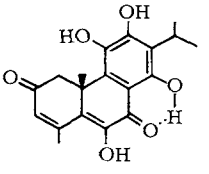
(2)



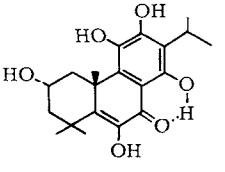
(3)



(4)



(5)



(6)

Compound *(2)* is probably built up from seven acetate residues; the compounds *(3)*—*(6)* are obviously derived from mevalonic acid (proved by tracer analysis in the case of coleon A [3]).

3. *Russupteridines.* The genus *Russula* (*Basidiomycetes*) is multicolored. The plants of this genus contain yellow, red, and blue pigments, along with colorless compounds that exhibit a very strong fluorescence in UV light (the green pigments appear to be a mixture). Isoelectric focusing in a pH-saccharose gradient proved to be suitable for the analytical separation of the water-soluble pigments; a preparative separation was accomplished by combined Sephadex and cellulose chromatography. Spectroscopic and chemical investigations have shown that the main red pigment in *R. sardonia* is a novel derivative of a dimeric pteridine riboside [4]. We also assume that the orange-red pigments from the peel of the fly agaric (*Amanita muscaria*) are probably pteridine derivatives.

Lecture at Berlin on January 12,
and at Konstanz on January 22, 1970 [VB 229 IE]
German version: Angew. Chem. *82*, 259 (1970)

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[1] *C. H. Eugster, R. Buchecker, Ch. Tscharner, G. Uhde*, and *G. Ohloff*, Helv. chim. Acta *52*, 1729 (1969).

[2] *R. Buchecker* and *C. H. Eugster*, unpublished.

[3] *D. Arigoni, C. H. Eugster et al.*, unpublished.

[4] *C. H. Eugster, E. F. Frauenfelder*, and *H. Koch*, Helv. chim. Acta *53*, 131 (1969).

SELECTED ABSTRACTS

The reaction between oxygen atoms and acetylene at room temperature has been investigated by *J. N. Bradley* and *R. S. Tse*. The oxygen atoms were produced from molecular oxygen by a microwave discharge. The concentration of O, H, and OH were determined from the ESR spectra of the reacting gas mixture. The results can be described essentially in terms of the following reaction sequence:

$$O + C_2H_2 \rightarrow CH_2 + CO \quad (1)$$

$$O + CH_2 \rightarrow CO + 2\,H \quad (2)$$

$$CH_2 + C_2H_2 \rightarrow C_3H_4 \quad (3)$$

$$H + C_2H_2 \rightarrow C_2H_2 + {}^1/_2\,H_2 \quad (4)$$

The values $k_1 = (1.1 \pm 0.1) \times 10^8$ l mole^{-1} s^{-1} and $k_2/k_3 = 2.6 \pm 0.3$ were derived for the (relative) rate constants. The side reaction

$$O + CH_2 \rightarrow CH + OH \quad (2a)$$

with $k_{2a}/k_2 = 0.06 \pm 0.02$ also occurs; the resulting OH radicals are consumed according to

$$OH + C_2H_2 \rightarrow H_2O + C_2H \quad (5)$$

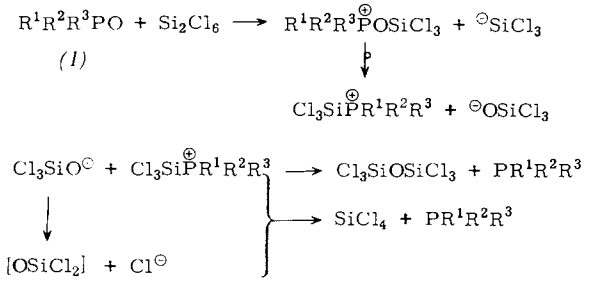
/ Trans. Faraday Soc. *65*, 2685 (1969) / —Hz. [Rd 145 IE]

The phase diagram of the niobium-hydrogen system has been studied by *J. H. Pryde* and *C. G. Titcomb* by measurement of pressure and electrical resistance at —78 to +300 °C, an atomic ratio of H : Nb = 0 : 1—0.65 : 1, and a hydrogen partial pressure of 10^{-7}—10^1 torr. Gaseous H_2 was rapidly taken up by the metal at all temperatures. The boundary of the two-phase region (solid solution + hydride) is symmetrical about the atomic ratio H : Nb = 0.256 : 1; the critical point lies at 211 °C, H : Nb = 0.256 : 1, 1×10^{-1} torr. At about 86 °C hysteresis phenomena become apparent in the two-phase region in the resistance-temperature diagram which indicate changes in the lattice structure of the hydride. / Trans. Faraday Soc. *65*, 2758 (1969) / —Hz. [Rd 144 IE]

A novel effect of CO_2 on catalyst properties in the dimerization of butadiene has been observed by *J. F. Kohnle, L. H. Slaugh*, and *K. L. Nakamaye*. In the absence of catalyst, butadiene slowly dimerizes to 4-vinyl-1-cyclohexene *(1)*; in the presence of $[(C_6H_5)_3P]_3Pt$ the product ist still compound *(1)* along with a small amount of *trans*-1,3,7-octatriene *(2)*, provided reaction is allowed to take place in an atmosphere of nitrogen or argon. However, if CO_2 is present and oxygen carefully excluded, $[(C_6H_5)_3P]_3Pt$ converts butadiene mainly into compound *(2)*. Similar results are obtained if $[(C_6H_5)_3P]_4Pd$ is used as catalyst. The $[(C_6H_5)_3P]_4Ni$- and $[(C_6H_5O)_3P]_4Ni$-catalyzed dimerizations of butadiene in the absence of CO_2

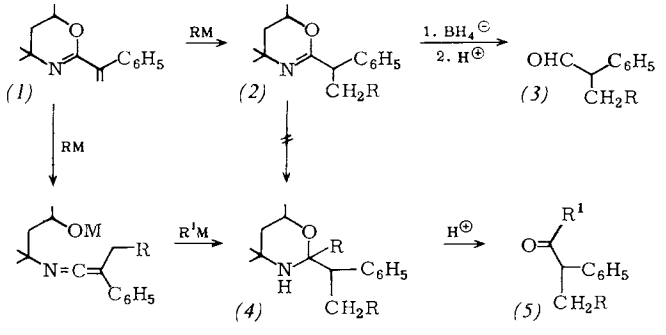
lead mainly to 1,5-cyclooctadiene; in the presence of CO_2 the major product is *(1)*. The above observations are of interest to those studying metal catalysis since CO_2 is frequently present in reaction systems. / J. Amer. chem. Soc. *91*, 5904 (1969) / --Ma. [Rd 151 IE]

The use of hexachlorodisilane as a reducing agent has been reported by *K. Naumann, G. Zon*, and *K. Mislow*. Optically active acyclic phosphine oxides *(1)* can be converted to phosphines with a high degree of stereospecificity and with inversion of configuration. Hexachlorodisilazane likewise reduces amine oxides to amines and sulfoxides to sulfides. The authors propose the following reaction scheme for the reaction of *(1)*:



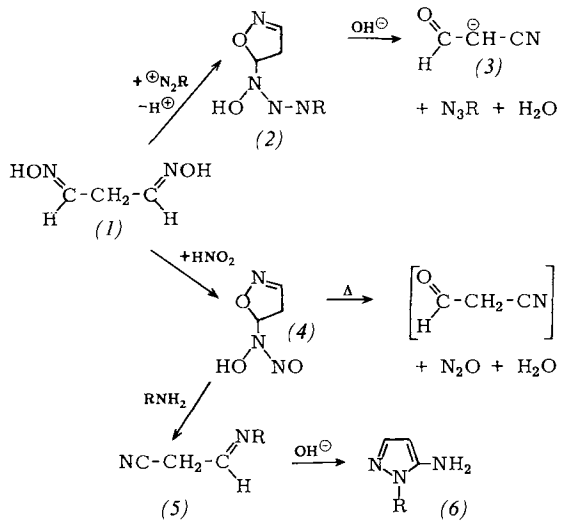
When carried out in refluxing benzene reduction is complete within about 5 minutes; if the contact time is extended beyond this period the optical purity of the product decreases. / J. Amer. chem. Soc. *91*, 7012 (1969) / —Kr. [Rd 148 IE]

A simple synthesis of α-phenylaldehydes and ketones is described by *A. I. Meyers* and *A. C. Kovelesky*. The readily accessible α-styryldihydro-1,3-oxazine *(1)* is treated with organometallic compounds, *e.g. n*-butylmagnesium bromide, to give *(4)* (R = R^1 = n-C_4H_9, 73% yield), which reacts with oxalic acid to give ketone *(5)* (overall yield 68%). Use of the



voluminous cyclohexylmagnesium bromide leads to the monoalkyl compound *(2)* only, which can be reduced with $NaBH_4$ to give the aldehyde *(3)* (R = cyclo-C_6H_{11}, total yield 98%). / Tetrahedron Letters *1969*, 4809 / —Kr. [Rd 150 IE]

Cyanoacetaldehyde derivatives and secondary products, *e.g.* 5-amino-pyrazoles, have been prepared by *H.-J. Sturm* and *H. Armbrust*. Dialkylaminoacroleins react with hydroxylamine to give malonoaldehyde dioxime *(1)*, which can occur in several isomeric forms and which, on treatment with aryldiazonium salts and HNO_2, yields the colorless coupling product *(2)* or *(4)*. In aqueous bases at room temperatures compound *(2)* decomposes exothermally to aryl azide and cyanoacetaldehyde *(3)*. Reaction of *(4)* with amines leads to



formation of the derivatives *(5)*, the hydrazones and thiosemicarbazones of which can be cyclized to the 5-aminopyrazoles *(6)* in good yields. / Liebigs Ann. Chem. *729*, 139 (1969) / —Kr. [Rd 153 IE]

***N,N*-Diethylaminooxysilanes** have been synthesized by *K. C. Pande* and *R. E. Ridenour* from chlorosilanes and an excess of *N,N*-diethylhydroxylamine in an inert solvent:

$$R_nSiCl_{4-n} + 2\,(4-n)\,(C_2H_5)_2NOH \rightarrow R_nSi[ON(C_2H_5)_2]_{4-n} + (4-n)\,(C_2H_5)_2NOH \cdot HCl$$

$n = 0$–3 *(1)*

Examples: *(1a)*, $n = 0$, R = CH_3, b.p. 95 °C/0.05 torr, yield 40%; *(1d)*, $n = 3$, R = CH_3, b.p. 44 °C/23 torr, yield 80%. $CH_3SiH[ON(C_2H_5)_2]_2$ *(2)* (b.p. 36 °C/0.2 torr, yield 45%), for example, was prepared in this way. Aminooxysilanes can be decomposed hydrolytically — *(1d)*, *e.g.*, decomposes to trimethylsilanol. Compound *(2)* reacts with *N,N*-diethylhydroxylamine to give *(1b)*:

$$CH_3SiH[ON(C_2H_5)_2]_2 + (C_2H_5)_2NOH \rightarrow CH_3Si[ON(C_2H_5)_2]_3 + H_2$$

(2) *(1b)*

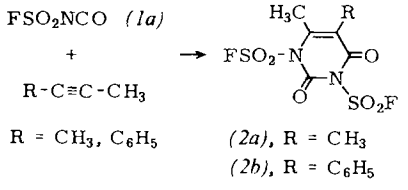
Tetrakis(diethylaminooxy)tetramethylcyclotetrasiloxane can also be prepared in this way. / Chem. and Ind. *1970*, 56 / —Kr. [Rd 155 IE]

Reactions of silicon fluorides with methanol have been investigated by *J. L. Margrave, K. G. Sharp*, and *P. W. Wilson*. A mixture of gaseous SiF_2, SiF_4, and methanol was condensed at —196 °C. On warming the mixture to room temperature, SiF_3H and CH_3OSiF_3 were formed as major products and $(CH_3O)_2SiF_2$ as secondary product:

$$CH_3OH + SiF_4 \rightarrow CH_3OSiF_3 + HF$$
$$SiF_2 + HF \rightarrow SiF_3H$$
$$CH_3OH + SiF_2 \rightarrow CH_3OSiF_2H$$
$$CH_3OSiF_2H + CH_3OH \rightarrow (CH_3O)_2SiF_2 + H_2$$

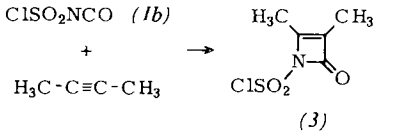
Formation of a secondary product by reaction of methanol with CH_3OSiF_3 does not take place. In the reactions described, a mechanism involving diradicals seems doubtful since products of the type $CH_3O(SiF_2)_nOCH_3$ were not observed. The two new methoxysilanes were identified, *inter alia*, by IR spectroscopy. / Inorg. nuclear Chem. Letters *5*, 995 (1969) / —Kr. [Rd 156 IE]

Cycloadditions of halogenosulfonyl isocyanates to alkynes is the subject of reports by *K. Clauss* and *H. Jensen*, and *K. D. Kampe*. Fluorosulfonyl isocyanate *(1a)* combines with 2-butyne in the molar ratio 2 : 1 at room temperature in chlorinated hydrocarbons to give dimethyluracil bis(sulfonyl fluoride) *(2a)* (m.p. 108.5 °C, 83% yield) while reaction of chlorosulfonyl isocyanate with 2-butyne leads to formation of a product (in 50% yield) having a m.p. of 57 °C and the structure of an azetinone derivative *(3)* (the valence isomer *(4)*, however, cannot altogether be ruled out). Phenylacetylene reacts with *(1a)* in the molar ratio 1 : 1 at temperatures

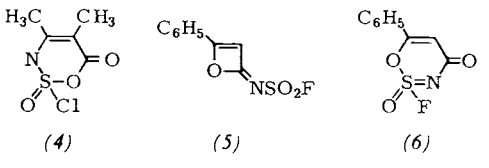


FSO_2NCO *(1a)* + $R-C\equiv C-CH_3$ → FSO_2-substituted azetinone

$R = CH_3, C_6H_5$ *(2a)*, R = CH_3; *(2b)*, R = C_6H_5



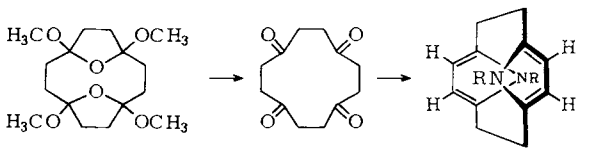
$ClSO_2NCO$ *(1b)* + $H_3C-C\equiv C-CH_3$ → *(3)*



(4) *(5)* *(6)*

below 35 °C to give the oxete derivative *(5)* [or the valence isomeric oxathiazinone derivative *(6)*], m.p. 100 °C, yield 36%. Reaction with methyl(phenyl)acetylene, on the other hand, leads to the uracil derivative *(2b)*, decomp. 145—149 °C. No crystalline products are obtained on reaction with *(1b)*. / Tetrahedron Letters *1970*, 119, 123 / —Kr. [Rd 157 IE]

***N,N*-Dimethyl[2.2](2,5)pyrrolophane** *(3)* has been prepared by *H. H. Wasserman* and *D. T. Bailey* from the tetramethoxy compound *(1)*, which can be obtained from [2.2](2,5)furanophane. Compound *(1)* can readily be converted into the tetraone *(2)* (m.p. 129—130 °C, 95% yield) by treatment with hydrochloric acid at room temperature. A solution of *(2)* in glacial acid is treated at 80 °C with anhydrous methylamine, adjusted to pH 10 by addition of ammonia, and then extracted with chloroform. The pyrrolophane *(3)* can be purified by chromatography (m.p. 144—145 °C, yield 42%). The signals



(1) *(2)* *(3)*

R = CH_3

due to the β-protons of the pyrrole ring appear at their normal positions ($\tau \approx 3.90$) in the NMR spectrum of *(3)*. The *anti*-configuration of *(3)* is thus confirmed. / Chem. Commun. *1970*, 107 / —Kr. [Rd 158 IE]

The yellow adduct (thiourea)$_2 \cdot I_2$, first described in 1912, has been shown to be a salt $[(H_2N)_2CS]_2I^+I^-$ *(1)* in an X-ray structure analysis carried out by *H. Hope* and *G. Hung-Yin Lin*. Compound *(1)* forms monoclinic crystals, space group C2/c, having $a = 22.27 \pm 0.02$, $b = 5.290 \pm 0.005$, $c = 9.808 \pm 0.005$ Å, $\beta = 115.31 \pm 0.03°$, and $Z = 4$. The I^I atom lies at the center of symmetry of the cation (∢ SIS 180.0 °); the interatomic distances are IS 2.629, SC 1.723, CN 1.298 and 1.318 Å; ∢ ISC 106.2 °. The ion is not perfectly planar, the $C(NH_2)_2$ groups being twisted 17 ° about the CS bond out of the CSISC plane. / Chem. Commun. *1970*, 169 / —HB. [Rd 161 IE]

The acidity of surface OH groups has been evaluated by *M. L. Hair* and *W. Hertl*. Hydroxyl band frequency shifts in the IR spectra of hydroxy compounds are known to be related to the acidity of the OH compound and to the basicity of the solvent. Comparison of the OH frequency shifts of methanol, phenol, and trichlorophenol in solutions and the OH frequency shifts of surface hydroxyl groups on adsorption of the corresponding solvents allowed the pK_a values of the surface OH groups to be correlated with the known pK_a values of alcohols and phenols. The pK_a values found were:

Mg—OH	15.5 ± 0.4
B—OH	8.8 ± 0.6
Si—OH	7.1 ± 0.5
P—OH	−0.4

For silica and a silica-alumina cracking catalyst, the same values were obtained which are in good agreement with an earlier value (≈ 7.0) obtained by titration. The surface groups have lower pK_a values than the first dissociation steps of the corresponding "molecular" acids. There is no obvious relationship between the two values. / J. physic. Chemistry *74*, 91 (1970) / —Hz. [Rd 163 IE]

BOOK REVIEWS

Messgrößenverarbeitung. Eine Einführung in die elektrische Messgrössenerfassung und -verarbeitung nichtelektrischer Grössen. (Treatment of measurements. An introduction to the electrical measurement and treatment of non-electrical quantities). By *E.-G. Woschni*. Verlag Chemie GmbH, Weinheim/Bergstr. 1969. 1st Edit., xii, 156 pp., 105 figures, 1 table, cloth, DM 24.—.

The book deals essentially with two topics: 1. the electrical measurement of non-electrical quantities, including the discussion of the principal types of recording instruments, and 2. the processing and output of the electrical analog quantities produced.

The value of the book lies mainly in the first part. This not only discusses the advantages and disadvantages of electrical measurements but also explains briefly, though precisely, the measurement principles of a series of detecting elements, and presents a sufficiently extensive mathematical discussion to show the limiting conditions for the measurement.

A particularly welcome feature is the abundance of hints about dynamic properties, since errors are repeatedly made here in practical measurements.

The subsequent discussion of the further treatment of analog values is also welcome. The list of types of bridges and their compensation criteria, for example, is very useful.

In the final third of the book, however, an attempt is made to cover too much ground in too little space, with the result that some chapters (*e.g.* on spectral analysis and on correlation computers) do not contain much more information than the

headings. To make up for this deficiency it would have been necessary to provide a much more comprehensive bibliography than that given.

The chapter on the execution of computations would have been better omitted, since it is too short to give adequate explanations (*e.g.* of the digital computer) and since it is not directly connected with the main subject.

Gerhard Quietzsch [NB 854 IE]

Einführung in die Kernchemie Introduction to Nuclear Chemistry). By *K. H. Lieser*. Volume I of the series "Kernchemie in Einzeldarstellungen" (Nuclear Chemistry Monographs). Verlag Chemie GmbH, Weinheim/Bergstr. 1969. 1st Edit., xvi + 720 pp., 230 figures, 103 tables, bound, DM 78.—.

The author, who lectures in nuclear chemistry at the Technische Hochschule Darmstadt, is to be congratulated on filling a long-standing gap in the German-language literature. Students or scientists wishing to acquaint themselves with nuclear and radiochemistry had in the past no alternative but to turn to American or British textbooks. Apart from the obvious language problem, there was the additional difficulty that "Nuclear Chemistry" in the USA leans far more heavily toward nuclear physics than does "Radio- und Kernchemie" as understood in Germany. Consequently, chemical aspects and methods tend to get somewhat neglected in these textbooks.

Lieser's book is oriented entirely toward the requirements of chemists wanting to learn about nuclear and radiochemistry. However, every interested reader will find in the book a thorough but readily digestible introduction to the theoretical principles, techniques, and applications of this domain.

In line with the "chemical" approach, the author begins with the periodic system of elements and the concept of isotopes. He continues with several chapters devoted to the physical principles of nuclear and radiochemistry, followed by discussions of the properties of atomic nuclei and radioactive radiation, decay processes, and nuclear reactions. The specialized techniques and equipment used are described in the chapters on radioactive radiation, major installations, separation and chemistry of radionuclides, and applications.

It is especially gratifying to find detailed sections on precisely those nuclear and radiochemical problems which are particularly interesting for the modern chemist and which are totally absent from other textbooks, *e.g.* isotopic effects and the chemical effects of nuclear reactions. They may not, strictly speaking, belong to the subject-matter of the book, but since these side effects are constantly encountered in nuclear and radiochemical experiments, it is right to mention them.

In addition to the physical principles and the most interesting chemical problems, the third main topic of the book consists of applications of radiochemistry and nuclear chemistry in science and industry. This is yet another pleasing feature, for many of the other textbooks only give these matters peripheral treatment. Individual chapters are devoted to nuclear fuels and reactor chemistry, isolation of radionuclides, synthetic elements, and isotope separation. Finally, the chapter dealing with applications includes radiochemical methods for analysis, biology, medicine, and cosmochemistry.

In conclusion, a few critical remarks are justified. At the same time, it is only fitting to point out that their brevity, and the fact that they concern in the main trivialities, bear witness to the excellence of the work. The reviewer would have preferred the sections on dating and activation analysis, which after all are among the most important subjects in nuclear and radiochemistry, and also that on nuclear models, to have been given more detailed treatment. The same may be said about the measurement of radioactive radiation, particularly as regards modern scintillation and semiconductor measuring techniques. These matters will of course be given due attention in a later volume in the monograph series. Nevertheless, since many readers, especially students, will buy only the "Introduction", it was wrong to curtail the chapter on measuring techniques in this way. Finally, the table of radionuclides in the Appendix does not seem to be very enlightening, whereas the inclusion of a nuclide chart is thoroughly commendable.

The table of nuclides, which finds its way into practically every textbook on nuclear and radiochemistry, contains scarcely any more information than the nuclide chart and is far less easy to refer to than the latter. For anyone seeking detailed information on a nuclide it will never replace a detailed table of isotopes. *G. K. Wolf* [NB 856 IE]

Synthetic Procedures in Nucleic Acid Chemistry. Vol. 1. Preparations of Purines, Pyrimidines, Nucleosides, and Nucleotides. Edited by *W. W. Zorbach* and *R. St. Tipson*. Interscience Publishers, John Wiley & Sons Ltd., London-New York 1968, 1st Edit., v + 570 pp., numerous figures, bound, approx. DM 75.—.

There can be no doubt that this book, the first volume in the series "Synthetic Procedures in Nucleic Acid Chemistry", is extremely useful and meets a definite need. More and more organic chemists and biochemists are submitting to the lure of the chemistry of the nucleic acids and nucleic-acid components, and they will find it a great advantage to have their first steps in this field guided by a collection of typical synthetic methods and tried and tested preparations of the main starting materials. For this reason, no library should be without this book.

On the other hand, some of the claims which the editors make in their preface are not justified. In its descriptions of synthetic techniques, analytical methods, and the preparation of the main compounds this book is not, with all due respect to its editors, completely up-to-date. Indeed, how could it be, when the literature from 1967 on could only be treated incompletely, if at all? One of many examples must suffice: the phosphorylation of nucleosides and nucleoside analogs, a very important reaction, is represented solely by the 2-cyanoethyl phosphate method, although more elegant and effective phosphorylation methods have become available since 1967.

The editors may well have intended to help the reader find his way through the very extensive literature of nucleoside and nucleotide chemistry by representative examples of the various syntheses, but unfortunately some of the authors are so sparing in their use of literature references that this opportunity has been missed.

Perhaps these comments will be taken into account in the subsequent volumes of this series.

Karl-Heinz Scheit [NB 860 IE]

Solute-Solvent Interactions. Edited by *J. F. Coetzee* and *C. D. Ritchie*. Marcel Dekker, Inc., New York-London 1969. 1st Edit., xiv + 653 pp., 53 figures, 138 tables, bound $ 29.50.

While brief summaries have been published on the influence of solvents on the rate and equilibrium position of organic reactions[1,2], there has been no comprehensive work on the solute-solvent interactions underlying this solvent effect. This gap has now been filled in exemplary fashion by the present book.

The first chapter (Heats and Entropies of Ionization) written by *J. W. Larson* and *L. G. Hepler* contains 44 pages giving a critical summary of thermodynamic data on the ionization of Brønsted acids in aqueous solutions. The second chapter (Medium Effects and pH in Nonaqueous Solvents, 51 pp.) by *R. G. Bates* deals with acidity scales in nonaqueous solvents

[1] Cf. Angew. Chem. internat. Edit. *7*, 158 (1968).

[2] Cf. Angew. Chem. internat. Edit. *8*, 465 (1969).

and the methods of determining them. In the third chapter (Acidity Functions, 121 pp.) *R. H. Boyd* discusses important aspects of the effect of the solvent on the acid-base equilibrium, also listing numerous tables of Hammett's H_0 and H_- functions for a large number of acids. The fourth chapter (Interactions in Dipolar Aprotic Solvents, 81 pp.) by *C. D. Ritchie* is concerned with the acidities of organic acids and the rates of proton-transfer reactions, but especially also with the effect of dipolar aprotic solvents on the rate of S_N1 and S_N2 reactions. The solvent polarity scale given in Table 4—13 on p. 281 requires some additions. In the fifth chapter (The Selective Solvation of Ions in Mixed Solvents, 41 pp.) *H. Schneider* describes the selective solvation of ions in binary solvent mixtures and their determination. While *E. M. Arnett* and *D. R. McKelvey* discuss the effect of changing over from H_2O to D_2O on the thermodynamic parameters of the solute in the sixth chapter (Solvent Isotope Effect on Thermodynamics of Nonreacting Solutes, 41 pp.), *P. M. Laughton* and *R. E. Robertson* in the seventh chapter (Solvent Isotope Effects for Equilibria and Reactions, 139 pp.) deal in detail with the effect of this solvent change on the equilibrium position and the rate of chemical reactions. The final chapter (Organoalkali Compounds in Ethers, 66 pp.) by *J. F. Garst* deals with the structure of the ethereal solutions of organometallic alkali metal compounds, with a detailed discussion of the effect of solvent polarity and cation and anion solvation on the formation and dissociation of ion pairs and their influence on equilibria and reaction rate. The book closes with a brief and rather fragmentary appendix dealing with purification methods for certain selected solvents.

There is no discussion of solvophobic interactions. Even the interactions between suitable acceptors (*e.g.* metal ions) and donor solvents ("coordinating solvents") are scarcely mentioned, despite their importance in coordination chemistry. In view of the scope of the subject matter some overlapping was seemingly unavoidable (*e.g.* Tables 2-2 on p. 52 and A II-9 on p. 199 are practically identical).

The book is interspersed with numerous examples, 53 figures and 138 tables. The bibliography lists nearly 1600 publications, and this, together with author and subject indexes, makes the book a useful reference work.

All in all, the present book gives an outstanding synopsis of all aspects of solvent-solute interactions, and no library should be without it. *Christian Reichardt* [NB 862 IE]

Oxidation: Techniques and Applications in Organic Synthesis. Vol. 1. Edited by *R. L. Augustine*. Marcel Dekker, Inc., New-York-London 1969. 1st Edit., x + 368 pp., numerous figures, $ 18.75.

The contents of this book are as follows: Chapter 1: Oxidation of hydrocarbons with transition metal compounds (*D. G. Lee*); Chapter 2: Oxidation of functional groups containing oxygen and nitrogen with transition metal compounds (*D. G. Lee*); Chapter 3: Oxidation reactions with selenium dioxide (*E. N. Trachtenberg*); Chapter 4: Glycol fission and related oxidation reactions (*A. S. Perlin*); Chapter 5: Oxidation reactions with peracids and peroxides (*S. N. Lewis*); Chapter 6: Ozonization (*J. S. Belew*).

This is the fourth book on oxidation reactions that I have had to review over the past five years[1]. In addition to this, the first volume of *K. Wiberg*'s "Oxidations in Organic Chemistry"[2] appeared during the same period, so that we may well ask ourselves whether a fifth book on the same subject is justified or necessary. In principle, this question can be answered in the affirmative. While the previous books for the most part considered oxidations from the mechanistic viewpoint, the present work is chiefly concerned with the methods used. Examples of tested operating procedures are thus given in heavy print. The preparation, purification, and analytical determination of the oxidants are mostly described in detail, as are the mode of action on the substrates and the reaction selectivity Mechanisms are invoked only to the extent that they are necessary for the comprehension of the mode of action.

It might appear that the editor intended to produce a sort of Houben-Weyl on oxidations. If this was the intention, however, the organization of the book is not very suitable, for the various chapters are arranged on the basis of oxidizing agent and not (with the sole exception of glycol fission) on the basis of the reaction to be performed. Thus, if we want to oxidize an unsaturated alcohol to an unsaturated aldehyde, we have to search through a number of chapters to find a suitable oxidizing agent, which means that we are still left with the consideration of the various alternatives and the choice of the best one.

Apart from this fundamental error in organization, the six chapters offer a wealth of valuable information. The literature is considered selectively up to 1968. Since all the authors have actually worked with the reactions they are describing, the subject material and the examples are based on personal experience. In many cases valuable tips which are not generally known have been given for the use (*e.g.* in Chapter 3 and 5) or for the preparation (*e.g.* in Capter 6) of oxidizing agents. The fact that someone with different experience (like the reviewer) might in many cases have chosen other examples or have given further tips, is no reflection on the authors' merit.

In addition to one or two easily recognizable printing errors, there are a few factual mistakes. For example, the statement on page 11 that the osmic ester obtained from OsO_4 gives metallic osmium (instead of Os^{IV} or Os^{II}) on reduction is as incorrect as the assertion that it would be reduced by alkaline mannitol solution (in actual fact, a transesterification occurs).

All in all this is a valuable book, particularly for chemists working with synthetic reactions. Its purchase is unhesitatingly recommended. *Rudolf Criegee* [NB 864 IE]

[1] Cf. Angew. Chem. internat. Edit. *4*, 380 (1965); *5*, 620 (1966).
[2] Cf. Angew. Chem. internat. Edit. *7*, 158 (1968).

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Inelastic Interactions of Slow Electrons with Adsorbed Particles

By Dietrich Menzel[*]

When slow electrons impinge on metal surfaces which are covered with an adsorbed layer, desorption of neutral particles as well as of positive ions, partly accompanied by fragmentation of the adparticles, is observed. The mechanism of these processes is of interest in connection with existing concepts of the surface bond. The effect can also be used as a probe for the investigation of complex adsorption layers.

Transfer of much smaller energies to the adsorbate can lead to vibrational excitation. This process may find application in the vibrational spectroscopic study of adsorbates.

If the energy transferred in the inelastic collision is high enough to ionize low-lying levels of the surface atoms, radiationless re-ordering of the electron configuration (Auger-effect) can occur subsequently. The secondary electrons of characteristic energy emitted in these processes can be used for qualitative analysis of the surface.

1. Introduction

When slow electrons (electrons with kinetic energies up to about a thousand electron volts) interact with matter, two basic kinds of interaction can be distinguished, which are normally designated as *elastic* and *inelastic*. We refer to *elastic* interactions when the collision leads to essentially zero energy transfer and the electrons are only deflected in the field of the atoms. As electrons possess wave properties, a phase relationship exists between incident and scattered beams, and interference may occur between the scattered electrons. When the scattering centers are arranged periodically, for instance in a defined crystal face, periodic extinction and re-inforcement of the scattered intensity are observed.

The method which uses this effect of electron diffraction for the investigation of crystal surfaces, is known under the acronym LEED (Low Energy Electron Diffraction) and has found wide application in recent years[1]. The small penetration depth of slow electrons in solids and the fact that their wavelengths are in the Ångstrom range, *i.e.* in the order of lattice parameters, are especially favorable for this use.

Such processes are relatively rare, however: above 50 eV, typically only a few percent of the impinging electrons are scattered elastically. The majority of the electrons interact *inelastically* and transfer part of their kinetic energy to the collision partner. In the case of isolated molecules this leads to rotational, vibrational[2], and electronic excitation or ionization[3]. The latter two processes are often followed by dissociation. These excitations and their coupling are investigated by "electron impact spectroscopy"[4]. The ionization processes are of importance for mass spectroscopy. When electrons collide with surfaces, all these processes can still occur. In addition others caused by interactions of the incident electrons with the electrons of the solid are possible: excitation of plasmons[5] and emission of secondary electrons[6]. These processes which are essentially caused by the

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[1] *J. J. Lander*: Recent Progress in Solid State Chemistry. Pergamon Press, N.Y. 1965, Vol. 2, p. 26; *G. A. Somorjai*, Ann. Rev. physic. Chem. *19*, 251 (1968); *E. Bauer*, Techniques of Metals Research, Interscience N.Y. 1969, Vol. II, 2, p. 559.

[2] *A. V. Phelps*, Rev. mod. Physics *40*, 399 (1968).

[3] *H. S. W. Massey*, Handbuch der Physik, Springer, Berlin 1956, 2nd ed., Vol. 36/II, p. 307; *L. J. Kieffer* and *G. H. Dunn*, Rev. mod. Physics *38*, 1 (1966).

[4] See *e.g. E. N. Lassettre, A. Skerbele, M. A. Dillon*, and *K. J. Ross*, J. chem. Physics *48*, 5066 (1968).

[5] *H. Raether*, Springer Tracts mod. Physics *38*, 84 (1965); Surface Sci. *8*, 233 (1967).

[6] *O. Hachenberg* and *W. Braun*, Advances Electronics Electron Physics *11*, 413 (1959).

properties of the solid will not be treated in the following. We shall confine the discussion to inelastic interactions with surface complexes (adsorbates) consisting of metal surface atoms (adsorbens) and adsorbed particles (adsorpt).

Three processes can be distinguished. The excitation and ionization of adsorbates followed by dissociation of the surface complex, *i.e.* by desorption of neutrals and ions, has been investigated for a number of systems. This "electron impact desorption", which necessitates the transfer of 5 to 25 eV, is interesting in itself and can be used as a probe for the investigation of complex adsorption layers. Recently two other processes have created some interest. In analogy to the electron spectroscopy of free molecules, higher vibrational states can also be excited in surface complexes by transfer of some tenths of an eV. If much more energy is transferred (50 to 1000 eV), low-lying electronic levels can be ionized. A rearrangement of the electron system, coupled with the emission of another electron (Auger effect), can follow. The energy of the emitted electron is characteristic for the atom excited. The latter method particularly is in a state of rapid development and will certainly be used increasingly in the near future.

In all the examples of surface investigations discussed below the exact definition of the experimental conditions is a very important prerequisite. The investigated surface must be cleaned first, then covered with an adsorbed layer in a defined way and kept free of contamination for the duration of the experiment. This is only possible with the use of modern ultrahigh-vacuum techniques [7] which will not be discussed here.

2. Electron Impact Desorption

(Excitation, ionization, desorption, and dissociation of adsorbed particles by slow electrons.)

2.1. Experimental Methods

Plumlee and *Smith* [8] and *Young* [9] were the first to show mass spectrometrically that the collision of slow electrons on metal surfaces can lead to the emission of positive ions from adsorbed layers of residual gases. In a similar way *Moore* [10] investigated adsorbates of CO and O_2 on molybdenum and observed O^+ ions. The formation of positive ions was subsequently used repeatedly for the explanation of anomalies observed in ionization gauges and mass spectrometer ion sources [11]. Using a partial pressure analyzer, *Pétermann* [12] found that electron impact on CO/Ni adsorbates liberates neutral CO molecules.

This work showed that slow electrons can lead to the emission of neutrals as well as ions from adsorbed layers. The later more detailed investigations can be subdivided into two groups according to the experimental method used: either the change caused by electron impact of a parameter coupled to the adsorption is followed, or the desorbed particles are detected directly.

The first group includes the work of *Menzel* and *Gomer* [13] who used the work function Φ of the metal and its change with adsorption, $\Delta\Phi$, measured with the field emission microscope (FEM; [14]) as the particular parameter (concerning the use of the FEM for adsorption measurements see also [15]).

The advantages of this method are:

1. The FEM tip which consists of a hemispherical single crystal (radius of curvature about 1000 Å) has a well characterized surface and can be cleaned and covered in a defined way.

2. A relatively large number of adsorption systems have already been investigated with this instrument [14, 15], making the interpretation easier.

3. The work function change $\Delta\Phi$ caused by an adsorbed layer can be easily measured by recording the current-voltage characteristics of the field emitter: according to *Fowler* and *Nordheim* the following equation describes this characteristic approximately [14, 15]

$$\log (i\,V^{-2}) = A - b\,\Phi^{3/2} V^{-1} \qquad (1)$$

where i and V are emission current and applied voltage, resp., and A and b are constants (b depends on the geometry of the tip only and is not changed by adsorption). A plot of $\log (i\,V^{-2})$ versus V^{-1} yields a straight line with the slope $m = -b\,\Phi^{3/2}$. If the characteristics are recorded before and after covering the surface with an adsorbed layer, the result is

$$\Phi_2 = (m_2/m_1)^{2/3} \cdot \Phi_1. \qquad (2)$$

If Φ_1 (of the clean surface) is known, Φ_2 and $\Delta\Phi = \Phi_2 - \Phi_1$ can thus be found.

4. If the pressure in the system is kept low enough such that re-adsorption is negligible, very small desorption effects can be detected by integrating over a long time.

An example of the FEM tube used for the investigation of the system CO/W is shown in Fig. 1 [13].

In order to enable one to utilize the integrating method of measurement as far as possible, the tube is baked and sealed

[7] *R. W. Roberts* and *T. A. Vanderslice*, Ultrahigh Vacuum and its Applications. Prentice-Hall, Englewood Cliffs 1963.

[8] *R. H. Plumlee* and *L. P. Smith*, J. appl. Physics *21*, 811 (1950).

[9] *J. R. Young*, J. appl. Physics *31*, 921 (1960).

[10] *G. E. Moore*, J. appl. Physics *32*, 1241 (1961).

[11] *P. Marmet* and *J. D. Morrison*, J. chem. Physics *36*, 1238 (1962); *P. A. Redhead*, Vacuum *12*, 267 (1962); *J. L. Robins*, Canad. J. Physics *41*, 1385 (1963); *T. E. Hartmann*, Rev. Sci. nstruments *34*, 1190 (1963).

[12] *L. A. Pétermann*, Nuovo Cimento, Suppl. *1*, 601 (1963).

[13] a) *D. Menzel* and *R. Gomer*, J. chem. Physics *40*, 1164 (1964); b) *41*, 3311 (1964); c) *41*, 3329 (1964).

[14] *R. H. Good* and *E. W. Müller*, Handbuch der Physik, Springer, Berlin 1956, 2nd ed., Vol. 21, p. 176; *R. Gomer*, Field Emission and Field Ionization, Harvard University Press, Cambridge, Mass. 1961.

[15] *W. M. H. Sachtler*, Angew. Chem. *80*, 673 (1968); Angew. Chem. internat. Edit. *7*, 668 (1968).

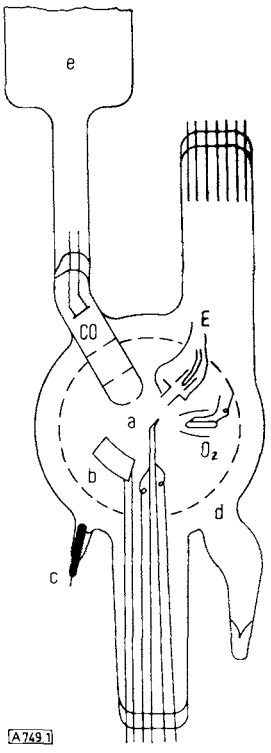


Fig. 1. FEM tube for electron impact desorption experiments (after [13], schematically).

a: Tungsten loop with field emission tip and potential leads; E: electron source; O_2: oxygen source; CO: source of carbon monoxide, with collimator; b: electron collector; c: anode contact; d: fluorescent screen; e: funnel for liquid hydrogen (for precooling of CO).

off from the vacuum line and immersed in liquid hydrogen or helium. Thus a residual pressure of below 10^{-15} torr is reached. The tip is cleaned and characterized by the recording of a F(owler)-N(ordheim) plot and then covered by a molecular beam liberated by heating one of the sources. The oxygen source consists of a heatable supply of CuO, the CO source of a platinum foil, onto which a small amount of CO, which has been introduced into the tube before seal-off, is condensed by cooling it with liquid hydrogen, while the tube is still warm; at the low temperature all molecules stick at the first collision. From a second F—N plot the work function change, $\Delta\Phi$, caused by this layer is measured. With the field emission voltage switched off, the tip is bombarded with electrons for a certain time; the change of the work function caused thereby is determined by recording another F–N characteristic. This procedure can be repeated as often as necessary. Thus the change of the work function as a function of the total number of impinged electrons is obtained. Besides the adsorption system CO/W the systems H_2/W, O_2/W, and Ba/W were investigated with similar tubes (see chapter 2.2.).

In a similar manner *Ermrich*[16] studied the system N_2/W, and *Bennette* and *Swanson*[17] the systems Cs/W and (Cs + O)/W. *Zingerman* and *Ishchuk*[18] used electron impact desorption, followed by the measurement of the change of $\Delta\Phi$ (with the retarding potential method), of oxygen on tungsten to distinguish O atoms above and below the metal surface.

Besides these indirect methods of recording electron impact desorption, the direct detection of the desorbed particles is possible. The above-mentioned work of *Plumlee* and *Smith*, *Young*, *Moore*, and *Pétermann* was of this type. In order to determine the effectiveness of the desorption of ions, *Redhead*[19] investigated the total ion emission (without mass analysis) from O_2 and CO on molybdenum with an apparatus, which allowed the kinetic energy of the desorbing ions to be measured at the same time (Fig. 2).

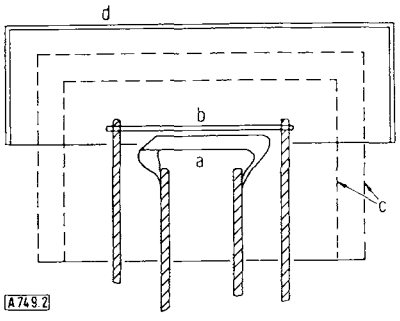


Fig. 2. Apparatus for the measurement of the intensity and the energy distribution of ions desorbed by electron impact (after [19], schematically).

a: anode (Mo); b: filament; c: grids; d: collector.

The anode (see Fig. 2) is a molybdenum ribbon, which is cleaned by flashing in ultrahigh vacuum and then covered with the gas to be investigated. It can be bombarded with electrons emitted from the filament; the potential difference between anode and filament determines their energy. The positive ions emitted from the anode are accelerated by the potentials at the grids and are intercepted by the collector, which is connected to an electrometer. The total ion current leaving the anode is thus measured, and the effectiveness of the ionic desorption is determined directly. If a retarding potential is established at one of the grids, only those ions with sufficient energy to surmount this barrier can reach the collector; thus by varying the retarding potential, the energy distribution of the ions can be recorded. Using a somewhat modified apparatus *Redhead* also investigated the system CO/W[20]. Similar experiments were done by *Yates et al.*[21] using CO, NO, O_2, and N_2 on W.

The mass spectrometric analysis of the electron induced ion emission introduced by *Moore* was extended by *Lichtman et al.*[22], *Degras* and *Lecante*[23], *Coburn*[24], and *Leck et al.*[25], who used the effect as a probe for the investigation of adsorption. The desorption of neutral particles, *e.g.* of CO from Mo, was observed by *Degras* and *Lecante*[23]. *Klopfer*[26] followed the processes caused by electron impact on adsorbed H_2O molecules by mass spectrometric analysis of the gas phase.

[16] *W. Ermrich*, Nuovo Cimento, Suppl. *5*, 582 (1967); Thesis, Technische Hochschule Aachen 1967.

[17] *C. J. Bennette* and *L. W. Swanson*, J. appl. Physics *39*, 2749 (1968).

[18] *Ya. P. Zingerman* and *V. A. Ishchuk*, Fiz. tverdogo Tela *7*, 227 (1965); *9*, 797, 3347 (1967).

[19] *P. A. Redhead*, Canad. J. Physics *42*, 886 (1964); Appl. Physics Letters *4*, 166 (1964).

[20] *P. A. Redhead*, Nuovo Cimento, Suppl. *5*, 586 (1967).

[21] *J. T. Yates jr.*, *T. E. Madey*, and *J. K. Payn*, Nuovo Cimento, Suppl. *5*, 558 (1967); *T. E. Madey* and *J. T. Yates jr.*, Surface Sci. *11*, 327 (1968).

[22] *D. Lichtman*, *R. B. McQuistan*, and *T. R. Kirst*, Surface Sci. *5*, 120 (1966); *D. Lichtman*, *F. N. Simon*, and *T. R. Kirst*, *ibid. 9*, 325 (1968).

[23] *D. A. Degras* and *J. Lecante*, Proc. Seventh int. Conf. Phenomena Ionized Gases, Beograd 1965, p. 124; Nuovo Cimento, Suppl. *5*, 598 (1967).

[24] *J. W. Coburn*, Surface Science *11*, 61 (1968).

[25] *D. R. Sandstrom*, *J. H. Leck*, and *E. E. Donaldson*, J. chem. Physics *48*, 5683 (1968).

[26] *A. Klopfer*, Nuovo Cimento, Suppl. *5*, 606 (1967).

The analysis of the desorbing ions and neutrals in the same system – although with different sensitivity – was possible using a small, sensitive mass spectrometer, which could be baked out to attain ultrahigh vacuum [27] (see Fig. 3).

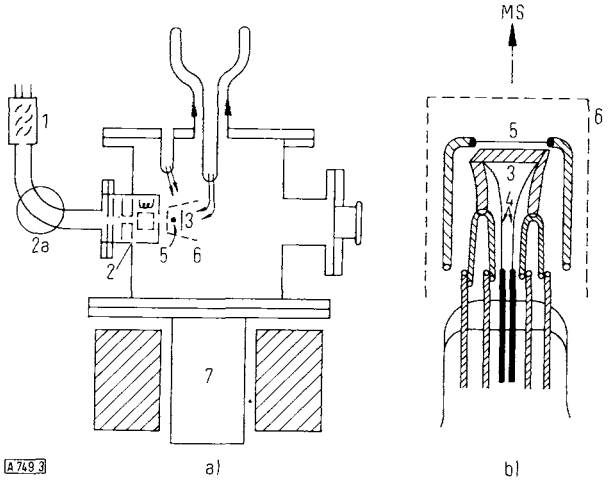


Fig. 3. a) Apparatus for the measurement of desorbed ions and neutrals (after [27], schematically). b) Target structure of a).

MS: mass spectrometer; 1: secondary electron multiplier; 2: ion source, 2a: magnet of MS; 3: target (tungsten ribbon); 4: potential leads; 5: cathode filament; 6: grid; 7: ion pump.

The anode structure corresponds essentially to that of *Redhead*, but is situated in front of the open ion source of the mass spectrometer. The target can be cooled by liquid nitrogen and heated to temperatures between 100 and 3000 K (measurement and regulation by the potential difference between the potential leads). After cleaning it is covered with the adsorbate by introducing the appropriate gas into the system. Electron bombardment of the adsorbate from the filament leads to desorption. If the desorbed *ions* are to be recorded, the ion source of the mass spectrometer is switched off, and the potentials are adjusted such that the ions originating on the surface are drawn into the mass spectrometer and analyzed. The secondary electron multiplier allows the measurement of very small ion currents. For the measurement of desorbed *neutrals*, the potentials are changed such that the surface ions cannot enter the mass spectrometer, and the ion source is switched on. A mass spectrum of the residual gas is then recorded. Desorbed neutrals are found by an increase of certain gas phase peaks upon turning on the electron beam to the surface, and a respective decrease when turning it off again. For the quantitative evaluation of these signals the pumping speed of the system has to be known. This cannot be determined accurately; for many purposes, however, a knowledge of the desorption signals in relative units suffices.

2.2. Results

As mentioned before, the earliest investigations [8 to 10, 12] had already shown that electron impact on adsorbates of electronegative gases such as oxygen, carbon monoxide *etc.* on metals liberates positive ions as well as neutral particles. *Moore* [10] was the first to notice that the number of desorbed particles of any kind (the other conditions remaining equal) is strictly proportional to the number of impinging electrons (see Fig. 4).

[27] a) *D. Menzel*, Z. Naturforsch. *23a*, 330 (1968); b) Ber. Bunsenges. physik. Chem. *72*, 591 (1968).

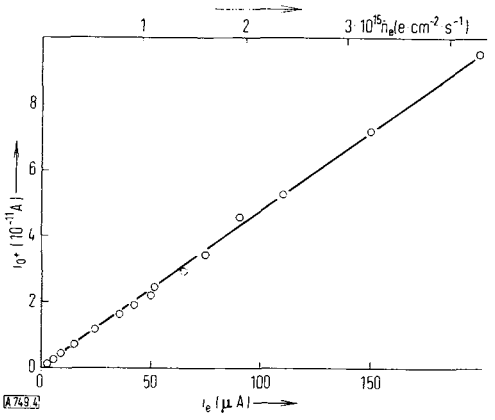


Fig. 4. Dependence of the O^+ desorption signal from CO/W on the electron current density (after [27]).

This linearity is only valid for electron currents which are not so high that the coverage of the surface is noticeably diminished by the bombardment. If the current is higher, the desorption signal decreases with bombardment time (this decrease can be used for the determination of the parameters of the interaction, as will be shown below). From the slope of the measured line the *probability* w of desorption of the particle concerned, *e.g.* the number of particles desorbed per impinging electron, can be derived for the measuring conditions:

$$w_{O^+} = \dot{n}_{O^+}/\dot{n}_e = i_{O^+}/i_e \qquad (3)$$

For electrons of 80 to 100 eV, which result in the maximum w values, numbers of $w_+ = 10^{-4}$ to 10^{-8} (ions) and $w_n \leq 10^{-2}$ (neutrals) were found.

The interaction is thus seen to be of first order in the number of electrons; *i.e.* the collision process between electrons and adsorbate is an isolated event. This suggests that the dependence of the number of desorbing particles on the number of adsorption complexes of a certain kind present on the surface is also linear. In this case the kinetics of electron induced desorption would be given by

$$-\frac{dN}{dt} = q \cdot \dot{n}_e \cdot N \qquad (4)$$

where N is the number of adsorbed particles of a certain kind per unit area, $\dot{n}_e$ is the number of electrons impinging per unit time and area, and q is a constant.

The term adsorbate *of a certain kind* has the following meaning in this context: It is well known from a number of investigations that at least the simple electronegative gases (hydrogen, oxygen, nitrogen, carbon monoxide *etc.*) on surfaces of simple geometry (single crystal faces, FEM tips, tempered ribbons and filaments; *not* powders and porous substances) are adsorbed in a few discrete *adsorption states*. These are characterized by the fact that parameters such as heat of adsorption, desorption rate, contact potential, geometrical structure, infrared spectrum *etc.* are virtually independent of the coverage N within such a state, and change abruptly from one state to the other [28]. The reason for this behavior must be that

[28] See *e.g. R. Gomer*, Discuss. Faraday Soc. *41*, 14 (1966).

the particle concerned can exist on the surface in different *binding states* (different electron configuration; possibly different geometrical orientation to the substrate as well). Applied to the work function change $\Delta\Phi$ used as the relevant parameter in [13], this means that within a certain adsorption state i

$$\Delta\Phi_i \sim N_i \tag{5}$$

i.e. all particles adsorbed in the state i have the same dipole moment (for CO on W this was confirmed experimentally by *Bell* and *Gomer* [29]).

The conjecture formulated in eq. (4) has been proven by *Menzel* and *Gomer* [13] in the following way:

As pointed out above, it was a characteristic of the experiments [13] to use such high electron currents i_e that the coverage N of the surface is decreased markedly by bombardment. By integration of eq. (4) and use of eq. (5) one then obtains for the time dependence of the coverage of an adsorption state i

$$N_i/N_i^0 = \exp(-q \cdot \dot{n}_e \cdot t) = \Delta\Phi_i/\Delta\Phi_i^0 \tag{6}$$

Here $\Delta\Phi_i$ is the change of work function caused by the state i (= difference between the momentary Φ and the Φ after total desorption of state i); N_i^0 and $\Delta\Phi_i^0$ are the values before electron bombardment.

As shown in Figs. 5 and 6, this equation is indeed valid.

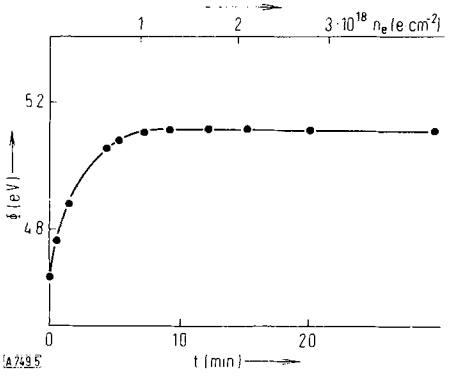


Fig. 5. Change of the work function of a tungsten tip covered with CO, by bombardment with 80 eV electrons (after [13]).

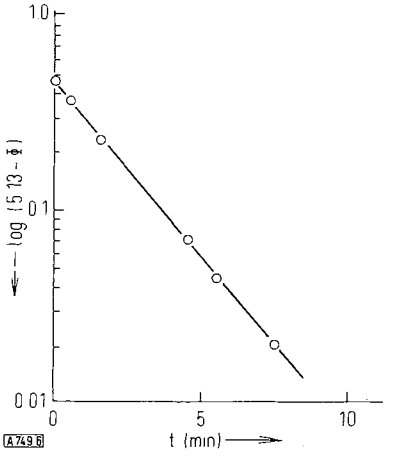


Fig. 6. Semilogarithmic plot of the change of Φ of Fig. 5.

[29] *A. E. Bell* and *R. Gomer*, J. chem. Physics *44*, 1065 (1966).

It was always found that the slopes of plots like that depicted in Fig. 6 were proportional to the electron current; by division through $\dot{n}_e$ a constant value of q was obtained. This result proves equations (5) and (6). The constant q is the interaction cross section used in collision experiments (dimension: area, *e.g.* cm^2), which describes the effectiveness of the interaction. The q value found in this way is obviously connected to the total desorption of state i, irrespective of desorption products, and is therefore called total desorption cross section. It can be found from the change occurring under bombardment of any parameter coupled linearly with the coverage N_i. For instance, it can also be found from the decrease of a desorption signal with bombardment time; according to eq. (4) every desorption signal is proportional to N_i (with the appropriate proportionality factor q_+ or q_n), and for its decrease under bombardment a relation similar to eq. (6) is obtained. In this way *Redhead* [19] used the decay of ion signals for the determination of q values; the same can be done with neutral signals [27]. As can easily be seen, for each desorption signal a relation holds

$$q_+ = w_+/N_i \quad \text{or} \quad q_n = w_n/N_i. \tag{7}$$

The total desorption cross section is of course

$$q = \Sigma q_+ + \Sigma q_n.$$

Using eq. (7) and assuming a plausible value of N, *Redhead* calculated from the directly determined values of w_+ and q that for the systems O_2/Mo and CO/Mo only a few percent of the desorbed particles are ions, and the predominant part consists of neutrals. The same was found for CO/W and H_2/W [27].

A further very important result was found by FEM measurements such as that shown in Fig. 5. *Different adsorption states of the same particle on the same surface have very different desorption cross sections q and can thus be easily distinguished.* The curve of Fig. 5 is so simple only because under the conditions used only one adsorption state of CO on W, the weakly bound "α-state", is desorbed with a measurable rate. The dipole of this state on the surface has its positive end outward, thus decreasing the work function. When it is desorbed Φ increases. The strongly bound "β-state" with a dipole moment in the opposite direction is present on the surface under the same conditions. However, its desorption cross section is smaller by about three orders of magnitude, as was found by measurements with much higher electron current, and therefore the decrease of Φ caused by its desorption is barely noticeable in Fig. 5. The change of Φ under bombardment of a surface which – by suitable pretreatment – contains a third adsorption state besides these two (weakly bound as α-CO, but with negative dipole as β-CO) is shown in Fig. 7.

Obviously the desorption cross section of α-CO is largest, as shown by the initial increase of Φ. After some time a decrease of Φ caused by desorption of the third state competes (the effect of desorption of β-CO

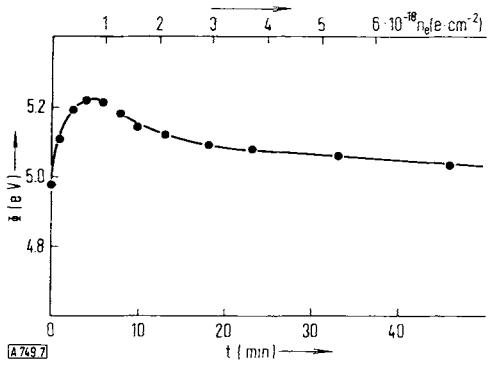


Fig. 7. Change of the work function of a tungsten tip containing three adsorption states of CO, by electron bombardment (after [13]).

is completely masked here). By extrapolation of the curve branches and semilogarithmic plotting, straight lines according to eq. (6) are again obtained (see Fig. 8). From the slopes the q values for the adsorption states can be found.

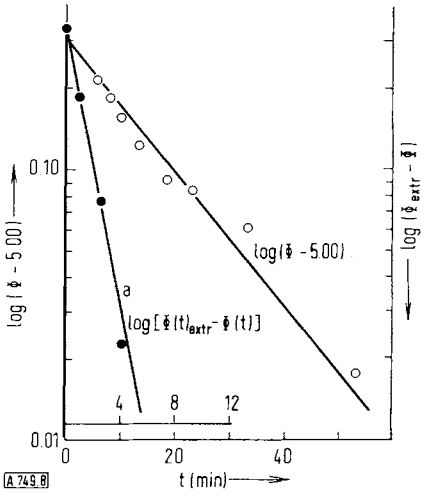


Fig. 8. Semilogarithmic plot of the extrapolated branches of the Φ(t) curve of Fig. 7 (after [13]).

In this way, one finds that $q = 3 \times 10^{-18}$ cm² for α-CO, $5-8 \times 10^{-21}$ cm² for β-CO and about 3×10^{-19} cm² for the third state (for electrons of 80–100 eV). As the total changes of Φ caused by electron desorption are proportional to the amount of the respective state present at the beginning of the experiment, such measurements can be used to study the coverages of the different states under different conditions and their changes and conversions by heating or by electron impact itself. Such measurements were performed extensively on the system CO/W [13c]. We shall come back to the conversion processes below.

It is seen that electron impact desorption is well suited to differentiate between adsorption states. Using the FEM method the above-mentioned three states, which had been characterized before with different methods, were identified. It was also shown that the α-state should be further subdivided [27]. Two states were found in each of the systems H_2/W and O_2/W. From the work of various authors one can make the generalization that for identical particles q is smaller the stronger the surface bond. In addition it was found [27] that different states can be characterized by different desorption products as well as by different q values. When tungsten is covered with CO at 100 K, electron impact causes emission of CO^+ and O^+ ions in a relation of about 10 : 1, in addition to the desorption of neutral CO. (A similar result was found for CO/Mo by *Degras* and *Lecante* [23].) When the target is heated stepwise in ultrahigh vacuum, so that no re-adsorption can occur, the CO^+ signal diminishes above 200 K (see Fig. 9).

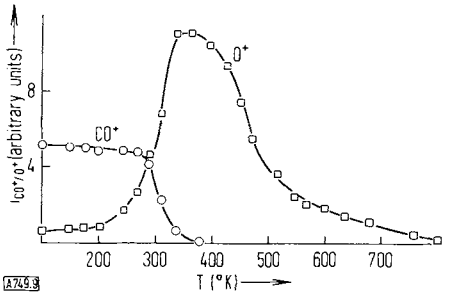


Fig. 9. Change of the CO^+ and O^+ signals from CO/W upon stepwise heating of the target ($\dot{n}_e = 2 \times 10^{13}$ e/cm² · s, 100 eV; after [27]).

This could simply be due to thermal desorption of the relevant state; that this takes place is shown by a transient increase of the CO pressure in the gas phase after each heating step. However, this thermal desorption is not the only cause of the decay of the CO^+ signal: the O^+ signal increases during the same interval and decays only after the CO^+ signal has virtually vanished. In these measurements the electron current density is kept so low that the change of surface coverage caused by electron impact desorption can be neglected; the electron beam is thus seen to serve only as a probe for the investigation of surface coverage and the processes observed are purely thermal. The explanation suggested for the reported observations is therefore as follows. The two ionic signals stem from two different adsorption states. The increase of the O^+ current, which implies an increase in the concentration of the corresponding state, must then be due to a conversion from the first state (characterized by CO^+ emission) caused by the temperature increase, besides desorption. Interestingly both *Redhead* [20] and *Yates et al.* [21] found that these two ionic signals also differ in the kinetic energy of the ions. Different adsorption states of the same particle on the same surface can thus be characterized by different q values, different desorption products and different kinetic energies of the desorbing ions.

The experiments discussed in this section demonstrate two different applications of eq. (4). Firstly, the surface can be bombarded with such high electron current densities that the coverage of adsorbed particles is diminished considerably; from such experiments the total cross section q can be evaluated according to eq. (6). Secondly, such small electron densities can be used that the change of surface coverage by electron impact desorption is negligible; then the desorption signals can be used as a perturbation free probe for coverage. This method was used for instance by

Lichtman et al. [22] to follow the kinetics of adsorption. A combination of both methods is found in the determination of q by *Redhead* [19] which has been mentioned above. A further example also serves to illustrate this application. As already mentioned, electron impact can lead to the conversion of one state into another; the coverage of each state can be followed by its desorption signal. For instance, if one starts with the same initial coverage as in the experiment of Fig. 9, but bombards the surface with a much higher electron density (*e.g.* by a factor 100), the curves of Fig. 10 result for the ionic signals as a function of bombardment time.

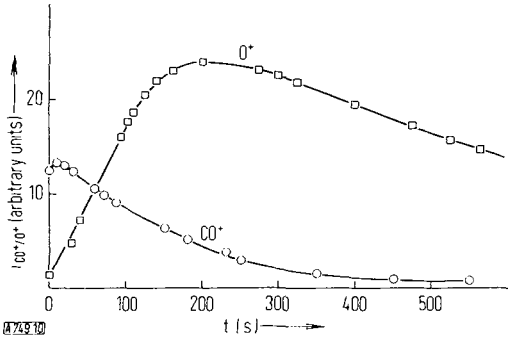


Fig. 10. Change of the CO^+ and O^+ signals from CO/W at 100 K caused by electron bombardment ($\dot{n}_e = 2 \times 10^{15}$ e/cm² · s, 100 eV (after [27]).

Again the CO^+ signal decreases; the O^+ signal at first increases, then goes through a maximum and finally decays also. The conversion of the state characterized by CO^+ emission, which can be induced thermally, is thus seen also to be obtained by electron impact. After removal of the first state by desorption and conversion, the second state is also diminished by further electron impact. Although other explanations of the observations cannot be excluded (see [27b] for further discussion), the ability of the electrons to cause conversions among adsorption states seems to be certain. *Menzel* and *Gomer* [13] observed such processes with the FEM; *Ermrich* and *van Oostrom* [30] found an electron induced state in the system N_2/W, which is not formed normally, *e.g.* thermally, and which possesses interesting characteristics.

All measurements discussed so far were done using electrons of 80 to 100 eV. In this energy range a maximum of the interaction cross sections is usually found for electron impact on free molecules. Usually the cross section decreases slightly towards higher energies and drops sharply towards lower energies. At the threshold energy it reaches the value 0. The value of the threshold energy is an interesting quantity, as it is the minimum energy required for the corresponding process. A similar behavior was usually found for the electron induced desorption processes, *e.g.* by *Moore* for O^+ desorption from CO/Mo [10]. An example of the energy dependence of a desorption signal is shown in Fig. 11.

[30] *W. Ermrich* and *A. van Oostrom*, Solid State Commun. *5*, 471 (1967).

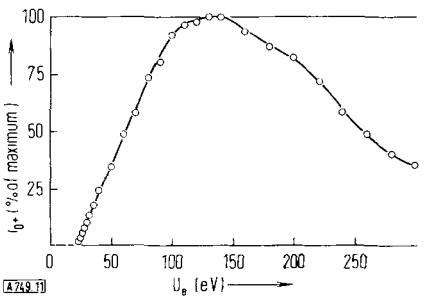


Fig. 11. Energy dependence of the O^+ desorption from CO/W (after [27]).

In some cases a further increase of the cross section was observed above 100 eV [20,27]; most probably this behavior was due to secondary effects. An interesting deviation from the usual energy dependence was reported recently by *Zingerman* and *Ishchuk* [18]. They found that the desorption cross section of oxygen from tungsten single crystal faces shows a periodic variation with energy, which they explain in terms of elastic scattering of the impinging electrons by the periodic surface structure. This effect needs further investigation.

Fig. 12 shows the range above the threshold for the desorption of CO^+ and O^+, and Fig. 13 the same range for the desorption of CO from the same state of CO/W [27]. The difference between the thresholds for CO^+ and O^+ is caused by the energy necessary for the rupture of the C–O bond and by the different

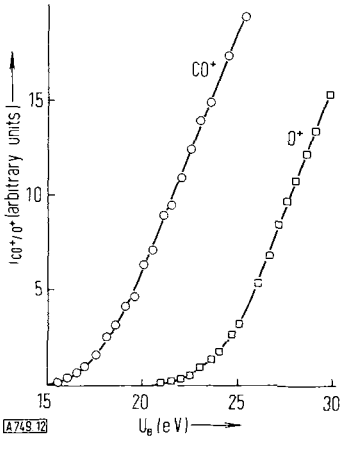


Fig. 12. Energy dependence of the desorption signals of CO^+ and O^+ from CO/W in the threshold region (after [27]).

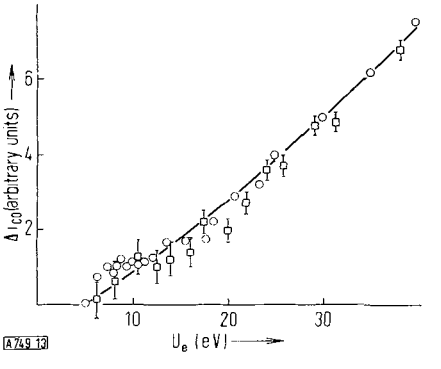


Fig. 13. Energy dependence of the desorption signal of CO from CO/W in the threshold region (after [27]).

heats of adsorption of CO and C. For a quantitative analysis the knowledge of the kinetic energies of the ions is necessary (*e.g.* see [21]). The large difference between the thresholds of CO^+ and CO shows that these two particles are formed in different ways. The q values quoted above (some 10^{-18} to 10^{-21} cm^2 for CO/W; the values for other systems lie in the same range for 100 eV electrons) are thus seen to be the maximum values. For similar electron induced processes in free molecules (excitation, ionization, dissociation), however, much higher maximum q values are found. Even for small molecules they amount to between 10^{-16} and 10^{-15} cm^2 and above. A mechanism which is to explain the experimental results must be able to account for this decreased "reactivity" of adsorbed particles with electrons. Metallic adsorbates are extreme cases in this respect: *Menzel* and *Gomer* [13] and *Bennette* and *Swanson* [17] found immeasurably small desorption cross sections for such layers.

2.3. Mechanism of the Electron Impact Desorption of Particles Adsorbed on Metal Surfaces

Because of the qualitative similarity of the processes it appears reasonable to assume that the interactions of electrons with adsorbed particles are, in principle, analogous to the processes with free particles, and that all special characteristics must be due to the bond with the metal surface. In free particles electron impact causes Franck-Condon transitions into excited or ionized states which can dissociate when the potential curves are suitably situated. As mentioned above, the maximum cross sections measured for such processes are at least in the range of 10^{-16} to 10^{-15} cm^2. Before the mechanism of the interaction with adsorbed particles is discussed, the most important findings will be summarized.

1. The impact of slow electrons on adsorbed layers of electronegative particles on metals causes desorption of neutral and positively charged particles, which can be accompanied by fragmentation. Normally the desorbed neutrals are in the majority and from threshold measurements, they appear to be formed in a different way from ions.

2. The maximum cross sections of these processes, which are found at electron energies of around 100 eV, just as with free particles, are smaller than those of comparable processes in free particles by several powers of ten.

3. Different binding states of the same adsorpt differ – in some cases appreciably – in their desorption cross sections. Sometimes the desorption products and the kinetic energy of desorbed ions are also different for different states.

4. Besides desorption, electron impact can lead to conversion of one binding state into another.

5. In the case of metallic, *i.e.* electropositive adsorpts, no electron impact desorption is found.

To explain these findings a mechanism has been proposed by *Menzel* and *Gomer* [13] which will now be covered briefly. A mechanism which is similar in many respects has been published independently by *Redhead* [19]. The starting point is the assumption that the binding of electronegative particles at a metal surface is caused by localized bonds which qualitatively are similar to the bonds in normal molecules. Electron impact should then lead to Franck-Condon transitions to excited or ionized surface complexes. In a one-electron approximation this means that an electron is lifted into a higher level within the surface complex or is taken into the metal or to infinity. In any case an electron vacancy is created in the adsorbate. If this view is correct and the respective levels are situated as shown in Fig. 14, the surface complex can dissociate subsequently, and a neutral or ionic particle can leave the surface.

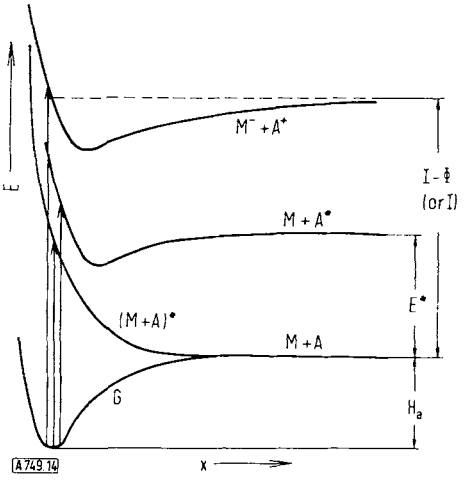


Fig. 14. Potential curves for the system metal–adsorbed particle, and possible transitions caused by electron impact.

M: metal; A: adsorbed particle; G: ground state of the adsorbate; $M^- + A^+$: ionic state of the adsorbate; $(M + A)^*$: antibonding state of the adsorbate; A^*: electronically excited state of the adsorpt; I: ionization potential of A; Φ: work function of M; H_a: heat of adsorption; E^*: excitation energy of A^*. The arrows indicate possible Franck-Condon transitions caused by electron impact.

As the bonds were assumed to be "normal", the interaction cross sections should be normal as well, *i.e.* in the order of 10^{-16} to 10^{-15} cm^2 at 100 eV. The much lower cross sections found in practice are then attributed to the closeness of the metal to the surface complex; the proximity of this practically infinite electron reservoir can lead to secondary processes. *Gomer* and *Swanson* [31] have shown in a different connection that the potential barrier between metal and adsorbate is easily penetrated by electrons, *i.e.* that the frequency of electrons tunneling through the barrier is high. By such a process the electron vacancy caused in the adsorbate by the excitation can be filled and the system returns to the ground state, desorption having been avoided. If these secondary processes are fast in terms of the lifetime of the excited states on the surface, then only a very small percentage of the initially excited particles are desorbed. The total desorption cross section will then be very small – as is observed. The number of the desorbed particles thus depends on

[31] *R. Gomer* and *L. W. Swanson*, J. chem. Physics *38*, 1613 (1963).

the tunneling rate through the surface barrier, which in turn will depend strongly (approximately exponentially) on the thickness of the barrier. This thickness is given by the binding state: for identical partners the bond length is known to be longer, the weaker the bond. The same should be true for surface bonds. This explains the large difference in the cross sections for different adsorption states: the weaker the bond, the greater the bond length, the smaller the tunneling rate, the smaller the proportion of the initially excited particles which can leave the surface before the bond is re-formed. Thus the weaker the bond, the larger the total desorption cross section – as found experimentally. This contains the assumption that the excited or ionized states for different adsorption states are identical. A quantitative estimate resulted in the correct order of magnitude for the observed effects [13b]. Depending on the position of the binding level of the adsorbate relative to the conduction band of the metal, the tunneling processes referred to above consist of resonance tunneling or two-electron transitions of the Auger type [40]. Even the latter seem to be fast enough to make the postulated mechanism possible.

Finally, the mechanism explains the likelyhood of conversions by electron impact. If several ground states exist, it is possible that the re-formation of the bond does not bring the particle back into the state it had occupied before the excitation, but to another: this is equivalent to a conversion. In reality these processes seem to be somewhat more complicated, however (see [13] and [27]).

The length of the arrows of Fig. 14 is determined by the minimum energy necessary for the transitions, *i.e.* the threshold energies. In the formation of an ion the electron set free in the ionization could enter the metal in a coupled process, so that only $(I - \Phi)$ eV would be necessary for its removal, or it could be lifted to the vacuum level, which would require the full ionization energy I. The experiment decided in favor of the latter possibility [27]. *Redhead* [19] assumed that desorbed neutral particles are formed *via* neutralization of ions by tunneling, while they are leaving the surface; *Menzel* and *Gomer* [13] envisaged the direct excitation of antibonding ((M + A)*) or excited (A*) states leading to neutral desorption. The difference in the threshold of ions and neutrals (see Figs. 12 and 13 above) showed the correctness of the latter assumption [27]. In the case of CO/W the desorption of electronically excited neutrals seems to occur, as suggested by observations of *Redhead* [20], *Baker* and *Pétermann* [32] and *Menzel* [27] (the threshold energy of Fig. 13 for desorption of neutral CO is compatible with this interpretation).

The discussed mechanism also explains why metallic adsorbates are not desorbed by electron impact. In metallic adsorption the bond is mainly formed by delocalized electrons: as the bonding levels of the adsorpt atoms are situated around the Fermi level of the metal substrate, they are broadened and a surface band is formed [31, 33]. It would thus make sense to speak of a surface alloy. The bonding electrons are thus included in the collective behavior of the metal electrons and alternate so fast between the adsorpt atoms and the interior of the metal that any excitation is transported into the bulk metal immediately and the surface remains free of excitation. This is seen to be an extreme case of the tunneling mechanism sketched above. Interestingly *Bennette* and *Swanson* [17] were able to show that cesium on tungsten *is* desorbed by electron impact when oxygen is also adsorbed. The presence of oxygen seems to modify the binding of the Cs atoms sufficiently to invalidate this concept of the electropositive bond.

The proposed mechanism thus appears to be plausible. It is further confirmed by the results of measurements of the temperature dependence of the cross sections [34], which seems to be determined by the vibrational structure of the adsorbate. It should be noted, however, that our treatment can only be a crude approximation. The use of a one-dimensional model (Fig. 14) is far from correct, especially as the two neglected coordinates, those parallel to the surface, are certainly important for defining the uniqueness of the different adsorption states – not to speak of the use of one-electron transitions in the place of many-body interactions. A better approximation will be very difficult, however. The good qualitative agreement with the experimental results shows, nevertheless, that the basic concepts used (excited and ionized adsorbate states and their potential curves, fast tunneling through the surface barrier) are appropriate.

2.4. Electron Impact Desorption as a Method and as a Disturbing Effect

Some examples of the use of electron stimulated desorption for the investigation of adsorbed layers have already been cited. These mainly rely on the difference of desorption cross sections and desorption products. So far only very simple systems have been investigated in such a way, and these turned out to be complicated enough. There is hope that the method can also be used for more complex layers. As the interaction between electron and adsorbate is an isolated process (see chapter 2.3. above), it is improbable that larger particles than those existing in the undisturbed adsorbed layer would be formed by secondary processes. The products of electron desorption should therefore allow conclusions about the composition and possibly the orientation of the adsorbates. An example of such conclusions can be given for CO/W. From the strongly bound states only desorption of O^+ ions, never of C^+ ions, was observed, although the dissociation of the free CO molecule by electron impact results in appreciably more C^+ than O^+. This suggests that the states concerned are bound to the metal *via* the C-end, which

[32] *F. A. Baker* and *L. A. Pétermann*, J. Vacuum Sci. Techn. *3*, 285 (1966).

[33] *R. W. Gurney*, Physic. Rev. *47*, 479 (1935); *T. B. Grimley*, Advances Catalysis and Related Subjects *12*, 1 (1960).

[34] *D. Menzel*, Surface Sci. *14*, 340 (1969).

has been concluded earlier from other investigations. Experiments on the investigation of complex adsorption layers (co-adsorption of several adsorpts, precursors of catalytic reactions) are under way.

It was remarked above that the effect of electron impact desorption can lead to disturbances in some instruments (see section 2.1). Another possibility of disturbance exists in LEED measurements. This method assumes that the surface structures shown by electron diffraction are identical with the structures existing without electron impact; the probe "electron beam" is assumed to create no changes. The electron current densities used in LEED are, however, in the order of magnitude of those used in the experiment of Fig. 10. Consequently the LEED electron beam can in fact change the adsorbed layer, especially if weak adsorption is being investigated. Besides mere diminution of coverage this change can consist of conversion processes and therefore result in qualitative changes in the adsorbate. In these circumstances the structure shown by LEED no longer corresponds to the undisturbed structure. This danger was pointed out by *Menzel*[35] some years ago; other authors actually demonstrated such effects during LEED investigations[36]. While the cross sections may be too small for such effects in cases of strong adsorption, care must be taken in LEED investigations of weak adsorption. In general, severe disturbances should be avoidable by decrease of the beam intensity or possibly by intermittent or pulsed operation; the value of the LEED method is therefore not seriously impaired.

3. Electron Impact Excitation of Vibrations of Adsorbed Particles

As electron impact can lead to vibrational excitation in free molecules, it should be expected that the same possibility exists for adsorbed particles. In principle the detection is possible, as in electron impact spectroscopy[4], by measuring the energy losses of the primary electrons. The experimental difficulties are appreciable here: the energy losses are of the order of 0.1 eV. The primary beam must therefore be very well monochromatized so as not to impair the resolution of the instrument (the electrons formed by thermionic emission from a cathode have a much broader distribution). The monochromator decreases the intensity considerably, and the subsequent energy analysis again selects only a very small part of the secondary electrons. The final intensities are therefore minute. *Probst* and *Piper*[37] succeeded in overcoming these difficulties; they found energy losses of very slow electrons occurring in the impact on adsorbed layers, which can be interpreted as vibrational excitation of the adsorbates. In at least one other laboratory work is in progress on the development of this method[38]. Fig. 15 shows the apparatus used by *Probst* and *Piper*.

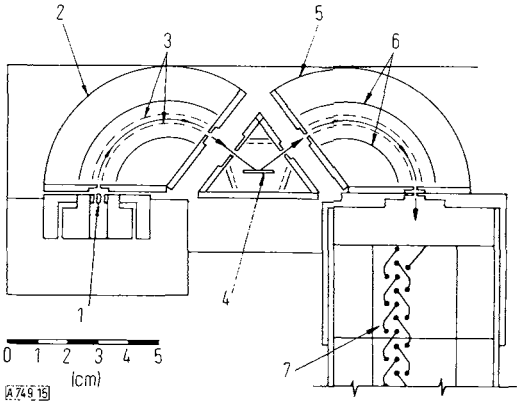


Fig. 15. Electron spectrometer for the measurement of vibrational excitation of adsorbates (after [37], with permission).
1: cathode; 2: monochromator; 3: deflection plates (grids); 4: target; 5: analyzer; 6: collection plates; 7: secondary electron multiplier.

A beam of very slow electrons (< 10 eV) is monochromatized in an electrostatic sector field (resulting half width < 50 meV) and hits the surface to be investigated. A fraction of the secondaries leaving the surface are analyzed in a second sector field according to their energy. The transmitted beam which corresponds to a particular energy loss is amplified by the secondary electron multiplier and recorded. By variation of the transmission condition of the second monochromator (analyzer) the distribution of the relative number of the secondaries as a function of their energy loss is obtained. As an example Fig. 16 shows this distribution for an adsorbed layer of hydrogen on a (100) face of tungsten.

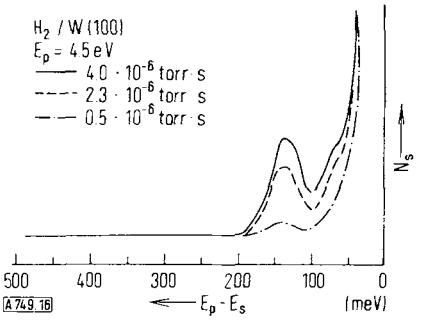


Fig. 16. Energy loss spectrum of very slow electrons from an adsorbed layer of hydrogen on (100) tungsten (from [37], with permission).

The maxima at energy losses of 135 and 69 meV are attributed to the vibrational excitation of atomically adsorbed hydrogen[37]. It can be expected that this new method will become of some importance, particularly as the recording of infrared spectra for adsorbates on well defined surfaces is not possible to date because of intensity limitations[*].

[35] *D. Menzel*, Surface Sci. *3*, 424 (1965).

[36] *C. W. Tucker jr.*, Surface Sci. *2*, 516 (1964); *L. Fiermans* and *J. Vennik*, Physics Letters *25 A*, 687 (1967); *J. Anderson* and *P. J. Estrup*, Surface Sci. *9*, 463 (1968).

[37] *F. M. Probst* and *T. C. Piper*, J. Vacuum Sci. Techn. *4*, 53 (1967).

[38] *D. A. Degras*, personal communication; *I. Ballu*, Rev. Physique appl. *3*, 46 (1968).

[*] Note added in proof: This may no longer be the case, see for example *A. M. Bradshaw*, *J. Pritchard*, and *M. L. Sims*, Chem. Commun. *1968*, 1519; *J. Pritchard* and *M. L. Sims*, Trans. Faraday Soc. *66*, 427 (1970).

4. Auger Electron Emission

(Ionization of "inner" levels of adsorbed particles by electron impact.)

Another new method for the investigation of adsorbed particles by electron impact is the spectroscopy based on the emission of Auger electrons. It was introduced to surface studies by *Lander*[39] in 1953, but has only found broader application in the last four years. This method is particularly well suited for the qualitative analysis of surfaces and adsorbed layers, as it can characterize the kinds of atoms present in the surface. If an "inner" electron (*e.g.* from a K or L shell) of an atom is removed by the action of electrons or energetic photons, then an electronic re-ordering can occur as a secondary process instead of the emission of an x-ray photon (see Fig. 17).

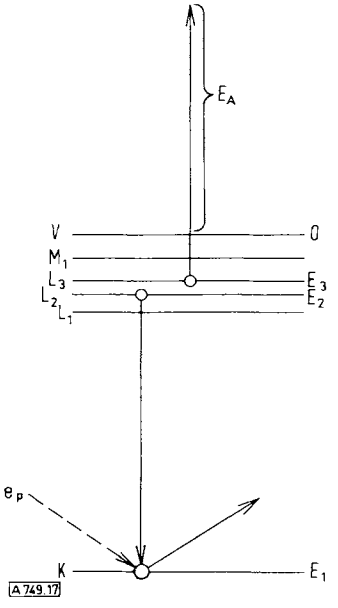


Fig. 17. Energy level diagram of a sulfur atom and schematic representation of the emission of a KL_2L_3 Auger electron.

An electron from a higher level falls into the low-lying vacancy; simultaneously a second electron is expelled from another (or the same) higher shell to balance the energy. The kinetic energy E_A of the emitted secondary (called Auger electron after the discoverer of the process[40]) is given by the energy balance as

$$E_A = E_1 - E_2 - E_3 \qquad (8)$$

where E_1 is the energy (relative to the vacuum level) of the primarily ionized level, E_2 is that of the level from which the electron filling the primary vacancy originates, and E_3 is that of the level from which the Auger electron stems. In the case shown the transition is called a KL_2L_3 Auger transition. As can be seen from eq. (8), E_A is independent of the energy of the incident primary electron (provided this energy is larger than E_1), and is given by the various possibilities of combination of the levels of the atom concerned.

Thus, if the energies of the Auger electrons emitted from a surface are measured, a qualitative analysis of the surface atoms is possible. The sensitivity to surface composition results from the small penetration depth of the slow primary electrons and the even smaller range of the secondaries in the solid. The combination of these two effects results in the majority of the Auger electrons originating from the first two to three atomic layers. As the Auger electrons stem from transitions between inner shells of the atoms, their energies are little influenced by the environment. Calibration spectra for different elements obtained from surfaces of known composition can therefore normally be used under other conditions.

The detection of Auger electrons is achieved by energy analysis of the secondary electrons emitted from the surface under electron bombardment. This can be done using different analyzer systems, *e.g.* with an electrostatic sector field[41] as in Section 3. or with a retarding potential method as in the energy analysis of electron impact desorbed ions (see Fig. 2). In the latter case the retarding field plot has to be differentiated for the energy distribution to be obtained. Particularly useful is the fact that the grid optics of a LEED system can also be employed efficiently as a retarding potential analyzer[42]. As most of the relevant Auger energies lie in the range between 50 and 1000 eV, primary energies of 1000 eV and higher must be used. Because of these high energies and the lack of a dependence of the Auger energies on the primary energies no monochromatization of the primary beam is necessary. The main problem lies in the fact that the number of the normal secondaries (*i.e.* those formed by interaction of the primaries with the collective electrons and the phonons of the solid) is far greater than that of the Auger electrons, which impedes their detection. However, the energy distribution of the normal secondaries is monotonic, so that the additional weak structure superimposed by the Auger electrons can be extracted by electronic means. This is done by modulation of the analyzer potential, which determines the energy loss of the electrons to be measured, with a small a.c. voltage; the a.c. component of the collector current is then detected selectively by a lock-in amplifier. With a suitable circuit the first derivative of the energy distribution of the secondaries (*i.e.* the second derivative of the retarding field plot, when LEED optics are used as analyzer) can be recorded directly. The structure caused by Auger electrons is then shown quite clearly. Fig. 18 shows the circuitry of *Palmberg* and *Rhodin*[43] which utilizes this principle in combination with a conventional display-type LEED optics.

The sensitivity of the analysis of surface atoms which, in the case of cesium on silicon has been reported as being 1/10 of a monolayer[44], can be further increased

[39] *J. J. Lander*, Physic. Rev. *91*, 1382 (1953).

[40] *P. Auger*, J. Physique Radium *6*, 205 (1925).

[41] *L. A. Harris*, J. appl. Physics *39*, 1419, 1428 (1968).

[42] *P. W. Palmberg*, J. appl. Physics *38*, 2137 (1967).

[43] *P. W. Palmberg* and *T. N. Rhodin*, J. appl. Physics *39*, 2425 (1968).

[44] *R. E. Weber* and *W. T. Peria*, J. appl. Physics *38*, 4355 (1967).

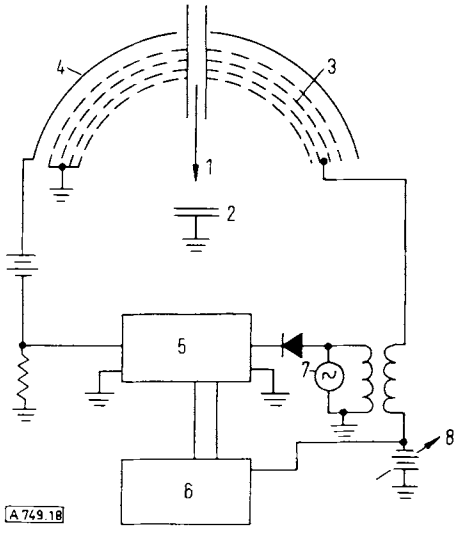


Fig. 18. Auger electron spectrometer based on a display-type LEED system (after [43]).

1: electron beam; 2: sample; 3: grids; 4: collector (LEED fluorescent screen); 5: amplifier; 6: recorder; 7: sine generator; 8: retarding potential.

by near-grazing incidence of the primary beam [45]. Sensitivity and speed of analysis can be further enhanced by the use of another type of analyzer [46].

Because of the ease of combination with a LEED system the method has already been used frequently for the examination of the cleanliness of surfaces for LEED investigations [47]. Fig. 19 shows an example of Auger spectra from a stainless steel surface which had been heated to various temperatures in ultrahigh vacuum for cleaning purposes [47a]. For some peaks the source atoms are given.

Segregation processes [41] on surfaces and grain boundaries and the surface composition of alloys [43] have also been investigated. It seems certain that the method can fruitfully be applied to other surface problems such as the investigation of the composition of metallic fracture planes, of active and poisoned catalysts, or of passive layers, to name only a few. A wider application of the method can therefore be safely predicted. This development will be further promoted by a refinement of the understanding of the underlying processes. In particular the investigation of the relationship between number of atoms present

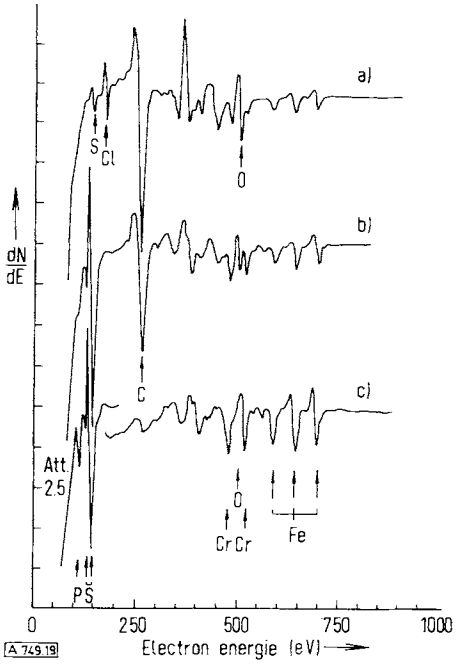


Fig. 19. Auger electron spectra of a stainless steel surface in ultrahigh vacuum (from [47a], with permission).

a: after bake-out; b: after 1 min at 600 °C; c: after 1 min at 820 °C.

and intensity of the peaks would allow an extension to quantitative analysis, and measurements of chemical shifts would give some information on environmental influences.

5. Conclusion

It was the aim of this survey to show that the specific processes brought about by energy transfer from slow electrons to adsorbed particles are well suited for the investigation of adsorbates. The three effects described differ in the amount of energy transferred ($\approx 10^{-1}$ eV for vibrational excitation, $\approx 10^{1}$ eV for electron impact desorption, $\approx 10^{2}$ eV for Auger emission) and in the kind of information obtained by them: spectroscopic data of the surface bond, elucidation of the kind and configuration of adsorbates and their binding states, and finally qualitative analysis of the surface atoms. As in all three cases the characteristics of the interaction depend on the parameters of the adsorbates, it may be expected that a better understanding of these processes will improve our theoretical concepts of the physical entities "surface" and "adsorbate".

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[45] *P. W. Palmberg*, Appl. Phys. Letters *13*, 183 (1968).

[46] *P. W. Palmberg, G. K. Bohn*, and *J. C. Tracy*, Appl. Phys. Letters *15*, 254 (1969).

[47] a) *N. J. Taylor*, J. Vacuum Sci. Techn. *6*, 241 (1969); b) *P. W. Palmberg*, 4th Intern. Material Sympos., Berkeley 1968, Wiley N.Y. 1969, p. 29.

Automatic Analysis of Amino-Acid Sequences in Proteins and Peptides[1]

By M. von Wilm[*]

The development of the widely used automatic method from Edman's manual sequence analysis of proteins and peptides has resulted from modification of the procedure and from the use of a physically novel principle. All reaction, centrifugation, extraction, and drying operations are carried out in a rotating vessel. At a minimal cost in time and material, for example, sixty amino acids have been split off consecutively from a single sample of myoglobin.

1. Introduction

In 1950, the Swedish physician and biochemist *Edman* published his first article on the method of sequence analysis that is nowadays generally known as Edman degradation[2,3]. This involves the elucidation of the primary structure of a protein or peptide by successive controlled chemical degradation of the peptide chain from the amino end, followed by identification of the amino acids split off.

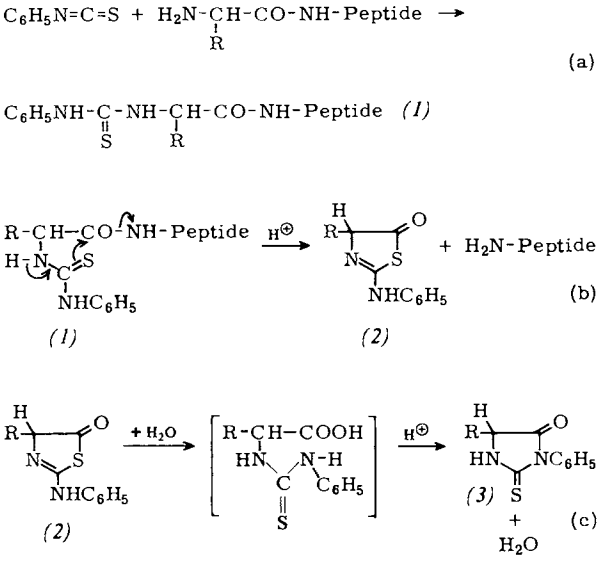
In 1967, *Edman* and *Begg*[4,5] described a protein sequenator, *i.e.* a device that allows the largely automatic analysis of the amino-acid sequences in proteins and peptides. This automatic method was first tested on myoglobin from the humpback whale; this substance, which is the oxygen-transferring protein of skeletal muscle, has a molecular weight of 17200. The sequence of the first sixty N-terminal amino acids of this protein was established in a single operation. Comparison with the known amino-acid sequence of sperm whale myoglobin[6] showed good agreement in all but six positions, in which different amino acids appeared.

Fifteen degradation steps could be carried out automatically with the sequenator in 24 hours. The quantity of substance required was about 5.0 mg; this corresponds to about 0.30 μmole of protein. The maximum number of degradation steps that was possible by the manual method was about 15, and each step took about two days. *Edman* reached the described perfection and automation of the method (1) by the use of a new principle in the reaction of the amino end group of the protein with the degrading reagent, and (2) by optimization of the reaction conditions on the basis of kinetic studies.

Edman recently reported the automatic degradation of a sequence of 22 amino acids of an antibody[7].

2. The Manual Edman Degradation

The reaction underlying the manual degradation involves the coupling of the peptides with phenyl isothiocyanate to give the phenylthiocarbamyl (PTC) derivative *(1)*, cyclizing cleavage to give the 2-anilino-5-thiazolinone derivative *(2)*, and rearrangement of *(2)* to give the 3-phenyl-2-thioxoimidazolidin-4-one (3-phenyl-2-thiohydantoin, PTH) derivative *(3)*.



The reaction of phenyl isothiocyanate with the α-amino end group of the peptide proceeds in accordance with equation (a) in pyridine/water, the pH value being adjusted to 8.5–9.0 with dilute sodium hydroxide solution. Pyridine and excess isothiocyanate are then extracted with benzene. Lyophilization of the aqueous phase containing the phenylthiocarbamyl derivative *(1)* of the peptide is followed by cleavage and rearrangement in a single step. The removal of the residual peptide and the rearrangement of the unstable *(2)* into *(3)* correspond to cyclizing transamidation.

The reactions (b) and (c) are carried out in glacial acetic acid HCl at 40 °C, or preferably in an anhydrous medium such as nitromethane HCl[2,3] to avoid hydrolysis of the peptide chain, at about 25 °C. Anhydrous trifluoroacetic acid has been in use for some time as the cleaving reagent[8,9]. The dissolved PTH-amino acid *(3)* is separated from the precipi-

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[2] *P. Edman*, Acta chem. scand. *4*, 283 (1950).

[3] *P. Edman*, Acta chem. scand. *10*, 761 (1956).

[4] *P. Edman* and *G. Begg*, European J. Biochem. *1*, 80 (1967).

[5] *P. Edman* in *F. Koller*, and *E. Beck*: Fibrinogen and Fibrin Turnover of Clotting Factors. Schattauer-Verlag, Stuttgart 1963.

[6] *A. B. Edmundson*, Nature (London) *205*, 883 (1965).

[7] *P. Edman* and *A. G. Cooper*, FEBS Letters *2*, 33 (1968).

[8] *D. T. Elmore* and *P. A. Toseland*, J. chem. Soc. (London) *1956*, 188.

[9] *P. Edman*, Proc. Roy. Austral. chem. Inst. *1957*, 434.

tated residual peptide by centrifugation, and identified by thin layer chromatography after distillation of the solvent. The peptide, which has been shortened by one amino acid, can now be allowed to react again with phenyl isothiocyanate (see Fig. 1). (For improvements of this method, see [10, 11].)

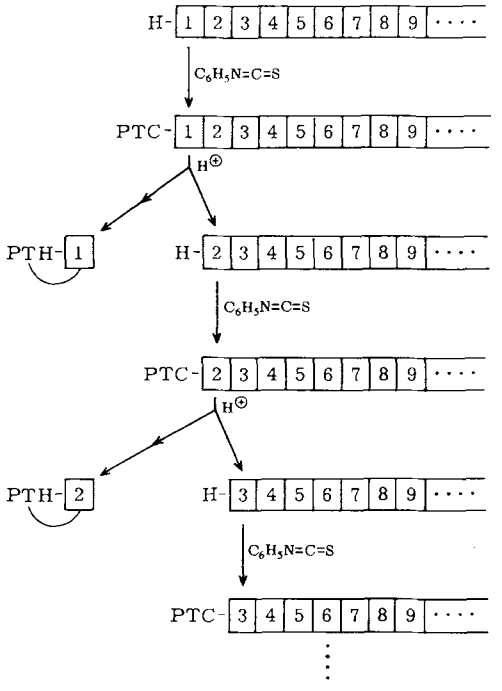


Fig. 1. Scheme of the Edman degradation.

The liquid phase procedure described is suitable only for proteins whose PTC derivatives are soluble in the acidic medium required for the cleavage. This condition is unfortunately not satisfied by most proteins. According to *Fraenkel-Conrat* [12], however, proteins that do not dissolve can be degraded by working on paper strips. Fourteen degradation steps were carried out on 1–2 mg of insulin by this method. The detection sensitivity is about 0.01 μmole per PTH-amino acid.

3. Methods for the Elucidation of the Primary Structure of Proteins and Peptides

3.1. Methods of End-Group Determination

The first efforts to elucidate the structure of peptides were based on the use of a reagent to label the α-amino or the α-carboxyl group of an amino acid situated at the end of a peptide chain, so that it could be qualitatively (and if possible quantitatively) detected after total hydrolysis of the peptide.

This requires reaction of the protein or peptide under the mildest possible conditions, to avoid hydrolysis of the peptide chain, which would lead to the formation of new end groups. Furthermore, the bond between the reagent and the amino end group must be resistant to vigorous hydrolysis.

Numerous reagents have been suggested for this end-group determination, which still plays an important part in the determination of the primary structure, particularly for the determination of the chain length and the number of chains with different sequences. A selection of the principal methods is presented in Table 1.

Table 1. Methods of end-group determination.



(4) *(5)* *(6)*

Reagent, method	Detection	Ref.
N-terminal:		
(4), DNP-method	paper, thin-layer, column chromatography	[13]
(5), Dansyl-method	thin-layer chromatography (fluorescence in UV)	[14]
(6)	thin-layer chromatography	[15]
C-terminal:		
H_2N-NH_2	amino acid analysis	[16]

Dinitrophenylation (DNP method), which was used by *Sanger* [13] with great success in the determination of the structure of insulin, has become very important, and has been perfected by combination with paper chromatography and more recently with thin layer chromatography.

The most recent method is the dansyl method, which was introduced in 1952 by *Weber* [14] and later modified by *Gray* and *Hartley* [17, 18], and which permits the qualitative determination of 0.5 nmole of amino end groups. This method is thus about 100 times as sensitive as the DNP method. It has found steadily growing use since the introduction of special polyamide plates for the fast thin layer chromatography [19] of these compounds.

The *Akabori* method [16], in which only the C-terminal amino acid is not in the form of the hydrazide after hydrazinolysis of all the peptide linkages, has proved suitable for the detection of the C-terminal amino acids. The hydrazides are precipitated as Schiff bases by reaction with benzaldehyde, while the C-terminal amino acid, which remains in solution, is identified chromatographically.

[10] *P. Edman*, Ann. New York Acad. Sci. *88*, 602 (1960).

[11] *B. Blombäck, M. Blombäck, P. Edman*, and *B. Hessel*, Biochim. biophysica Acta *115*, 371 (1966).

[12] *H. Fraenkel-Conrat*, J. Amer. chem. Soc. *76*, 3606 (1954).

[13] *F. Sanger*, Biochem. J. *39*, 507 (1945).

[14] *G. Weber*, Biochem. J. *51*, 155 (1952).

[15] *A. Signor, A. Previero*, and *M. Terbojevich*, Nature (London) *205*, 596 (1965).

[16] *S. Akabori, K. Ohno*, and *K. Narita*, Bull. chem. Soc. Japan *25*, 214 (1952).

[17] *W. R. Gray*, Methods in Enzymol. *11*, 139 (1967).

[18] *W. R. Gray* and *B. S. Hartley*, Biochem. J. *89*, 59 (1963).

[19] *K. R. Woods* and *K. T. Wang*, Biochim. biophysica Acta *133*, 369 (1967).

3.2 Methods of Sequence Analysis

Investigators did not remain satisfied for long with the ability to determine only the N- or C-terminal amino acid. A search was therefore started for reactions by which the degradation process could be repeated many times. To be suitable for this purpose, a reagent must satisfy the following conditions:

1. The coupling reaction must proceed under very mild conditions, since hydrolysis of the peptide chain would also allow non-terminal amino acids to react.

2. The reagent used for substitution of the terminal amino acid must weaken the first peptide linkage in the chain, to enable the remainder of the peptide to be split off under mild conditions.

3. The derivative of the amino acid must allow easy chromatographic identification.

4. The detection sensitivity for this derivative should be as high as possible.

The first compound to be suggested for this purpose [20] was phenyl isocyanate, but this did not satisfy the requirements. The degradation with this reagent, which was considerably improved by *Brockmann* and *Abderhalden* [21] by finding much milder reaction conditions for the cyclizing cleavage, and which was first tested on a tripeptide, may be regarded as a precursor of the Edman reaction. Instead of phenyl isocyanate, *Edman* used phenyl isothiocyanate, which reacts more rapidly. He was able to show that the cyclizing cleavage was then possible under much milder conditions.

The most important of the compounds proposed for sequence analysis are listed in Table 2. Apart from the Edman degradation, however, these methods have not become generally accepted.

Table 2. Methods of sequence analysis.

Reagent	Detection	Ref.
N-terminal:		
$C_6H_5N=C=O$	m.p.	[20, 21]
$C_6H_5N=C=S$	paper, thin-layer, column chromatography	[2,3]
$S=C=S$	paper chromatography	[22]
$N=C=O^{\ominus}$	amino acid analysis after retrodegradation	[23]
leucine-aminopeptidase	amino acid analysis	[24]
C-terminal:		
$N=C=S^{\ominus} + (CH_3CO)_2O$	subtraction method	[25, 26]
carboxypeptidase A and B	amino acid analysis	[27]

The only method suitable for stepwise degradation from the C-terminus was first introduced in 1926 by *Schlack* and *Kumpf* [25] and was recently considerably improved by *Stark* [26].

In many cases, use is made of the possibility of obtaining information about the N- or C-terminal sequences of peptides by the action of peptidases. The enzymes most commonly used in this method are leucine aminopeptidase [24] and carboxypeptidase A and B [27].

4. Degradation of the Tertiary and Secondary Structures of Proteins

4.1. Modification of the Functional Groups and Cleavage into Single Chains

In the elucidation of the primary structure of proteins, the sequence analysis is the final step, which must be preceded not only by the isolation and purification of the protein, but also by many controlled degradation processes, some of which are very complicated and laborious. By systematic degradation of the tertiary and secondary structure, the peptide chains are prepared for the sequence analysis after cleavage into fragments of suitable size. The "chains" referred to here are parts of the molecule that are not bound by hydrogen and/or disulfide bridges. By following the degradation steps shown in Scheme 1, it is necessary above all to answer four questions:

1. How many chains constitute a molecule?

2. What is the molecular weight of each chain?

3. What amino acids do the chains contain and in what quantities?

4. What is the sequence of the amino acids in the individual chains?

The steps that decide the success of the sequence analysis are:

1. the modification of the functional groups in the amino-acid side chains of the protein molecule;

2. the cleavage into single chains by breaking the hydrogen bonds (denaturation) and by opening the disulfide bridges;

3. the subsequent enzymatic or chemical cleavage into peptide subunits.

The non-covalent intermolecular and intramolecular bonds, particularly the hydrogen bonds in the helical regions, are broken by urea or by heat.

Several reactions are used to open intermolecular and intramolecular disulfide bridges in order to break the protein molecule down into single chains:

Reduction of the disulfide bridges with thioglycolate [28] or mercaptoethanol [29] yields thiol groups,

[20] *M. Bergmann, E. Kann,* and *A. Miekeley,* Liebigs Ann. Chem. *458*, 56 (1927).

[21] *E. Abderhalden* and *H. Brockmann,* Biochem. Z. *225*, 386 (1930).

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[23] *G. R. Stark* and *D. G. Smyth,* J. biol. Chemistry *238*, 214 (1963).

[24] *R. E. Canfield,* J. biol. Chemistry *238*, 2699 (1963).

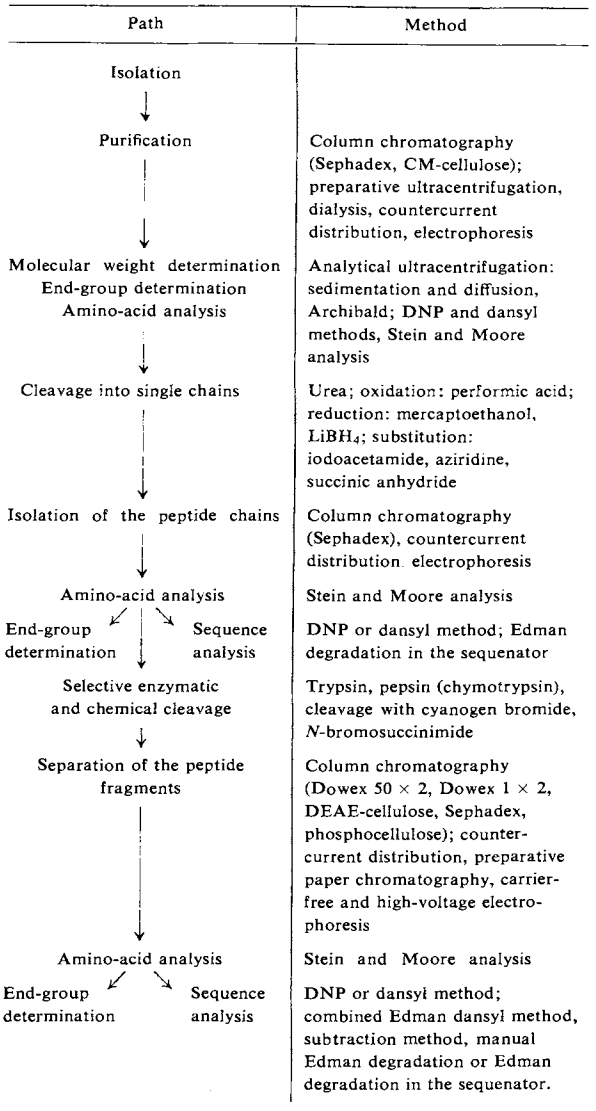
[25] *P. Schlack* and *W. Kumpf,* Hoppe-Seylers Z. physiol. Chem. *154*, 125 (1926).

[26] *G. R. Stark,* Biochemistry *7*, 17969 (1968).

[27] *G. Guidotti, R. J. Hill,* and *W. Konigsberg,* J. biol. Chemistry *237*, 2184 (1962).

[28] *E. Katchalski, G. S. Benjamin,* and *V. Gross,* J. Amer. chem. Soc. *79*, 4069 (1957).

[29] *E. O. P. Thompson* and *I. J. O'Donnell,* Biochim. biophysica Acta *53*, 447 (1961).



Scheme 1. Scheme of the systematic controlled degradation for the determination of the primary structure of proteins.

which can be carboxymethylated with iodoacetamide [30–32]. Simultaneous alkylation of the ε-amino group of lysine can be avoided by suitable choice of the reaction conditions.

A second possibility is the oxidation of the disulfide bridges with performic acid [33], in which cystine is converted into cysteic acid, and methionine into its sulfone. However, any tryptophan present in the chain will be quantitatively decomposed in this case.

The introduction of additional carboxyl groups into hydrophobic regions of the peptide chains, particularly those containing cystine, by carboxymethylation or by succinylation of the ε-amino groups of lysine makes the peptides formed on subsequent enzymatic cleavage more readily soluble in aqueous media.

[30] *H. G. Gundlach, S. Moore*, and *W. H. Stein*, J. biol. Chemistry *234*, 1754a (1959).

[31] *H. G. Gundlach, S. Moore*, and *W. H. Stein*, J. biol. Chemistry *234*, 1754b (1959).

[32] *S. Moore, R. D. Cole, H. G. Gundlach*, and *W. H. Stein*, Protein-Symposium, IV. Int. Congr. Biochem., Vienna 1958.

[33] *G. Toennies* and *R. P. Homiller*, J. Amer. chem. Soc. *64*, 3054 (1942).

The principal enzymes used for enzymatic degradation are trypsin and pepsin, and in some cases also chymotrypsin and papain. The initial cleavage is usually carried out with the very specific trypsin, and then further cleavage with pepsin or other proteases. The end groups are determined in the chromatographically separated and isolated peptides, and it is usually possible to deduce the structure of the peptide from the overlapping sequences obtained in this way.

The enzymatic cleavage is very strongly influenced by modification of the functional groups of the molecule. For example, aminoethylation [34] of the thiol groups formed by reduction of the cross-linking disulfide bridges, which results in the conversion of cysteine into *S*-aminoethylcysteine, allows the cleavage of the peptide chain by trypsin at this point. Otherwise trypsin breaks only peptide linkages of the basic amino acids lysine and arginine, the cleavage occurring on the carboxyl side. Difficulties in structural elucidation due to the presence of trypsin-resistant "core" regions can in some cases be overcome in this way.

The peptide chain an also be selectively broken down by chemical methods. Thus cyanogen bromide [35] breaks the chain after methionine, while *N*-bromosuccinimide [36] breaks it after tryptophan. However, chemical degradation has the important disadvantage that no overlap occurs, with the result that the assignment of the fragments is more difficult.

5. Results of Sequence Analysis

The first great success for sequence analysis was the elucidation of the primary structure of insulin. The sequences of the A and B polypeptide chains of this hypoglycemic pancreatic hormone, which contains a total of 51 amino acids, were determined by *Sanger* [13] between 1945 and 1954 by the DNP method. Neither amino-acid analysis by automatic column chromatography nor a sophisticated method for the Edman degradation was available at that time.

Between 1956 and 1960, the amino-acid sequence of ribonuclease, a chain of 124 amino acids, was published by *Hirs, Stein*, and *Moore* [37] and by *Anfinsen* [38]. Important contributory factors in the success of this work were the automatic amino-acid analysis method published in 1958 [39,40], and the Edman degradation, which had by that time been reported.

[34] *M. A. Raftery* and *R. D. Cole*, Biochem. biophysic. Res. Commun. *10*, 467 (1963).

[35] *E. Gross* and *B. Wikop*, J. biol. Chemistry *237*, 1856 (1962).

[36] *A. Patchornik, W. B. Lawson*, and *B. Witkop*, J. Amer. chem. Soc. *80*, 4748 (1958).

[37] *C. H. W. Hirs, S. Moore*, and *W. H. Stein*, J. biol. Chemistry *235*, 633 (1960).

[38] *R. R. Redfield* and *C. B. Anfinsen*, J. biol. Chemistry *221*, 385 (1956).

[39] *S. Moore, D. H. Spackman*, and *W. H. Stein*, Analytic. Chem. *30*, 1185 (1958).

[40] *S. Moore, D. H. Spackman*, and *W. H. Stein*, Analytic. Chem. *30*, 1190 (1958).

Further important sequence analyses then appeared in quick succession: in 1960/1961, *Tsugita*[41] and *Schramm et al.*[42] reported that elucidation of the protein of tobacco mosaic virus, which contains a total of 158 amino acids; in 1961, *Braunitzer et al.*[43] established the sequence of human hemoglobin A, consisting of two α and two β chains with a total of 574 amino acids.

We now know, in whole or in part, the sequences of lysozyme, chymotrypsinogen, cytochrome c, catalase, myoglobin, and corticotropin, as well as many other peptide hormones and enzymes. Chains of 500 and more amino acid residues can nowadays be sequenced without great difficulty by the Edman method. So far, 12000 primary structures have been published.

6. The Edman-Begg Protein Sequenator

6.1. The Improved Edman Degradation

By spectroscopic investigation of the reaction course in the degradation, *Edman*[3,4] was able to establish optimum conditions for the automatic sequence analysis. He found that the cyclizing cleavage [eq. (b)] and hence the formation of the thiazolinone *(2)*, which is unstable and therefore unsuitable for detection, proceeds very rapidly under mild conditions in the presence of anhydrous acids, while the rearrangement (c) is relatively slow. It therefore seemed reasonable, in a departure from the manual degradation procedure, to separate the two reactions. The revised procedure involved extraction of the thiazolinone *(2)* and conversion into the stable phenylthiohydantoin *(3)* by hand outside the newly developed instrument. By the removal and separate rearrangement of the thiazolinone, the residual protein with one amino acid less is removed from the action of strong acid in aqueous media, and the danger of hydrolysis of the peptide chain is thus avoided.

Finally, *Edman* found that the phenylthiocarbamyl grouping is very readily desulfurized by oxygen. This side reaction, which brings the degradation to a standstill, can be avoided by working under nitrogen.

The question how many successive degradation steps are possible on one peptide or protein depends on the maximum yield obtainable in each. If we assume, like *Edman*, that the overall yield after n degradation cycles has fallen to 30% and that further degradation seems undesirable in view of the increasing complexity of the results, then with an average yield of 97, 98, or 99% per degradation step we find that a total of 40, 60, or 120 degradation cycles are possible. By means of the above improvements in the reaction conditions, and by automation of the process with the sequenator, *Edman* achieved an average yield of 98% per degradation cycle, and hence a total of 60 degradation steps, for myoglobin.

6.2. A Novel Principle for the Reaction of the Protein

The physically novel principle first used by *Edman* for all the reaction, centrifugation, extraction, and drying processes required for a complete degradation cycle consists in the use of a cylindrical glass vessel rotating under an evacuable glass bell (see Fig. 2). The protein is deposited on the inner wall of the vessel as a very thin film on removal of the solvent under vacuum.

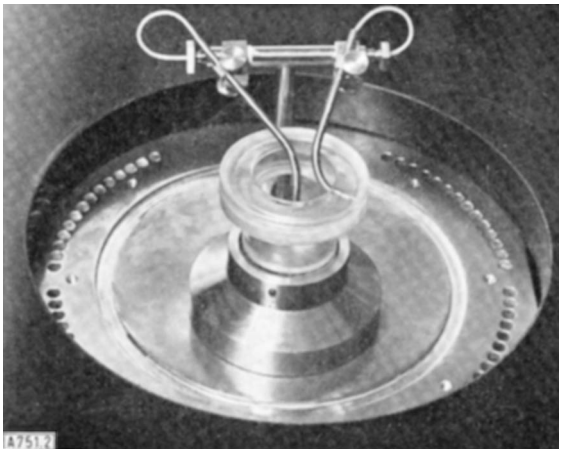


Fig. 2. Rotating reaction vessel of the Edman-Begg protein sequenator with glass bell removed. The figure shows the Teflon tube through which reagents and solvents are added, and the draw-off tube which is arranged tangentially in a groove at the edge of the vessel, and which is connected *via* a three-way valve with the fraction or drainage collector. Inlet and outlet holes for the circulating hot air (50 °C, temperature constant to within ± 0.2 °C) can be seen on the heatable base plate. Diameter of the base plate 18 cm. (Works photograph of Beckman Instruments GmbH, München).

The coupling reaction [eq. (a)] is now carried out on this protein film under nitrogen by dropwise addition of reagent and buffer through a capillary tube. The centrifugal force causes the reagents to rise slowly in a thin layer on the wall of the vessel until the protein is completely covered. After the reaction, the glass bell is evacuated again to remove the solvent and most of the excess reagent from the vessel.

The subsequent extraction of the buffer and of the residual phenyl isothiocyanate is carried out with a thin film of solvent, which runs over the protein layer and is finally sucked off from a groove in the upper third of the reaction vessel by a tangential Teflon tube. The vacuum drying after the extraction is greatly facilitated by the large surface and the stabilizing centrifugal force. Finally, the cleavage [eq. (b)] with anhydrous n-heptafluorobutyric acid is carried out under nitrogen by the same principle. After removal of the acid under vacuum, the thiazolinone *(2)* formed is extracted as described with 1-chlorobutane and collected in a fraction collector.

The purity of the reagents and solvents is extremely important in the automatic Edman method. Thus the smallest traces of aldehydes must be completely removed, since these form Schiff bases with the amino end groups and rapidly reduce the yields.

6.3. Identification of the Degradation Products

The rearrangement of the unstable thiazolinone-amino acids *(2)* collected into the PTH-amino acids

[41] *A. Tsugita, D. T. Gish, J. Young, H. Fraenkel-Vonrat, C. A. Knight,* and *W. M. Stanley,* Proc. nat. Acad. Sci. USA *46*, 1463 (1960).

[42] *F. A. Anderer, H. Uhlig, E. Weber,* and *G. Schramm,* Nature (London) *186*, 922 (1960).

[43] *G. Braunitzer, R. Gehring-Müller, N. Hilschmann, K. Hilse, G. Hobom, V. Rudloff,* and *B. Wittmann-Liebold,* Hoppe-Seylers Z. physiol. Chem. *325*, 283 (1961).

(3) in accordance with eq. (c) is carried out by hand outside the instrument in 1 N HCl at 80 °C within 10 minutes. Numerous methods have been devised for the identification of the PTH-amino acids. The thin layer chromatography method, which was formerly regarded as the best, has now been displaced by the gas-chromatographic determination of free or silylated PTH-amino acids, which has been considerably improved by *Pisano et al.* [43a]. Apart from its speed and its great sensitivity, the principal advantage of gas-chromatography is that it enables the entire degradation process to be followed accurately and quantitatively, a need that very soon appeared in the first investigations using the sequenator.

The following methods may be used for the identification of the PTH-amino acids:

1. Paper chromatography [44–46].
2. Partition column chromatography [47].
3. Thin layer chromatography on silica gel [48,49] and polyamide plates [50].
4. Gas chromatography [51–55]. However, this leads to partial decomposition of the PTH derivatives of Ser, Thr, Asn, and Gln, as well as of the basic amino acids.
5. Improved gas chromatography [43a].
6. Mass spectrometry [56, 57].
7. Cleavage by alkaline or acid hydrolysis [58] followed by identification after *Stein* and *Moore*. In this case, difficulties arise in the detection of Asn and Gln, which undergo the amide cleavage. PTH- Ser and PTH-Thr are also degraded to Gly, and PTH-Arg to Orn. The yields are poor in every case.
8. Thin layer electrophoresis for PTH-Arg and PTH-His [4, 59].

Mention should be made here of two indirect detection methods, which have acquired importance in particular in the determination of the constitution of short-chain peptides.

In the subtraction method [60], the rearrangement and identification of the thiazolinone-amino acids *(2)* removed are omitted. An aliquot is taken instead from the residual peptide after each degradation step, and used after hydrolysis for the column-chromatographic identification of the amino-acid components. The sequence is found from the missing amino acid.

In the combined Edman-dansyl method [61,62], an aliquot of the peptide is used before each degradation step for end-group determination by the dansyl method. After total hydrolysis, the terminal amino acid is identified by thin layer chromatography. The next amino acid, which is now known, is then split off. In this way the Edman degradation can be continuously checked by the end-group determination.

An important disadvantage of both methods is the relatively large quantities of material required.

7. Limitations of the Method

The universal applicability of the automatic Edman degradation in the sequenator is unfortunately subject to certain limitations:

1. Owing to the progressive decrease in the yields as a result of non-specific hydrolysis during the degradation and to the overlap of successive steps when reactions (a) and (b) are incomplete, there is a limit beyond which the results can no longer be interpreted.
2. Very long chains consisting mainly of hydrophobic amino acids present solubility problems, despite the introduction of additional hydrophilic groups.
3. The degradation cannot be continued to the carboxyl end, since the solubility differences between short-chain peptides and the thiazolinone amino acids are so small that the latter compounds can no longer be extracted. For the same reasons, the method cannot yet be applied to short-chain peptides (for preliminary experiments see [54]).
4. PTH-Asn and PTH-Gln suffer partial hydrolysis to PTH-Asp and PTH-Glu. PTH-Ser and PTH-Try are partly decomposed by the anhydrous acid used for the cyclizing cleavage.

8. Conclusions

The method of automatic sequence analysis described above opens up a number of new prospects and possibilities:

1. The systematic degradation of the primary structure by enzymatic and chemical cleavage will become simpler and less time-consuming, and may be com-

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[56] *F. Weygand*, Lecture, The Chemical Society Anniversary Meetings, Exeter, 1967.

[57] *A. Dijkstra, H. A. Billiet, A. H. Van Doninck, H. Van Velthuyzen, L. Maat*, and *H. C. Beyerman*, Recueil Trav. chim. Pays-Bas *86*, 65 (1967).

[58] *B. Africa* and *F. H. Carpenter*, Biochem. biophysic. Res. Commun. *24*, 113 (1966).

[59] *C. G. Honegger*, Helv. chim. Acta *44*, 173 (1961).

[60] *C. H. W. Hirs*, Ann. New York Acad. Sci. *88*, 611 (1960).

[61] *L. B. Smillie* and *B. S. Hartley*, Biochem. J. *101*, 232 (1966).

[62] *W. R. Gray*, Methods in Enzymol. *11*, 469 (1967).

pletely eliminated in some cases, since much longer chains can now be sequenced than formerly.

2. Because of the good yields in the sequenator and the increased detection sensitivity for amino acids, the quantity of material required for sequence analysis will be considerably reduced.

3. The time required for the actual sequence analysis has already been greatly reduced, and 15 degradation steps can now be carried out in 24 hours. (The determination of the sequence of insulin by the DNP method took *Sanger* and three coworkers ten years, while *Braunitzer* and five colleagues, using a greatly improved method, spent six years on the sequencing of hemoglobin. The determination of the sequence of a chain of 150 amino acids by the classical manual Edman method takes two people about two years.)

4. It may be possible to apply the Edman principle of automatic degradation to other macromolecular substances, such as nucleic acids, if repeatable degradation reactions can be developed for these compounds.

5. It is not unlikely that one of the reactions allowing controlled successive degradation from the C-terminus can be improved sufficiently to allow this degradation reaction [26] to be carried out in the sequenator. This would allow the sequence analysis to be carried out from both ends of the chain. The assignment would be greatly facilitated by overlapping in the middle of the chain.

6. It may be possible to overcome the problem presented by the similar solubilities of short-chain peptides and of thiazolinone amino acids by modification of the peptides or by the use of more suitable solvents. The latter alternative has already been followed successfully by *Niall et al.* [54] in studies on pig thyrocalcitonin, a distinctly hydrophobic peptide hormone consisting of 32 amino acids.

7. Thought must also be given to the fixation of the carboxyl end of the peptide to a polymeric support by covalent bonds [57,63,64] that can be broken again under mild conditions. In the automatic Edman method the support is the residual molecule itself, which is extracted toward the end.

8. An interesting new contribution to the strategy of sequence analysis is the simultaneous analysis of peptide mixtures proposed by *Gray* [65]. This method appears to allow the simultaneous automatic analysis of a mixture of ten or more peptides with different sequences, with the result that the time required for the elucidation of primary structures is again drastically reduced.

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Translated by Express Translation Service, London

[63] *R. A. Laursen*, J. Amer. chem. Soc. *88*, 5344 (1966).
[64] *G. R. Stark*, Federat. Proc. *24*, 225 (1965).
[65] *W. R. Gray*, Nature (London) *220*, 1300 (1968).

Problems and Possibilities of the Free-Radical Addition of Thiols to Unsaturated Compounds [**]

By Karl Griesbaum [*]

In view of the growing importance of photochemically initiated reactions in industry, the use of free-radical additions of thiols to unsaturated compounds also seems promising. The present article is intended to demonstrate the possibilities and limitations of reactions of this type in organic synthesis.

1. Introduction

Since its discovery [1] and its much later formulation as a free-radical chain reaction [2], the anti-Markownikoff addition of thiols to unsaturated compounds has been the subject of many reviews [3].

The present article was stimulated mainly by recent developments as a result of which the economical industrial use of such reactions has for the first time become a possibility. Free-radical additions originally

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[**] Based on a lecture at Wayne State University, Detroit (USA) on May 16, 1967.

[1] *T. Posner*, Ber. dtsch. chem. Ges. *38*, 646 (1905).

[2] *M. S. Kharasch, A. T. Read*, and *F. R. Mayo*, Chem. and Ind. *57*, 752 (1938).

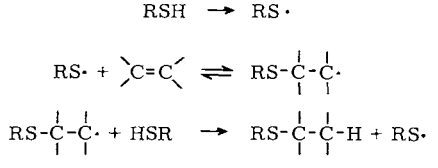
[3] Most pertinent review articles: a) *F. R. Mayo* and *C. Walling*, Chem. Reviews *27*, 351 (1940); b) *I. L. Knunyants* and *A. V. Foken*, Usp. Chim. *19*, 545 (1950); c) *C. Walling*: Free Radicals in Solution. Wiley New York 1957; d) *E. E. Reid*: The Organic Chemistry of Bivalent Sulfur. Chemical Publishing Co., New York 1958, Vol. 1, and 1959, Vol. 2; e) *E. N. Prilezhaeva* and *M. F. Shostakovskii*, Usp. Chim. *32*, 897 (1963); Russ. chem. Reviews (English transl.) *32*, 399 (1963); f) *F. W. Stacey* and *J. F. Harris jr.*, Organic Reactions *13*, 165 (1963); g) *G. Sosnovsky*: Free Radical Reactions in Preparative Organic Chemistry. Mac-Millan, New York 1964; h) *A. A. Oswald* and *K. Griesbaum* in *N. Kharasch*: The Chemistry of Organic Sulfur Compounds. Pergamon Press, New York Vol. 2, Chapt. 9, 1966.

had to be initiated either by exposure to UV radiation or by additon of chemical initiators. In the first case special apparatus was required, in the second case undesirable by-products were formed. This situation has changed with the successful use of radioactive waste products as initiators. With ^{60}Co radiation sources, for instance, free-radical reactions can nowadays be carried out safely and reliably on an industrial scale [4] without serious restrictions as to the material or the design of the reactor. Consequently, even free-radical reactions that require high pressures or extreme purity can now be carried out on an industrial scale.

2. Reaction Course

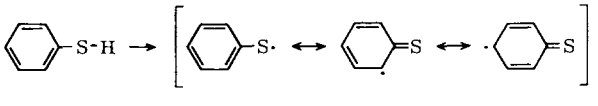
2.1. The Steps of the Reaction

The free-radical addition of thiols is a typical chain reaction, and is accordingly initiated by the addition of peroxides, azo compounds, *etc.* or by exposure to UV or other radiation. The initial products are alkylthiyl or arylthiyl radicals, which subsequently add to the unsaturated substrate to form a C radical, the latter usually being reversible. The C radical then reacts with a thiol molecule to give the final product and a new thiyl radical, thus propagating the radical chain.

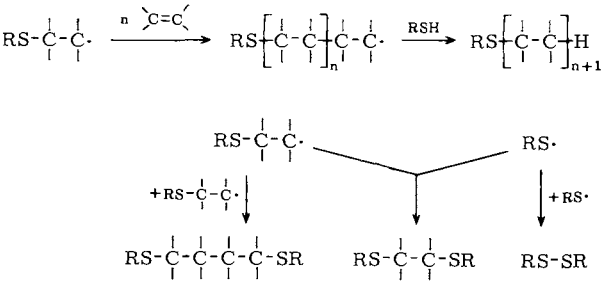


Both the addition of the thiyl radicals (referred to below as the primary reaction) and the chain transfer are normally exothermic, with the result that the overall reaction is fast and has kinetic chain lengths between a few hundred and several thousand cycles [5]. Most of these additions can therefore be treated kinetically as steady state systems.

The chain transfer is generally the rate-determining step. Since this involves the cleavage of a S–H bond, its rate will be strongly influenced by the structure of the thiol to be added. Thus, aromatic thiols are better chain transfer agents than aliphatic thiols, since in the former case the energy required to break the S–H bond is lowered by the resonance stabilization of the thiyl radical formed.

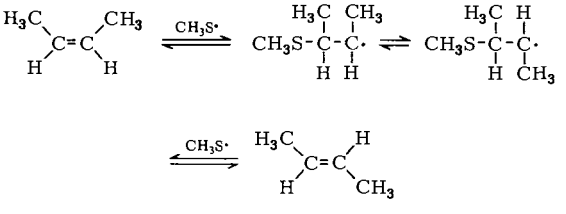


The rate of the chain transfer influences all the variables that depend on the lifetime of the intermediate C radical, such as the degree of reversibility of the primary reaction, the stereochemical course of the overall reaction, possible rearrangements of the intermediate C radical, and the extent of telomerization and chain termination reactions. Telomerization occurs when on an average the intermediate C radical reacts more rapidly with the unsaturated substrate than with the chain-transferring thiol, while chain termination occurs when combinations of free radicals can compete with the chain transfer.



2.2. The Reversibility of the Primary Reaction and Possible Consequences

The first indication for possible reversibility of the addition of thiyl radicals to unsaturated compounds was provided by the overall activation energy, which was found to be negative in several reactions [6]. Chemical evidence is provided by the fast *cis/trans* isomerization of the 2-butenes by small quantities of methanethiol [7] and by the reversibility of the co-addition of thiol and carbon monoxide to ethylene [8].



As can be seen from the isomerization of the butenes, the reversibility can have important practical consequences. For example, attempts to make the addition proceed stereospecifically often fail due to previous isomerization of the substrate.

However, the degree of reversibility of the primary reaction can have a decisive influence not only on the stereochemistry but also on the direction of the reaction. Thus, the reaction of equimolar quantities of ethanethiol and allyl phenyl sulfide *(1)* gave a mixture of adducts that contained only 6% of the expected

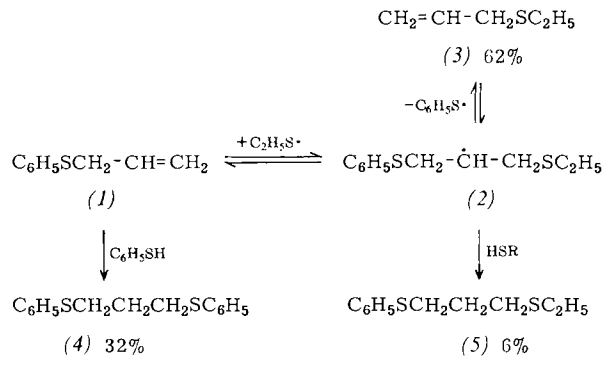
[4] *W. A. Pryor*, Chem. Engng. News *46*, 3, p. 70 (1968).

[5] *R. Back, G. Trick, C. McDonald*, and *C. Sivertz*, Canad. J. Chem. *32*, 1078 (1954).

[6] *C. Sivertz, W. Andrews, W. Elsdon*, and *K. Graham*, J. Polymer Sci. *19*, 587 (1956).

[7] *C. Walling* and *W. Helmreich*, J. Amer. chem. Soc. *81*, 1144 (1959).

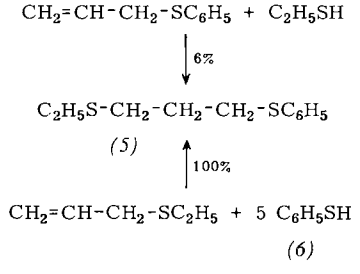
[8] *R. E. Foster, A. W. Larchar, R. D. Lipscomb*, and *B. C. McKusick*, J. Amer. chem. Soc. *78*, 5606 (1956).



mixed bis-sulfide *(5)*, together with 62% and 32%, respectively, of the sulfides *(3)* and *(4)* [9].

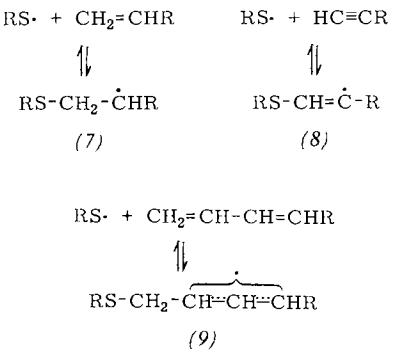
The decisive factor here is the tendency of the intermediate radical *(2)* to decompose into the resonance-stabilized phenylthiyl radical and allyl ethyl sulfide *(3)* prior to the chain transfer (β'-elimination, see Section 4.1.3).

The extent of reversibility of C–S bond formation depends mainly on the structure. The addition of thiyl radicals to terminal olefins, to olefins that lead to resonance stabilized free-radical intermediates and in particular to monosubstituted alkynes [10] is much less reversible than the addition to olefins with non-terminal double bonds. This reversibility can also be suppressed to a greater or lesser degree, *e.g.* by lowering the reaction temperature [*] or by accelerating the hydrogen transfer. Hydrogen transfer can be accelerated by the use of a thiol having a labile S–H bond in high concentration or by the use of a particularly active hydrogen donor (*e.g.* HBr) as a chain transfer agent [12]. The success of such measures is shown by the synthesis of the mixed bis-sulfide *(5)*, the selectivity of which could be increased from its original value of 6% to 100% [9].



2.3. Orientation and Stereochemistry of the Addition

As in other free-radical additions, the anti-Markownikoff orientation in the addition of thiols to unsymmetrically substituted multiple bonds is explained by the preferred formation of the more stable intermediate C radical [**]. Accordingly, the addition of thiyl radicals to simple olefins, alkynes, or conjugated olefins, takes place preferentially at the less substituted end of the unsaturated system to give the more highly substituted and hence more stable alkyl *(7)*, vinyl *(8)*, or allyl radical *(9)*.



Though the preferred direction of attack of the primary addition can be predicted fairly reliably by this principle, the final result of the addition depends on a number of other factors, which are discussed in Section 4.

The stereochemical course of thiol additions is strongly dependent on whether the intermediate radical can retain its stereochemical identity up to the chain transfer. If so, addition occurs preferentially in a *trans* (*anti*) direction, *i.e.* the chain-transferring thiol attacks the C radical on the side opposite to that of the RS group.

Stereoselectivity has been observed in the addition of thiols to some cyclic olefins [15–19] and to alkynes [20, 21]. The stereoselectivity in the former case is probably due to the restriction of free rotation. This explanation has been advanced for the preferred formation of the *cis*-adduct *(11)* from 1-chlorocyclohexene by axial attack of the RS group and rapid saturation of the resulting radical *(10)*. Since the chlorine in *(10)* assumes a quasi-equatorial position and the thiyl substituent an

[9] *D. N. Hall, A. A. Oswald,* and *K. Griesbaum,* J. org. Chemistry *30*, 3829 (1965).

[10] *E. A. Haiba* and *R. M. Dessau,* J. org. Chemistry *32*, 3837 (1967).

[*] Thus in the UV-catalyzed reaction of thioacetic acid with the isomeric 2-butenes, isomerization was observed at room temperature, but not at −78 °C [11].

[11] *N. P. Neureiter* and *F. G. Bordwell,* J. Amer. chem. Soc. *82*, 5354 (1960).

[12] *P. S. Skell* and *R. G. Allen,* J. Amer. chem. Soc. *82*, 1511 (1960).

[**] Two more recent suggestions, according to which the orientation in the addition depends on the selective cleavage of an intermediate bridged radical [13] or on the relative bond strengths of the two possible C–S bonds [14] lead to the same predictions, and will therefore not be dealt with in more detail here.

[13] *P. S. Skell:* Organic Reaction Mechanisms. Special Publication No. 19, The Chemical Society (London) 1965, p. 131.

[14] *J. I. G. Cadogan* and *I. H. Sadler,* J. chem. Soc. (London) *1966*, *B* 1191.

[15] *H. L. Goering, D. I. Relyea,* and *D. W. Larsen,* J. Amer. chem. Soc. *78*, 348 (1956).

[16] *E. S. Huyser* and *J. R. Jeffrey,* Tetrahedron *21*, 3083 (1965).

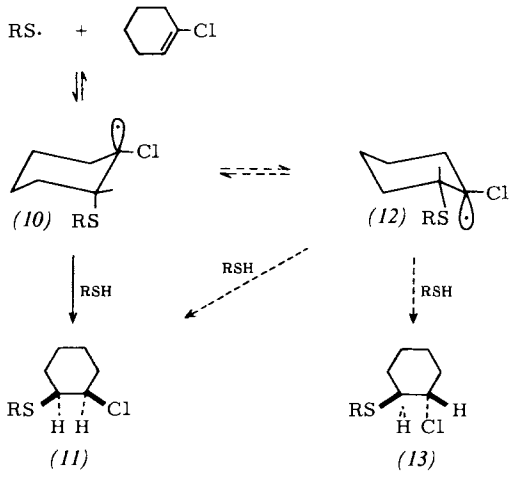
[17] *P. D. Readio* and *P. S. Skell,* J. org. Chemistry *31*, 759 (1966).

[18] *E. S. Huyser, H. Benson,* and *H. J. Sinnige,* J. org. Chemistry *32*, 622 (1967).

[19] *N. A. Le Bel* and *A. De Boer,* J. Amer. chem. Soc. *89*, 2784 (1967).

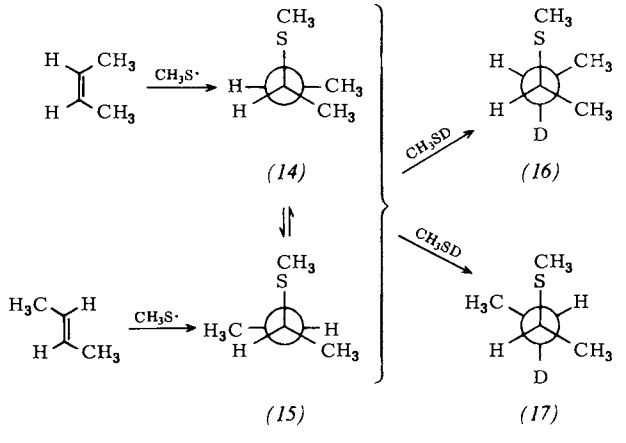
[20] *A. A. Oswald, K. Griesbaum, B. E. Hudson jr.,* and *J. M. Bregman,* J. Amer. chem. Soc. *86*, 2877 (1964).

[21] *J. A. Kampmeier* and *G. Chen,* J. Amer. chem. Soc. *87*, 2608 (1965).



axial position, the chain transfer takes place from the axial direction to give the *cis*-adduct *(11)*, provided that the chain transfer is faster than the conversion of *(10)* into *(12)*. Both the *cis-(11)* and the *trans*-adduct *(13)* could be formed if *(12)* is an intermediate, since in this case both substituents are in the equatorial position and thus attack of the thiol on the free-radical center can take place from either side. In agreement with this explanation, the *cis*-selectivity can be considerably increased by acceleration of the chain transfer [15].

Additions to acyclic olefins, on the other hand, are not stereoselective. In cases where the addition of the thiyl radical is reversible and the substrate isomerizes before the actual addition reaction, the non-stereospecificity is self-explanatory. Even when isomerization of the substrate was suppressed by the use of very low temperatures, however, the addition of CH_3SD to *cis*- and to *trans*-2-butene gave the same mixture of *threo*- *(16)* and *erythro*-3-deuterio-2-methylthiobutane *(17)*. Evidently the incipient free radicals *(14)* and *(15)* are mutually converted by rotation before chain transfer occured [12].



3. Influence of the Structure of the Addend

The reaction course described is valid for the addition of many classes of thiols to unsaturated compounds. Depending on the structure of the addend, however, slight differences may occur, which in some circumstances necessitate changes in the reaction conditions. Two such examples are described below.

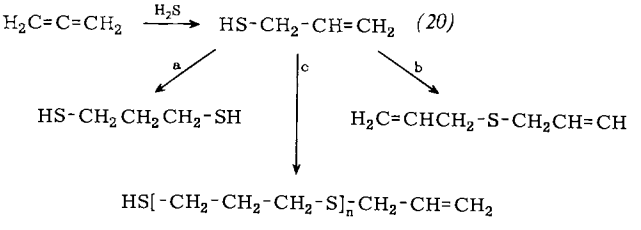
3.1. The Addition of Hydrogen Sulfide

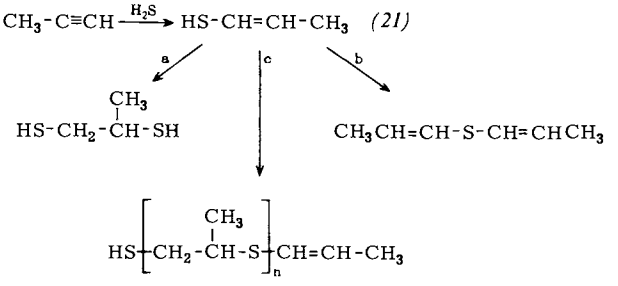
The free-radical addition of hydrogen sulfide to unsaturated compounds yields thiols by the usual reaction scheme *(18)* [3f]. Since thiols are generally more reactive than hydrogen sulfide, some of the thiol formed immediately reacts further to form the symmetrical sulfide *(19)*.

$$CH_2{=}CHR + H_2S \rightarrow HS{-}CH_2{-}CH_2R \qquad (18)$$

$$HS{-}CH_2{-}CH_2R + CH_2{=}CHR \rightarrow RCH_2{-}CH_2{-}S{-}CH_2{-}CH_2R \qquad (19)$$

Hence, if the products required are thiols *(18)*, the reaction must be carried out with a large excess of hydrogen sulfide. However, this procedure is unsuitable when the addition of H_2S is required to yield an unsaturated thiol such as allylthiol *(20)* (obtained from allene [22]) or vinylthiols *(21)* (obtained from alkynes [23]). In this case there are three competing reactions in which the original thiol is consumed. These are (a) the formation of dithiol with excess H_2S, (b) the formation of sulfide with excess substrate, and (c) the self-addition (polymerization) of the monothiol.





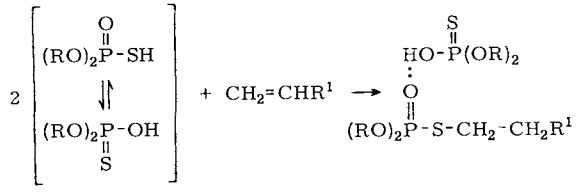
Since hydrogen sulfide is not a particularly good chain transfer agent, telomerization of the substrate also occurs in many cases (see Section 2.1). Some of these secondary reactions oppose one another. The measures for increasing the selectivity are therefore often very limited, and the optimum conditions must be worked out separately for each individual case.

[22] *K. Griesbaum, A. A. Oswald, E. R. Quiram*, and *P. E. Butler*, J. org. Chemistry *30*, 261 (1965).

[23] See *e.g.* a) *F. W. Stacey* and *J. F. Harris jr.*, J. Amer. chem. Soc. *85*, 963 (1963); b) *O. P. Strausz, T. Hikida*, and *H. E. Gunning*, Canad. J. Chem. *43*, 717 (1965).

3.2. Addition of *O,O'*-Dialkylthiophosphoric Acids

Whereas in the addition of H_2S the monoadduct and the substrate enter into secondary reactions, part of the thiol is prematurely consumed in the addition of *O,O'*-dialkylthiophosphoric acids. On the basis of the stoichiometry (two moles of dialkylphosphoric acid are required per mole of unsaturated compound) and the spectroscopic detection of hydrogen bonds of the type $-P{=}O\cdots HO-$, it is assumed that one molecule of dialkylthiophosphoric acid is tied up by one molecule of the adduct [24].



Selective *S*-alkylation was always observed in the free-radical addition of the tautomeric *O,O'*-dialkylthiophosphoric acids [24], whereas, depending on the substrate [25], considerable *O*-alkylation has been observed in cationic additions.

4. Influence of the Structure of the Unsaturated Compounds

The course of the addition depends mainly on the structure and the geometry of the unsaturated compound, which thus ultimately determines the orientation of the primary reaction, the nature of the intermediate free radical, and the result of the chain transfer.

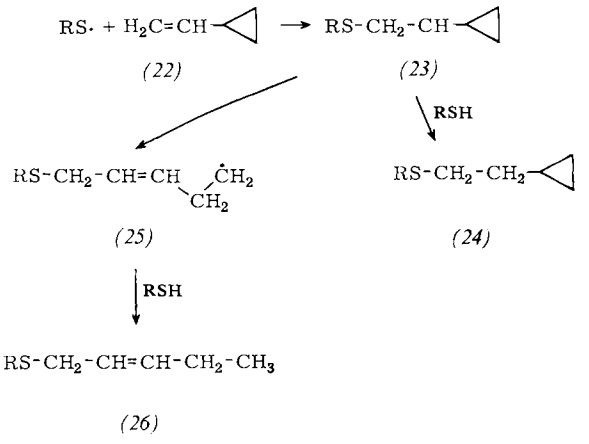
4.1. Compounds with One CC Double Bond

4.1.1. Hydrocarbons

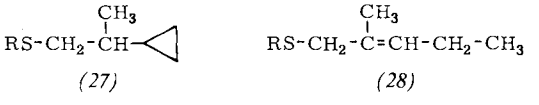
Additions to symmetrical molecules such as ethylene or the 2-butenes are generally slower than additions to olefins having an unsymmetrically substituted, particularly terminal, double bond.

Provided that the intermediate free radical is stable up to the chain transfer, additions to unsymmetrical olefins usually proceed in such a way that the principal product is derived from the more stable free radical intermediate. Thus, the anti-Markownikoff adducts of the terminal olefins styrene, propylene, and isobutylene and the adduct of the unsymmetrically trisubstituted olefin 2-methyl-2-butene have been obtained in very high yields (> 90 %) [3f].

Thiol additions to vinylcyclopropanes *(22)* occasionally follow a more complicated course. The first step leads to a free radical *(23)* which, depending on the rate of the chain transfer [*], either gives the normal adduct *(24)* or *via* the isomeric allylmethyl radical *(25)* gives the open-chain adduct *(26)*.



In agreement with this explanation, the addition of the good chain transfer agent thiophenol to 2-cyclopropylpropene gave only the normal adduct *(27)*, whereas addition of the poorer chain transfer agent methanethiol gave both adducts *(27)* and *(28)*. By varying the methanethiol/olefin ratio in the latter case, the proportion of the ring cleavage product could be varied between 38 % (10.8-fold excess of thiol) and 88 % (5-fold excess of olefin) [27].

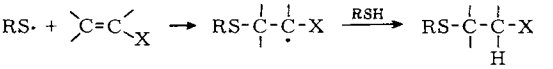


Vinylcyclopropane and ring-substituted vinylcyclopropanes behave similarly [28].

4.1.2. Substrates with Hetero Atoms or Hetero-Atom Groups in a Vinylic Position

Hetero atoms or hetero-atom groups have a strong activating and directing influence. If the double bond is substituted on only one side with such groups, the additions generally proceed very rapidly and very selectively (see Table 1).

If the double bond is substituted on both sides, but with different groups, it is sometimes difficult to pre-



[*] Free-radical cyclopropylmethyl/allylmethyl rearrangements have been repeatedly observed in recent years; they may involve homoallyl radicals as intermediates [26].

[24] *W. H. Mueller* and *A. A. Oswald*, J. org. Chemistry *32*, 1730 (1967).

[25] *W. H. Mueller* and *A. A. Oswald*, J. org. Chemistry *31*, 1894 (1966).

[26] *T. A. Halgren, M. E. H. Howden, M. E. Medof*, and *J. D. Roberts*, J. Amer. chem. Soc. *89*, 3051 (1967); *L. K. Montgomery* and *J. W. Matt, ibid. 89*, 934 (1967), and literature cited therein.

[27] *E. S. Huyser* and *J. D. Taliaferro*, J. org. Chemistry *28*, 3442 (1963).

[28] *I. S. Lishanskii, A. M. Guliev, A. G. Zak, O. S. Fomina*, and *A. S. Khachaturov*, Doklady Akad. Nauk SSSR *170*, 1084 (1966).

Table 1. Free-radical additions of thiols to substrates bearing hetero atoms or hetero-atom groups in the vinyl position [3f].

$RSH + R^1HC{=}CHX \rightarrow RS{-}CHR^1{-}CH_2X$

R	R^1	X	Yield (%)
$HOCH_2CH_2$	H	Cl	100
C_2H_5	H	OC_4H_9	97
CH_3	H	$OCOCH_3$	93
CH_3	H	CHO	86
$HOCH_2CH_2$	H	CN	91
$C_6H_5CH_2$	CH_3	COOH	95

dict the preferred orientation, since the orientation can often be decided by seemingly insignificant structural differences. For example, the orientation in the addition of aliphatic thiols to substituted methyl β-alkylthioacrylates or β-arylthioacrylates *(29)* is strongly dependent on the nature of the alkyl or aryl group R^1 [29].

$$RSH + R^1S{-}CH{=}CH{-}COOCH_3 \rightarrow R^1S{-}CH_2{-}\underset{SR}{CH}{-}COOCH_3$$
(29) *(30)*

+

$$\begin{matrix} RS \\ \diagdown \\ CH{-}CH_2{-}COOCH_3 \\ \diagup \\ R^1S \end{matrix}$$
(31)

R	R^1	*(30)*, Yield (%)
CH_3	C_6H_5	95
C_2H_5	CH_3	75
CH_3	CH_3CO	50

The ability of the double bond to take up thiyl radicals can be appreciably decreased by substitution of both sides with similar hetero atoms or hetero-atom groups.

Thus, diallyl maleate and diallyl fumarate are attacked only on the allyl double bond by methanethiol and trimethylenedithiol [30] whereas in allyl acrylate, the acrylic double bond, which is substituted on only one side, reacts preferentially [31].

4.1.3. Substrates with Hetero Atoms or Hetero-Atom Groups in an Allylic Position

Additions to substrates of the type *(32)* lead in the first step to a β,β′-disubstituted radical *(33)*, which can in principle react further in three ways, *i.e.* by dissociation into the starting components, β′-elimination to form the allyl sulfide *(34)*, or chain transfer to give the adduct *(35)*.

$$RS\cdot + CH_2{=}CH{-}CH_2X$$
(32)

$$\Downarrow\Uparrow$$

$$RS{-}CH_2{-}\dot{C}H{-}CH_2X \xrightarrow{RSH} RS{-}CH_2{-}CH_2{-}CH_2X$$
(33) *(35)*

$$\Downarrow\Uparrow$$

$$RS{-}CH_2{-}CH{=}CH_2 + X\cdot$$
(34)

The relative importance of these competing reactions depends on several factors, such as the relative stability of the radicals RS· and X· and the rate of the transfer step. The results of some thiol additions to allyl sulfides and allyl halides are listed in Table 2.

The first two examples in Table 2 again show the results of the thiol additions to allyl sulfides discussed in Section 2.2. A similar situation is found for allyl halides. Bromides suffer more β′-elimination than chlorides, and the β′-elimination in the case of chlorides can be almost completely suppressed by using the good hydrogen donor thiolacetic acid [32]. Additions to substrates with more than one halogen substituent in the allyl position [33,34] also proceed anomalously, as is shown by the following example:

$$C_6H_5SH + H_2C{=}CH{-}CCl_3 \rightarrow C_6H_5S{-}CH_2{-}CHCl{-}CHCl_2 + C_6H_5S{-}CH_2{-}CH{=}CCl_2$$

Table 2. Reaction products of allyl sulfides and allyl halides with equimolar quantities of thiols.

Thiol	Substrate	Normal addition, adduct *(35)*	Rel. yield (%) [a]	β′-Elimination *(34)* and further products	Rel. yield (%) [a]	Ref.
C_2H_5SH	$CH_2{=}CH{-}CH_2{-}SC_6H_5$	$C_2H_5S{-}(CH_2)_3{-}SC_6H_5$	6	$C_2H_5S{-}CH_2{-}CH{=}CH_2$ + $C_6H_5S{-}(CH_2)_3{-}SC_6H_5$	62 32	[9]
C_6H_5SH	$CH_2{=}CH{-}CH_2{-}SC_2H_5$	$C_2H_5S{-}(CH_2)_3{-}SC_6H_5$	93	–		[9]
CH_3SH	$CH_2{=}C(CH_3){-}CH_2Cl$	$CH_3S{-}CH_2{-}CH(CH_3){-}CH_2Cl$	69	$CH_3S{-}CH_2{-}C(CH_3)_2Cl$	31	[32]
C_2H_5SH	$CH_2{=}C(CH_3){-}CH_2Cl$	$C_2H_5S{-}CH_2{-}CH(CH_3){-}CH_2Cl$	72	$C_2H_5S{-}CH_2{-}C(CH_3)_2Cl$	28	[32]
CH_3COSH	$CH_2{=}C(CH_3){-}CH_2Cl$	$CH_3COS{-}CH_2{-}CH(CH_3){-}CH_2Cl$	100	–		[32]
C_6H_5SH	$CH_2{=}CH{-}CH_2Br$	$C_6H_5S{-}(CH_2)_3{-}Br$	0	$C_6H_5S{-}CH_2{-}CHBr{-}CH_3$	78	[32]

[a] Based on the sum of all the reaction products. The conversions are between 57 and 100%.

The additions to vinyloxiranes *(36)*, which result in ring cleavage, also belong to this group formally. However, since both a C–O and a C–C bond can be broken, depending on the substitution of the oxirane ring, and since vinylcyclopropanes can also undergo this reaction (see Section 4.1.1), the attachment of a hetero

[29] *W. H. Mueller*, J. org. Chemistry *31*, 3075 (1966). The reaction mechanism is further complicated by cleavage of thioacetoxyl (R = acetyl) from the primary radical.

[30] *A. A. Oswald* and *W. Naegele*, Makromolekulare Chem. *97*, 258 (1966).

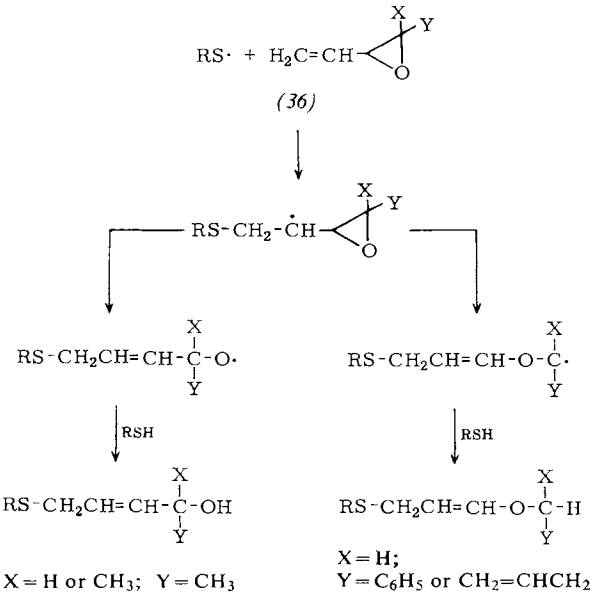
[31] *A. A. Oswald* and *W. Naegele*, Abstracts of Papers, 149. Meeting Amer. chem. Soc., Detroit, Mich. 1965, p. 47 P.

[32] *D. N. Hall*, J. org. Chemistry *32*, 2082 (1967).

[33] *A. N. Nesmeyanov*, *R. Kh. Freidlina*, *R. G. Petrova*, and *A. B. Terent'ev*, Doklady Akad. Nauk SSSR *127*, 575 (1959); *A. N. Nesmeyanov*, *R. Kh. Freidlina*, *A. B. Terent'ev*, and *R. G. Petrova*, *ibid. 138*, 859 (1961).

[34] *R. Kh. Freidlina*, *V. N. Kost*, and *M. Ja. Khorlina*, Russ. chem. Reviews *31*, 1 (1962).

atom to the allyl position cannot be the sole reason for the anomalous course of the addition. There is one difference, however: while only partial ring opening occurs in the addition to vinylcyclopropanes, the heterocycle in vinyloxiranes is completely opened in one direction or the other [35].



4.2. Compounds with Several CC Double Bonds

4.2.1. Isolated Double Bonds

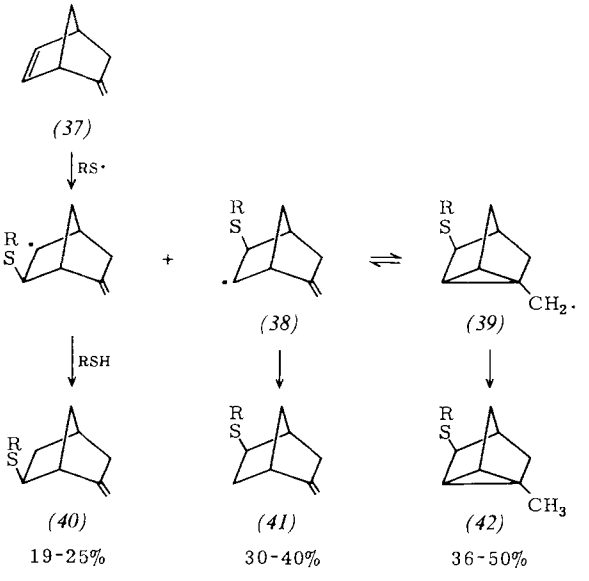
On addition of thiols to compounds with two or more isolated double bonds, the double bonds are attacked independently of one another and in the ratio of their individual reactivities, unless special steric factors are operative. The additions are governed by the same rules as in the case of monoolefins.

If, on the other hand, the double bonds are unequally activated, selective addition is often possible. Examples for this behavior with acyclic substrates are the preferred reactivity of the acrylic double bond in allyl acrylate and -methacrylate [31] and the exclusive addition of thiols to the allyl double bonds in allyl maleate and allyl fumarate [30], as mentioned earlier:

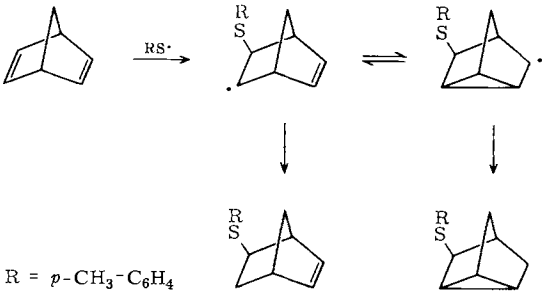
$$2\,RSH + H_2C{=}CH{-}CH_2{-}OCOCH{=}CHCOO{-}CH_2{-}CH{=}CH_2 \rightarrow (RS{-}CH_2{-}CH_2{-}CH_2{-}OCOCH)_2$$

The selective addition is particularly pronounced for many cyclic diolefins. In dicyclopentadiene [36–38] and in 5-methylenenorbornene *(37)* [39], for example, attack takes place preferentially on the strained double bond in the bicyclic system, while the unchlorinated double bond is preferentially attacked in the chlorinated olefins aldrin [37,38], hexachloronorbornadiene *(44)* [40,41], and hexachloromethylenenorbornene *(43)* [42].

The addition to bicyclic systems of this nature is often accompanied by rearrangements. Thus the addition of thiophenol to *(37)* leads not only to the two isomers *(40)* and *(41)* to be expected from an *exo* addition to the more reactive double bond but also to considerable quantities of the tricyclic adduct *(42)* [39]. This latter product is evidently formed by intermediate cyclization of the homoallyl radical *(38)* to give the cyclopropylmethyl radical *(39)*.



The partial formation of tricyclic compounds has also been reported for the addition of *p*-thiocresol to norbornadiene [43].



The strong tendency for cyclopropylmethyl radicals to be formed in these cases is probably due to the special steric conditions in the bicycloheptane system. Addi-

[35] *E. L. Stogryn* and *M. H. Gianni*, Lecture 1. Middle Atlantic Regional Meeting Amer. chem. Soc., February 1966.

[36] *H. A. Bruson* and *T. W. Riemer*, J. Amer. chem. Soc. *68*, 8 (1946).

[37] *A. A. Oswald* and *F. Noel*, J. org. Chemistry *26*, 3948 (1961).

[38] *A. A. Oswald, K. Griesbaum*, and *B. E. Hudson jr.*, J. org. Chemistry *28*, 1262 (1963).

[39] *S. J. Cristol, T. W. Russel*, and *D. I. Davies*, J. org. Chemistry *30*, 207 (1965).

[40] *J. A. Claisse, D. I. Davies*, and *C. K. Alden*, J. chem. Soc. (London) *C 1966*, 1498.

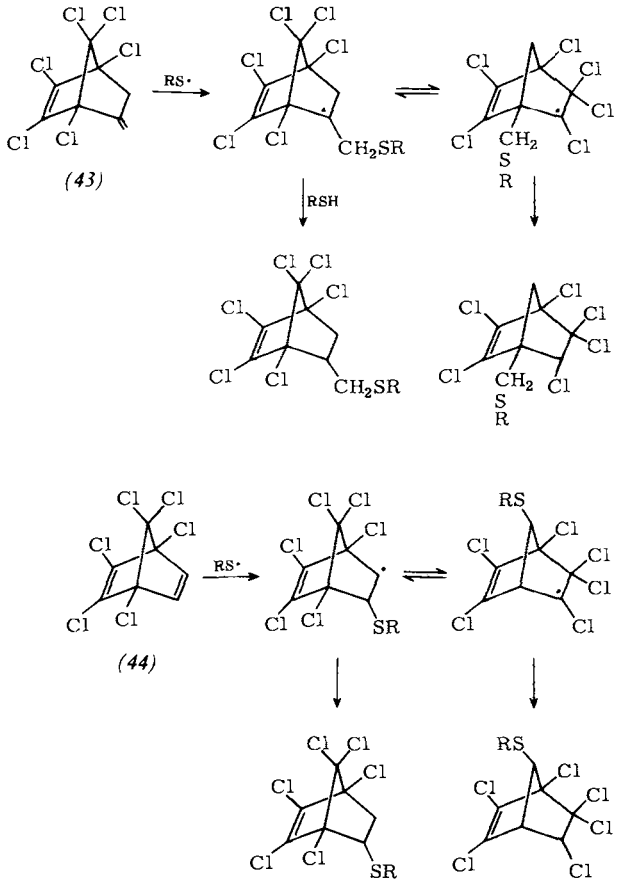
[41] *C. K. Alden, J. A. Claisse*, and *D. I. Davies*, J. chem. Soc. (London) *C 1966*, 1540.

[42] *C. K. Alden* and *D. I. Davies*, J. chem. Soc. (London) *C 1967*, 1018.

[43] *S. J. Cristol, G. D. Brindell*, and *J. A. Reeder*, J. Amer. chem. Soc. *80*, 635 (1958).

tions to vinylcyclopropanes and vinyloxiranes, on the other hand, are accompanied by ring opening, as discussed in Sections 4.1.1. and 4.1.3.

Unlike in the reactions of *(37)* and of norbornadiene, skeletal rearrangements were observed instead of homoallyl rearrangements in the addition of thiols [44] to the partly chlorinated systems *(43)* and *(44)*.

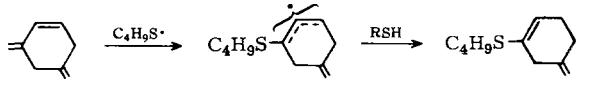


(43)

(44)

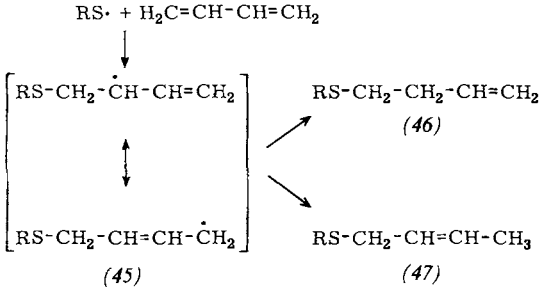
4.2.2. Conjugated Double Bonds

Additions to conjugated systems are generally faster than additions to comparable isolated double bonds, owing to the additional stabilization of the intermediate allyl radicals by resonance. Therefore, selective addition to the conjugated system can often occur in substrates that contain double bonds of both types [45].



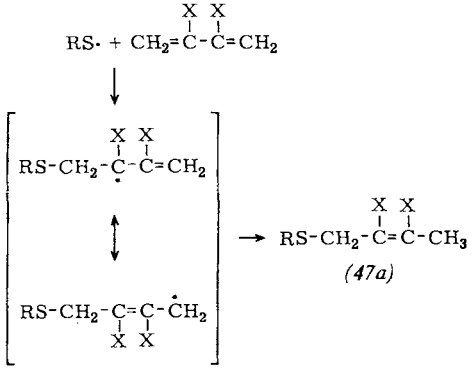
However, this increased reaction rate is possible only if the double bonds are truly conjugated. This is not so *e.g.* in the ground state of *cis*-1,3-cyclooctadiene, since energy factors favor a conformation in which the arrangement of the double bond system is non-planar. In agreement with this, *cis*-1,3-cyclooctadiene reacts only 2.9 times faster than 1-octene with thiophenol, whereas the truly conjugated substrates 1,3-cyclohexadiene and 2,3-dimethylenebicyclo[2.2.1]heptane react 2520 and 3078 times faster, respectively [46].

The orientation is a more complicated problem in the additions of thiols to conjugated systems than in the additions to simple olefins. The primary attack of the thiyl radical is again such as to lead preferentially (but not always exclusively [47]) to the more highly substituted allyl radical. Since such a radical [*e.g. (45)*] has two potential reaction centers, however, the resulting orientation is now additionally dependent on the course of the chain-transfer reaction and can lead both to a 1,2- *(46)* and to a 1,4-adduct *(47)*.



(45) *(46)* *(47)*

It has been shown in a detailed study however that the chain transfer occurs preferentially at the less substituted free-radical center of the intermediate allylic radical, with the preferential formation of adducts of a thermodynamically controlled reaction [48]. In agreement with this, additions to the non-terminally substituted dienes 2,3-dimethylenebicyclo[2.2.1]heptane [46],



(47a)

chloroprene, isoprene, and 2,3-dimethylbutadiene [48] lead with selectivities of 75–99 % to the 1,4-adducts *(47a)*, whereas the addition to the terminally substi-

[44] In the addition to *(43)*, only aliphatic thiols reacted at appreciable rates, whereas *(44)* also reacted rapidly with aromatic thiols.

[45] *R. E. Benson* and *R. V. Lindsey jr.*, J. Amer. chem. Soc. *81*, 4253 (1959).

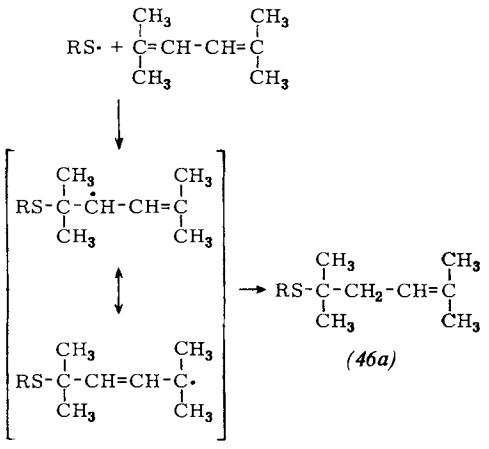
[46] *J. A. Claisse* and *D. I. Davies*, J. chem. Soc. (London) *1965*, 4894.

[47] Thus, in the addition to isoprene and piperylene, up to 25% and up to 20%, respectively, of the 4,1-adducts were found; these were presumably formed *via* the less stable radicals

$RS-CH_2-\dot{C}H-CH=CH_2$ and

$RS-CH(CH_3)-\dot{C}H-CH=CH_2$.

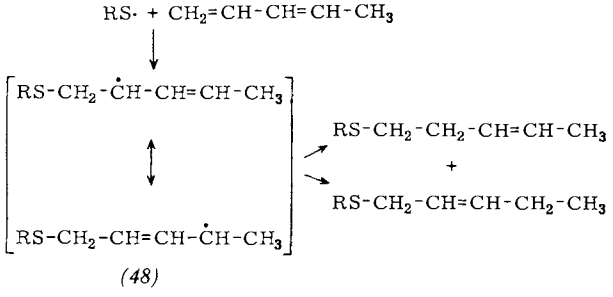
[48] *A. A. Oswald, K. Griesbaum, W. A. Thaler*, and *B. E. Hudson jr.*, J. Amer. chem. Soc. *84*, 3897 (1962).



(46a)

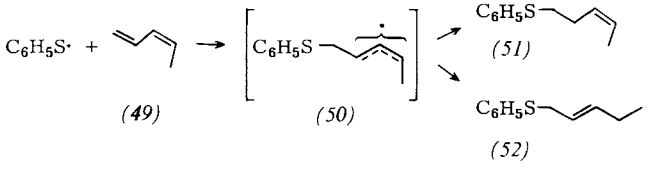
tuted system of 2,5-dimethyl-2,4-hexadiene leads mainly to 1,2-adducts *(46a)* [49,50].

If the two free-radical centers of the intermediate allylic radical are comparably substituted, neither of the two orientations is appreciably favored. Examples of such cases are cyclopentadiene [46], cyclohexadiene [46], and piperylene [48], which give secondary allyl radicals such as *(48)*, and thus yield 1,2- and 1,4-adducts in roughly equal proportions [47].



(48)

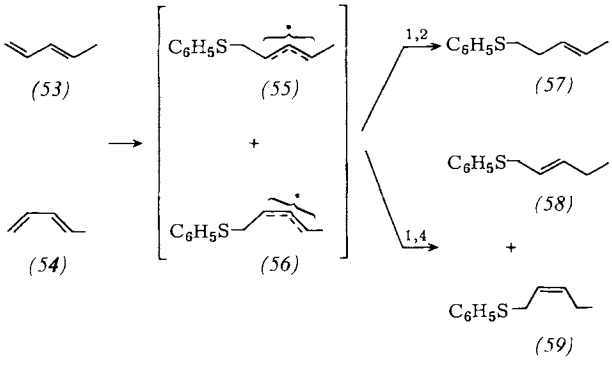
The stereochemistry of these additions has been examined in detail for the additions to piperylene [51]. With fast chain transfer [addition of thiophenol or co-oxidations (see Section 5.2)], the additions proceed stereoselectively with substantial retention of the geometry of the initially formed allyl radical. Thus the 1,2-adduct of thiophenol and *cis*-piperylene *(49)* contained 92 % of the *cis* isomer *(51)*, and the 1,4-adduct which was also obtained, contained 99.9 % of the *trans* isomer *(52)*. The following explanation was advanced for



(49) *(50)* *(51)* *(52)*

this result: *cis*-piperylene exists only in the transoid form *(49)*; thus, if the intermediate free radical *(50)* can retain its conformation until chain transfer occurs, it must give the adducts *(51)* and *(52)* obtained.

The 1,2-adduct obtained from *trans*-piperylene and thiophenol contained 96 % of the *trans* isomer *(57)*, while the 1,4-adduct contained the *cis* *(59)* and the *trans* isomer *(58)* in a ratio of 9:91, respectively. This is explained by assuming that *trans*-piperylene exists in a transoid form *(53)* and in a cisoid form *(54)*. If the geometry is retained in the allyl radical [*(55)* and *56)*], this must lead to two 1,4-adducts [*(58)* and *(59)*].

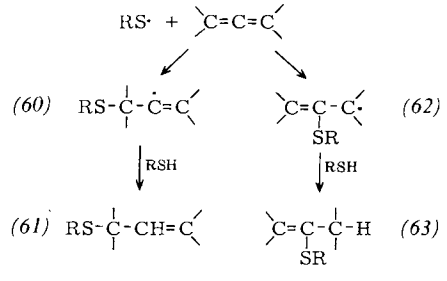


(53) *(54)* *(55)* *(56)* *(57)* *(58)* *(59)*

For the stereoselectivity observed with piperylene, it is an essential prerequisite that the olefin does not isomerize during the reaction, and that the chain transfer takes place before any possible isomerization of the intermediate allylic radical. The latter condition does not appear to be fulfilled in the addition of aliphatic thiols to piperylene, since these additions are not stereoselective, though piperylene does not isomerize during the addition [51].

4.2.3. Cumulated Double Bonds

Additions to allenes can proceed in two directions. Attack on the end of the cumulated system leads to an allyl sulfide *(61)*, while attack at the center yields a vinyl sulfide *(63)*.



(60) *(61)* *(62)* *(63)*

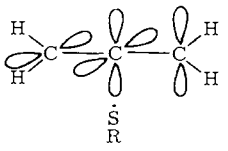
It may appear at first sight that the second path, *i.e.* attack on the central C atom, should be favored, since it involves a resonance stabilized allylic radical *(62)*, whereas a vinyl radical *(60)* is formed in the alternate case.

Since the double bonds are perpendicular to each other, however, resonance stabilization is impossible in the allene system; the first intermediate *(62)* is accordingly only an *alkyl* radical.

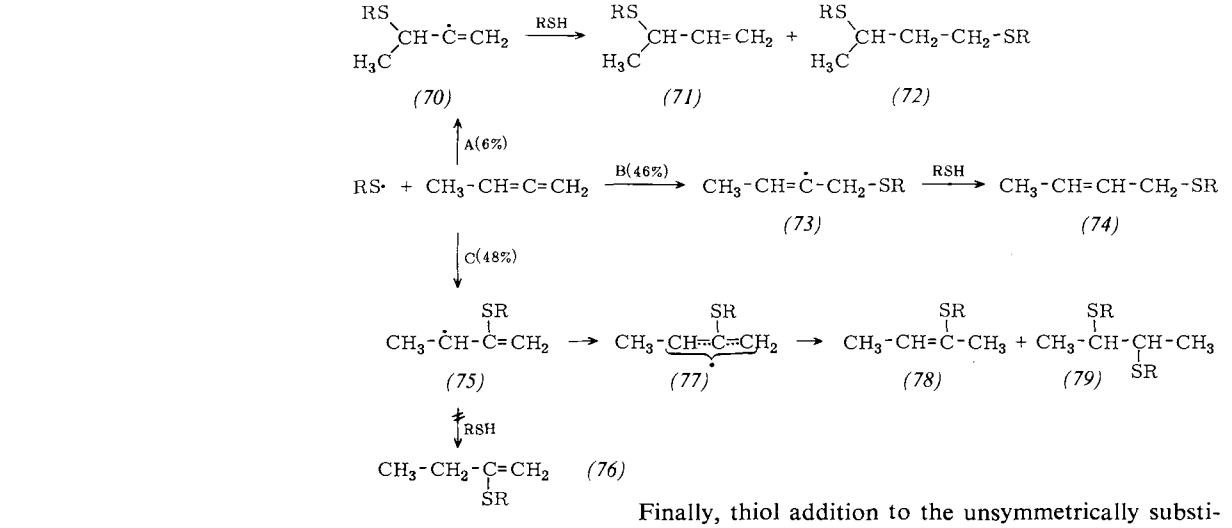
[49] *A. A. Oswald, B. E. Hudson jr., G. Rodgers,* and *F. Noel,* J. org. Chemistry *27*, 2439 (1962).

[50] Since no terminally substituted 1,3-dienes had been studied earlier only 1,4-additions were known for a long time. This occasionally led to the inaccurate conclusion that conjugated dienes undergo only 1,4-additions, irrespective of their structure [3f]. This hypothesis is no longer tenable according to [48, 49].

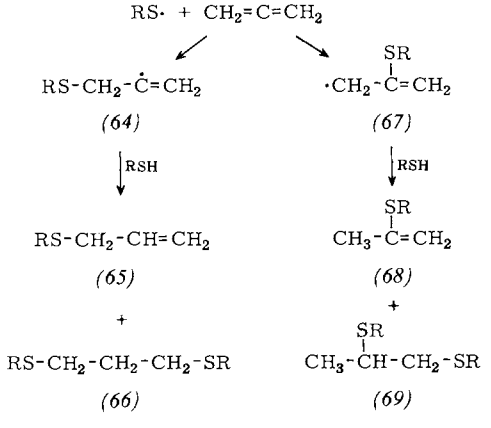
[51] *W. A. Thaler, A. A. Oswald,* and *B. E. Hudson jr.*, J. Amer. chem. Soc. *87*, 311 (1965).



Hence, attack on the central C atom must not be energetically favored necessarily, since the difference in stability between vinyl and alkyl radicals is smaller than that between vinyl and allyl radicals. It has been found that the point of attack of the thiyl radical on the allene system at room temperature depends on the substitution of the allene [52]. Thus allene, in which a vinyl radical *(64)* competes with a primary radical *(67)*



gives only about 10 to 20 % of adducts resulting from attack on the central C atom [*(68)* and *(69)*], but 80 to 90 % of adducts formed by reaction on the terminal C atom [*(65)* and *(66)*] [52, 53].



In the case of methylallene, on the other hand, the first intermediates are vinyl [*(70)* and *(73)*] and secondary alkyl radicals [*(75)*] and the adducts *(78)* and *(79)* resulting from attack on the central C atom (path C) and the adducts *(71)*, *(72)*, and *(74)* resulting from the two possible attacks on the ends of the allene system (paths A and B) are formed in roughly equal quantities [52]. It is interesting to note that path C does not yield the adduct *(76)* to be expected on abstraction of hydrogen from *(75)* but rather the adducts *(78)* and *(79)*.

This can be explained by the conversion of the initial *secondary* radical *(75)* into the *allyl* radical *(77)* prior to chain transfer. The subsequent reaction of *(77)* will then be governed by the same rules as in the reactions of conjugated dienes, *i.e.* the hydrogen is transferred to the least substituted atom of the free-radical system. This leads to the thermodynamically more stable monoadduct *(78)*.

Finally, thiol addition to the unsymmetrically substituted 1,1-dimethylallene, in which vinyl [*(80)* and *(81)*] and tertiary alkyl radicals *(82)* could be formed, leads exclusively to the adduct *(84)* [52], which results from attack on the central C atom. As in the case of methylallene, the hydrogen is transferred to the least substituted atom of the free-radical system of the allylic radical *(83)* that evidently occurs as a secondary intermediate.

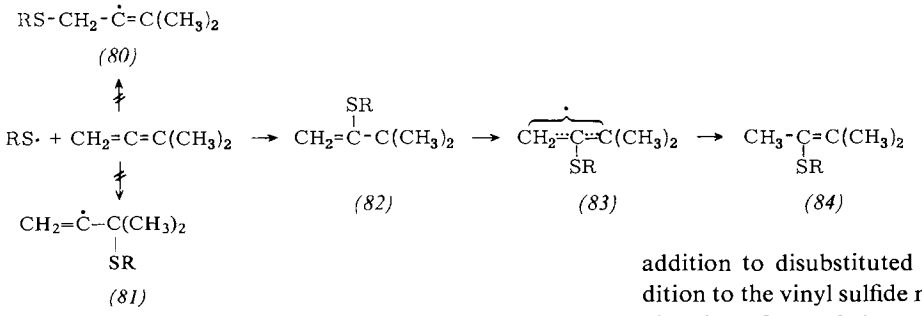
The dependence of the orientation on the reaction conditions has been investigated in some detail for allene. The selectivity for an attack on the end of the allenic system decreases with rising temperature [53, 54]. This phenomenon is particularly pronounced when the reactions are carried out in solvents. Thus, the reaction of a 1 molar solution of thiophenol and allene in benzene yields about 80 % of adducts resulting from a peripheral attack at 20 °C, about 51 % at 81 °C, about 31 % at 120 °C, and only 4 % at 140 °C [54, 55]. The thiol/allene ratio also appears to influence the orientation. The ratio of products resulting from peripheral attack to those formed by central attack increases linearly with increasing thiol concentration and reaches a constant value of approximately 3:1 if a threefold or higher excess of thiol is used [54].

[52] *T. L. Jacobs* and *G. E. Illingworth jr.*, J. org. Chemistry *28*, 2692 (1963).

[53] *K. Griesbaum, A. A. Oswald, E. R. Quiram*, and *W. Naegele* J. org. Chemistry *28*, 1952 (1963).

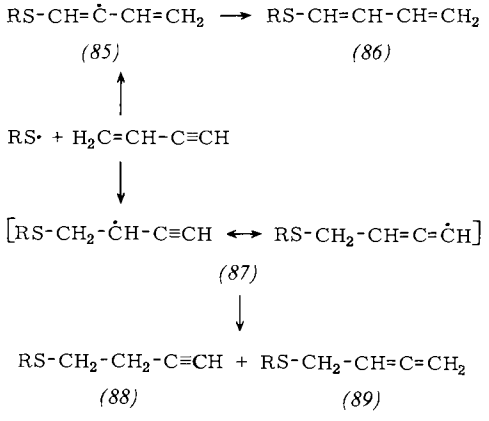
[54] *E. A. Haiba*, J. org. Chemistry *31*, 776 (1966).

[55] Similar observations were made earlier, though not in a systematic study of this matter: *H. J. Van der Ploeg, J. Knotnerus*, and *A. F. Bickel*, Recueil Trav. chim. Pays-Bas *81*, 775 (1962).



4.3. Compounds with CC Triple Bonds

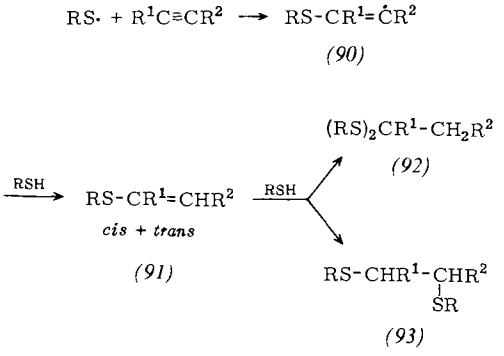
The course of free-radical additions of thiols to alkynes is basically similar to that described for alkenes. The few comparative studies carried out so far have shown however, that alkenes react more rapidly than the analogous alkynes. For example, in an equimolar mixture of propene and propyne, the propene reacts about 1.2 times as rapidly as the propyne [10]. This difference is still more pronounced in vinylacetylene, which, depending on the thiol, gives between 10 and 100 % of the products *(88)* and *(89)* resulting from addition to the double bond [56]. The high selectivity in this case may, however, also be due to the fact that the radical *(87)* can be stabilized by resonance [57] whereas in the vinyl radical *(85)* this would require the loss of the double bond conjugation.



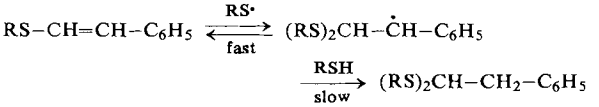
Addition to the triple bond leads *via* a vinyl radical *(90)* to *cis-trans* isomeric vinyl sulfide monoadducts *(91)* which can then add a further molecule of thiol more or less selectively and rapidly, depending on the substituents R, R^1, and R^2.

Thus the most important problems in such additions are: the orientation in the two addition steps and their relative rates, as well as the stereochemical course of the monoaddition.

The *orientation* is basically governed by the same rules as in the addition to alkenes. Monosubstituted acetylenes are attacked on C-1, whereas the position of the addition to disubstituted acetylenes and of the diaddition to the vinyl sulfide monoadducts depends on the directing effect of the substituents. Monoalkylacetylenes generally give vicinal diadducts [*(93)* where R^1 = H], while monoarylacetylenes give geminal diadducts [*(92)*, where R^1 = H].



Since the vinyl sulfides or vinyl thiols formed in the first addition step are generally more reactive than the alkynes from which they are derived, most thiol additions to alkynes are accompanied by at least partial diaddition. Exceptions to this rule are additions to aryl-substituted acetylenes, in which, owing to the stability of the intermediate benzyl radical *(94)*, the addition of the second thiyl radical is strongly reversible and thus reduces the extent of the diaddition:



The *stereochemistry of the addition* has been studied in detail on phenylacetylene [20] and 1-hexyne [21]. The stereoselectivity was strongly dependent on the molar ratio of the reactants, particularly in the additions to phenylacetylene. With excess thiol, the ratio of the isomers *(98)* and *(99)* corresponded to that of the thermodynamic equilibrium. If, on the other hand, equimolar quantities or an excess of the alkyne were used, the *cis*-adducts could be obtained with very high selectivities in some cases (Table 3).

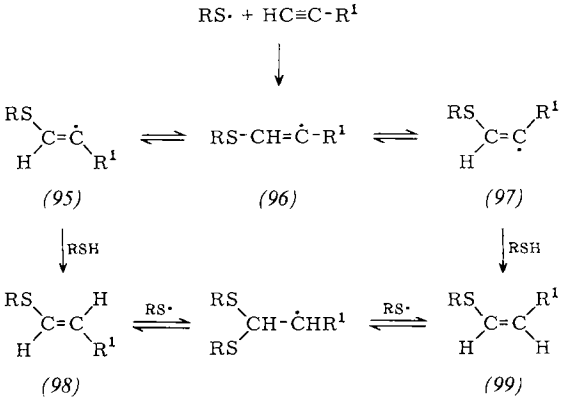
Table 3. Dependence of the stereochemical course of the additions to alkynes on the relative concentrations of the reactants.

Thiol	Alkyne	Thiol : Alkyne	*cis*-Adduct (%)	Ref.
C_6H_5SH	$C_6H_5C{\equiv}CH$	20 : 1	16	[20]
C_6H_5SH	$C_6H_5C{\equiv}CH$	1 : 1	56	[20]
C_6H_5SH	$C_6H_5C{\equiv}CH$	0.05 : 1	>95	[20]
CH_3SH	$C_6H_5C{\equiv}CH$	1 : 1	84	[20]
CH_3COSH	$C_4H_9C{\equiv}CH$	1 : 1	73	[21]
CH_3COSH	$C_4H_9C{\equiv}CH$	0.002 : 1	83	[21]

[56] *I. G. Sulimov* and *A. A. Petrov*, Ž. obšč. Chim. *2*, 767 (1965).

[57] Propargyl radicals, like allyl radicals, can be considerably stabilized by delocalization: *M. M. Martin* and *E. B. Sanders*, J. Amer. chem. Soc. *89*, 3777 (1967).

The question of the course of these stereoselective additions is very closely linked with that concerning the geometry of the intermediate vinyl radical. While it has been suggested occasionally that, like the alkynes from which they are formed, these reactive intermediates have a linear structure *(96)*, it has been deduced from more recent results that this is not so [58], but that the radicals *(95)* and *(97)* have a bent structure and equilibrate very rapidly with a low energy barrier [58a]. It is not certain whether the preferential formation of the *cis*-adducts *(99)* is due to preferred formation of the *cis*-radical *(97)* or merely to preferred chain transfer of this radical as compared to the *trans*-radical *(95)* that exists in equilibrium with it. This question is difficult to answer, since attempts at intercepting these radicals with excess thiol are always accompanied by side effects (isomerization of the monoadducts and/or diadduct formation).



5. Three-Component Reactions

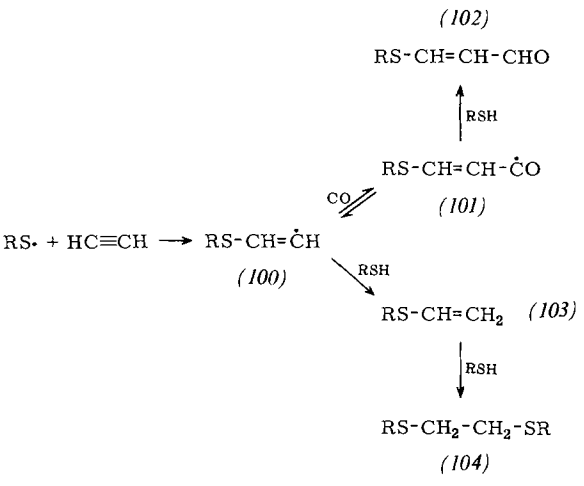
The addition of thiols to unsaturated compounds can be decisively modified by a third component. This third component may or may not be incorporated into the adduct.

5.1. Co-Carbonylations

The simultaneous action of thiols and carbon monoxide on alkenes [8] or alkynes [59] leads to partial formation of the ω-alkyl (or aryl) thioaldehyde containing one additional C atom, *e.g. (102)*. Since thiols are relatively good chain transfer agents, however, and since the reaction of the intermediate radical, *e.g. (100)*, with CO is reversible, these reactions also lead partly to the normal adducts, *e.g. (103)* and *(104)* even at high CO pressures.

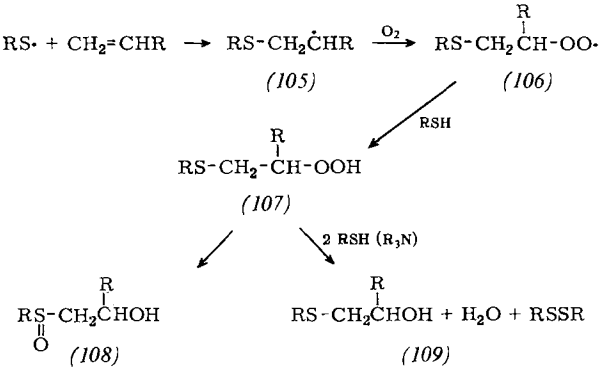
[58] For recent work on this problem see: a) *J. A. Kampmeier* and *R. M. Fantazier*, J. Amer. chem. Soc. *88*, 1959 (1966); b) *R. M. Fantazier* and *J. A. Kampmeier*, *ibid. 88*, 5219 (1966); c) *L. A. Singer* and *N. P. Kong*, *ibid. 88*, 5213 (1966); d) *O. Simamura*, *K. Tokumaru*, and *H. Yui*, Tetrahedron Letters *1966*, 5141; e) *L. A. Singer* and *N. P. Kong*, *ibid. 1966*, 2089; f) J. Amer. chem. Soc. *89*, 5251 (1967); g) Tetrahedron Letters *1967*, 643; h) *P. H. Kasai* and *E. B. Whipple*, J. Amer. chem. Soc. *89*, 1033 (1967).

[59] *J. C. Sauer*, J. Amer. chem. Soc. *79*, 5314 (1957).



5.2. Co-Oxidations

Upon simultaneous interaction of oxygen and thiols with unsaturated compounds, the initially formed C radical [*(105)* and *(110)*] combines spontaneously with the O_2-diradical. The resulting peroxy radical [*(106)* and *(111)*] then undergoes chain transfer with the thiol to form a hydroperoxide [*(107)* and *(112)*]. In the presence of sufficient oxygen, therefore, a free-radical combination step is inserted between the addition of the thiyl radical and the normal chain transfer [60, 61].



The initially formed hydroperoxides *(107)* have been isolated in several cases of co-oxidations of alkenes [62–65]. On prolonged standing, however, particularly in solution, they are transformed into the isomeric hydroxy sulfoxides *(108)*. On the other hand, they can also be converted into the alkylthio or arylthio alcohols *(109)* by amine-catalyzed reduction with an excess of thiol. Since the addend and the reducing agent are identical in this case (RSH), the co-oxidation

[60] *M. S. Kharasch*, *W. Nudenberg*, and *G. J. Mantell*, J. org. Chemistry *16*, 524 (1951).

[61] *H. Bredereck*, *A. Wagner*, and *A. Kottenhahn*, Chem. Ber. *93*, 2415 (1960).

[62] *J. F. Ford*, *R. C. Pitkethly*, and *V. O. Young*, Tetrahedron *4*, 325 (1958).

[63] *A. A. Oswald* and *F. Noel*, J. org. Chemistry *26*, 3948 (1961).

[64] *A. A. Oswald*, *B. E. Hudson jr.*, *G. Rodgers*, and *F. Noel* J. org. Chemistry *27*, 2439 (1962).

[65] *A. A. Oswald*, *K. Griesbaum*, and *W. Naegele*, J. Amer. chem. Soc. *86*, 3791 (1964).

can also be directed in such a way that the alcohols *(109)* are formed directly by the use of an excess of thiol and addition of a tertiary amine as a catalyst [66].

$$3\ RSH + CH_2{=}CHR + O_2 \xrightarrow{(R_3N)} RS{-}CH_2{-}\underset{R}{CHOH} + RSSR + H_2O$$

(109)

The co-oxidation of thiols and phenylacetylene leads to the phenylglyoxal monothiohemiacetals *(113)*, presumably *via* the unstable vinyl hydroperoxide *(112)* [67].

$$RS\cdot + HC{\equiv}C{-}C_6H_5 \longrightarrow [RS{-}CH{=}\dot{C}{-}C_6H_5 \xrightarrow{O_2}$$

(110)

$$RS{-}CH{=}C(C_6H_5)OO\cdot \xrightarrow{RSH} RS{-}CH{=}C(C_6H_5)OOH]$$

(111) *(112)*

$$\rightarrow RS{-}\underset{HO}{CH}{-}\overset{O}{C}{-}C_6H_5$$

(113)

5.3. Thiol-Phosphite-Olefin Reactions

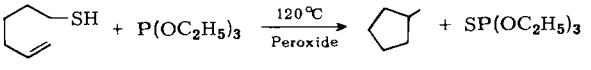
By combination of the well-known individual reactions (a) to (c)

$$RS^{\bullet} + P(OC_2H_5)_3 \rightarrow R^{\bullet} + SP(OC_2H_5)_3 \quad (a)$$

$$R^{\bullet} + CH_2{=}CHR^1 \rightarrow RCH_2{-}\dot{C}HR^1 \quad (b)$$

$$RSH + RCH_2{-}\dot{C}HR^1 \rightarrow RS^{\bullet} + RCH_2{-}CH_2R^1 \quad (c)$$

5-hexenylthiol *(114)* has been converted into the sulfur-free cyclization product *(115)* with a selectivity of up to 50 % [68].



(114) *(115)*

Preliminary attempts to extend this reaction principle to intermolecular alkylations have so far been unsuccessful.

6. Potential Applications

Derivatives of monothiophosphoric and dithiophosphoric acids, some of which have proved to be very active insecticides, play an important part in modern agricultural chemistry. Examples of such compounds are metasystox *(116)* and malathion *(117)* [69].

$$(CH_3O)_2P(O){-}S{-}CH_2{-}CH_2{-}SO{-}C_2H_5$$

(116)

$$(CH_3O)_2P(S){-}S{-}CH(CH_2{-}COOC_2H_5)COOC_2H_5$$

(117)

Compounds of this nature have in the past mainly been prepared by ionic substitutions or additions of *O,O'*-dialkyl monothiophosphates and -dithiophosphates with halogen compounds or unsaturated compounds respectively [70]. Compounds of this type have recently also been synthesized by direct free-radical addition of *O,O'*-diesters of monothiophosphoric and dithiophosphoric acids to dienes and alkynes [71]. These reactions led mainly to unsaturated adducts, of which *e.g.* the 1,4-monoadducts *(118a)–(118c)* with conjugated olefins and the 1,2-adducts *(119a)* and *(119b)* with allene have been described as very effective pesticides [72].

$(RO)_2P(S){-}S{-}CH_2{-}CX{=}CH{-}CH_3$ *(118)*

(a), R = CH_3, X = H
(b), R = C_2H_5, X = H
(c), R = C_2H_5, X = CH_3

$(RO)_2P(S){-}S{-}CH_2{-}CH{=}CH_2$ *(119)*

(a), R = CH_3
(b), R = C_2H_5

Derivatives of *O,O'*-dialkyldithiophosphoric acid are also important as oxidation inhibitors, and are widely used in motor oils [73]. Adducts formed by free-radical addition of *O,O'*-dialkyldithiophosphoric acids to dienes have recently also proved useful in this application [72, 74].

Among the co-oxidations, the reaction of the acetylenes, which leads to substituted glyoxal monothiohemiacetals *(120)* as the first isolable products (see Section 5.2), could be of preparative interest. These compounds are thermally very unstable, and can be decomposed in good yields into the corresponding thiol and glyoxal *(121)* by simple vacuum distillation, particularly when a very volatile thiol is used. Since the thiol is recovered, the overall reaction is thus a selective addition of one molecule of oxygen to the CC triple bond under the directing influence of a thiol [75].

$$RSH + O_2 + HC{\equiv}C{-}R^1 \rightarrow RS{-}CHOH{-}CO{-}R^1 \quad (120)$$

$$RS{-}CHOH{-}CO{-}R^1 \xrightarrow{\Delta} RSH + OHC{-}CO{-}R^1 \quad (121)$$

$$HC{\equiv}C{-}R^1 + O_2 \xrightarrow{(RSH)} OHC{-}CO{-}R^1$$

[66] *A. A. Oswald, K. Griesbaum,* and *B. E. Hudson jr.*, J. org. Chemistry *28*, 2351 (1963); *28*, 2355 (1963).

[67] *K. Griesbaum, A. A. Oswald,* and *B. E. Hudson jr.*, J. Amer. chem. Soc. *85*, 1969 (1963).

[68] *C. Walling* and *M. S. Pearson*, J. Amer. chem. Soc. *86*, 2262 (1964).

[69] For a compilation see *e.g.*: *O. Johnson, N. Krog,* and *J. L. Poland*, Chemical Week *1963*, 118.

[70] For a summary of this reaction see: *K. Sasse* in *Houben-Weyl-Müller*: Methoden der organischen Chemie. Thieme, 4. Edit., Vol. XII, Part 2, p. 652ff and 692ff.

[71] *A. A. Oswald, W. H. Mueller,* and *F. A. Daniher*, Abstracts of Papers, American Chemical Society Meeting, Miami Beach, April 1967, Division of Agricultural and Food Chemistry, Lecture No. 55.

[72] *A. A. Oswald* and *K. Griesbaum*, US-Pat. 3340332 (1967), Esso.

[73] *J. Teubel* and *K. Drescher* in: Additives. „Additives für Schmierstoffe: Oxidationsinhibitoren und Detergent-Dispersant-Zusätze". VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1962, p. 61ff.

[74] *A. A. Oswald, K. Griesbaum,* and *B. E. Hudson jr.*, Preprints of Papers, American Chemical Society Meeting, Los Angeles, April 1963, Division of Petroleum Chemistry, p. 5ff.

[75] *K. Griesbaum* and *A. A. Oswald*, US-Pat. 3321525 (1967), Esso.

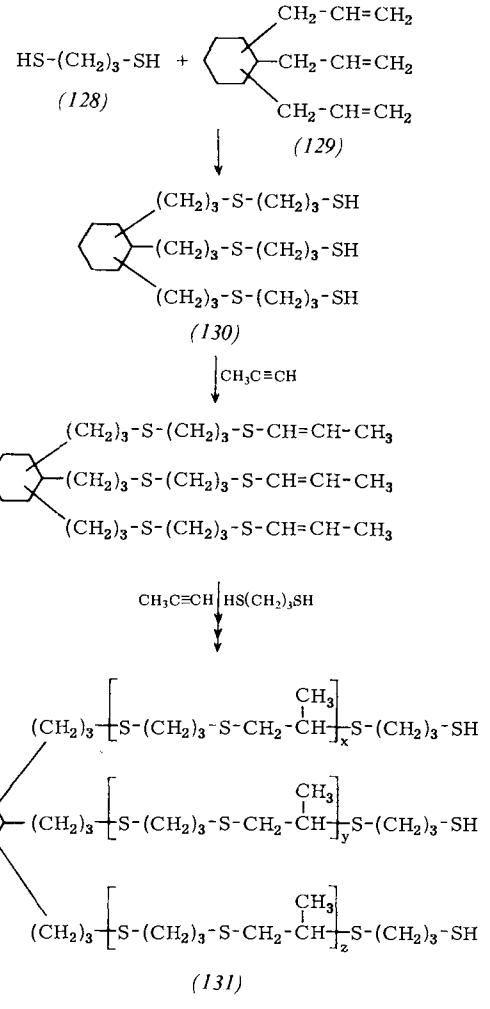
Polymers containing sulfur atoms in the chain are more or less resistant to hydrocarbon solvents, depending on their sulfur content, and are very widely used because of this property. The most important class are the Thiokols, which consist of alternating alkyl or alkoxy and polysulfide groups. Polymers containing only monosulfide groups, on the other hand, have so far found little use. The principal attempts to prepare such polymers were based on the polyaddition of dithiols to α,ω-dienes [76]. This approach had the disadvantage that the only readily obtainable α,ω-dienes, *i.e.* conjugated dienes, led to an adduct *(122)* with non-terminal double bonds, which are relatively inactive for further chain growth:

$$H{-}S{-}R{-}S{-}H + 2\ CH_2{=}CH{-}CH{=}CH_2 \rightarrow CH_3{-}CH{=}CH{-}CH_2{-}S{-}R{-}S{-}CH_2{-}CH{=}CH{-}CH_3$$

(122)

On the other hand, reactions of dithiols with allene or with propyne yield the adducts *(124)* and *(126)* respectively, which are more reactive than allene and propyne, and thus allow rapid chain growth. It was possible in this way to synthesize a series of polythioethers [77, 78]. The dithiol used was mainly trimethylenedithiol *(123)*, which is obtainable from allene and hydrogen sulfide [22, 79].

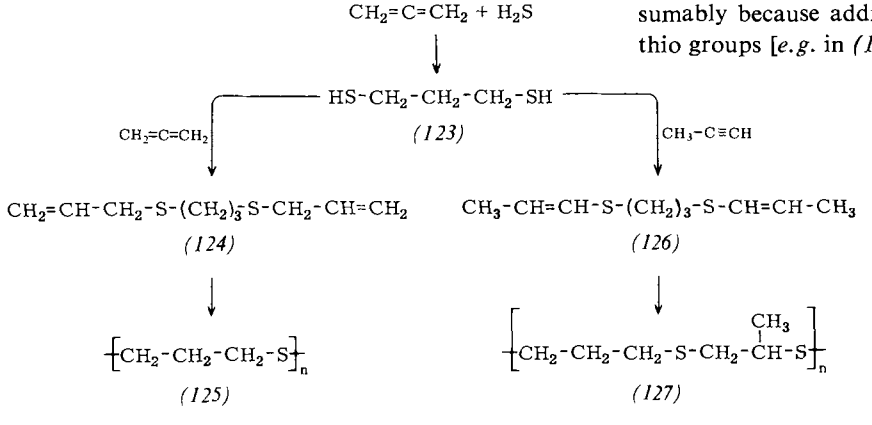
When this dithiol reacts with allene, the predominant addition to the terminal C atoms [53, 54] leads to a substantially linear polymer *(125)*, in which linear C_3 groups are separated by sulfur atoms. In accordance with this linear structure, polymers of this type are crystalline even at relatively low molecular weights [77]. On the other hand, the reaction of trimethylenedithiol with an alkyne, *e.g.* propyne, yields a polymer *(127)* in which linear and branched C_3 groups are separated by sulfur atoms [79]. This reaction is therefore suitable for the synthesis of strictly alternating copolymers *(127)* [78].



(131)

Such copolymers *(127)* do not tend to crystallize, presumably because additions of dithiols to 1-propenylthio groups [*e.g.* in *(126)*] do not proceed stereoselectively and thus lead to atactic products. Hence, these polymers are suitable for use as prepolymers for elastomers [78]. Owing to the simple stepwise growth, definite end groups can be introduced. An excess of dithiol gives polymers with terminal thiol groups, which can be used for vulcanization reactions or converted into other reactive end groups.

The stepwise growth also permits the introduction of additional functional groups into polymers of this type. For example the addition of a trithiol to the monomer



(123) *(124)* *(125)* *(126)* *(127)*

[76] For a summary see *N. G. Gaylord* in *N. G. Gaylord*: High Polymers. Interscience, New York 1962, Vol. 13, Part III, p. 164ff.

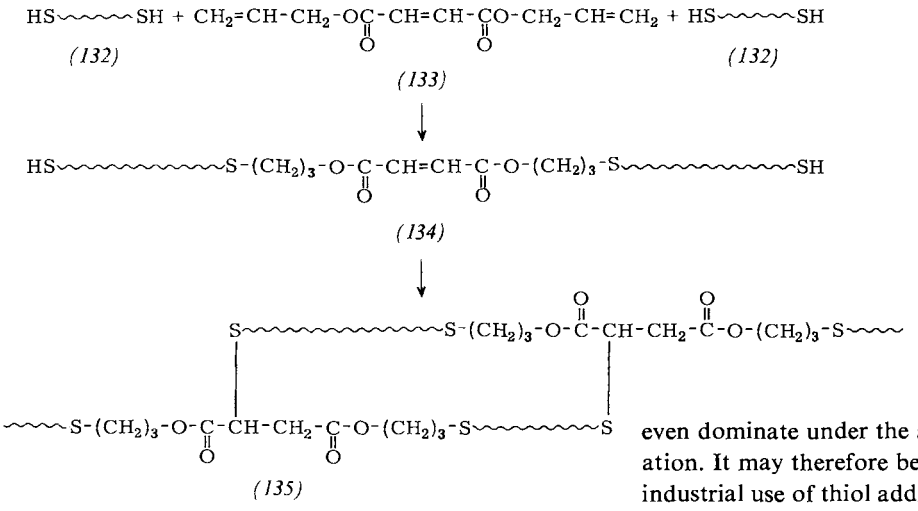
[77] *A. A. Oswald, K. Griesbaum*, and *D. N. Hall*, Preprints of Papers, American Chemical Society Meeting, Miami Beach, April 1967, Polymer Division, Vol. 8, No. 1, p. 743ff; US-Pat. 3403187 (1968), Esso.

[78] *A. A. Oswald, D. N. Hall, K. Griesbaum*, and *W. H. Mueller*, Preprints of Papers, American Chemical Society Meeting, San Francisco, April 1968, Polymer Division, Vol. 9, No. 1, p. 648ff and p. 657ff.

[79] *K. Griesbaum* and *A. A. Oswald*, US-Pat. 3488270 (1970), Esso.

mixture gives trifunctional polymers, *e.g. (131)*, in quantities corresponding to the quantity of this third component added. These polymers are capable of undergoing the oxidative vulcanization with lead dioxide that is commonly used in Thiokol technology. The same result can be achieved by the addition of a reactive triolefin such as trivinylcyclohexane *(129)* to the reaction mixture. This method has the advantage that the initially formed trithiol *(130)* is as reactive as the dithiol *(128)* used for further growth [78].

An interesting variant is the introduction of hidden functional groups into the polymer chain. By making use of the difference in reactivity between the allyl and the central double bond [30] (see Section 4.2.1), for example, diallyl maleate or diallyl fumarate *(133)* can be



built into the growing chain *(132)* in such a way that the central double bond is retained. On the other hand, since this double bond reacts very rapidly with thiols under ionic conditions, the initially formed linear polymer *(134)* can be crosslinked to give vulcanizates of the type *(135)* [78] simply by addition of catalytic quantities of an amine and without adding special vulcanizing agents.

These examples may suffice to illustrate the possibilities of the free-radical addition of thiols to unsaturated compounds. It has been reported for most of the examples described that the reactions were initiated both by UV radiation and by γ radiation and that no difference was found in the selectivity of the reactions. This is a very important observation, since fears have occasionally been expressed that undesirable reactions, particularly ionic additions, which are known to exhibit different orientation effects, could compete or even dominate under the action of high-energy γ radiation. It may therefore be assumed that interest in the industrial use of thiol additions will grow concurrently with the increasing use of γ-ray sources in industry.

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The Differential Calorimetric Study of the Reactivity of Unstable Compounds

By Erhard Koch[*]

The detection of unstable intermediates in chemical, photochemical, and radiation-chemical reactions can be greatly facilitated by the use of thermoanalytical methods. Special advantages are offered by differential thermal analysis (DTA), since it permits fast, easy investigation, from about −150 °C upward in some cases, over a wide temperature range. In this way processes that under normal conditions follow one another with immeasurable rapidity can be separated on the basis of their different temperature dependences. The great sensitivity of the method also allows the use of very dilute solutions, so that the studies can be confined to unimolecular processes.

The value of the method for the determination of energetic and kinetic data is illustrated by its application to the photochemically obtainable, unstable, ozonide-like epidioxydihydrofurans.

1. Introduction

Chemical reactions in solution usually comprise several individual processes, sometimes proceeding concurrently and sometimes consecutively. The strongest possible evidence of the fundamental correctness of an assumed reaction mechanism is the detection of an expected intermediate. However, the preparative isolation of substances that occur as intermediates is usually difficult. This is true in particular in radiation-chemical and photochemical reactions, in which the processes directly following the electronic excitation are so fast as to defy direct investigation.

Unstable intermediates can be made accessible even in these cases by the use of low temperatures if their further reaction requires appreciably higher activation energies than their formation. Even in photochemical processes, whose first propagation steps have very small activation energies [1–3], it is often possible to intercept intermediates, sometimes at extremely low temperatures [4–7].

However, attempts to isolate and identify unstable substances at low temperatures are frustrated by further difficulties in practice. On the one hand any concentration of reactive substances causes an increase in the importance of bimolecular processes, in which the substances change further. On the other hand, detection in solution is often difficult, since the current methods, such as NMR, IR, and UV spectroscopy, are not always selective enough, with the result that they also register solvents, catalysts, sensitizers, and starting materials.

These difficulties vanish if instead of the intermediates themselves, one investigates their reactions in solution. Since practically every reaction liberates or consumes heat, the change in temperature may be used as a general measuring criterion. Thus if a solution of an unstable substance is steadily heated, temperature changes characteristic of reactions of the intermediate are superimposed. Conversely, the absence of thermal effects in this investigation indicates that no unstable product was present.

This is the method of differential thermal analysis (DTA), which has found increasing use in the study of physical and chemical problems [8–12] since its discovery by *le Chatelier* (1887), *Callendar* (1897), and *Stansfield* (1898). These investigations were at first concerned with solid samples in the fields of geology, mineralogy, ceramics, metallurgy, and inorganic chemistry. The introduction of special thermocouples later made the use of temperatures above 2000 °C possible [13]. The extension of the working range to low temperatures [14–17] also opened the way to new applications.

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[1] *J. G. Calvert* and *J. N. Pitts jr.*: Photochemistry. Wiley, New York 1966, p. 645ff.

[2] *E. Koch*, Tetrahedron *24*, 6295 (1968).

[3] *E. Koch*, Tetrahedron *23*, 1747 (1967).

[4] *G. O. Schenck* and *D. E. Dunlap*, Angew. Chem. *68*, 248 (1956).

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[10] *Y. Chiang* and *W. J. Smothers*, J. chem. Educat. *29*, 308 (1952).

[11] *D. Schultze*: Differentialthermoanalyse. Verlag Chemie, Weinheim 1969.

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[14] *J. Jaffray*, C. R. hebd. Séances Acad. Sci. *224*, 1346 (1947).

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[17] *A. K. Mal'tsev*, Trudy Mosk. Chim. Technol. Inst. *1963*, 44; Chem. Abstr. *62*, 8682 (1965).

In the investigation of liquid systems, it was possible to approach the investigation technique of isothermal calorimetry; owing to the uniformity of temperature that could be achieved in this case, the situation could be expected to be simpler than in the solid phase. With adequate mixing, it was possible to obtain experimental curves that allowed the determination not only of the thermochemical data but also of reaction rate constants over a wide temperature range (over 100 °C), and hence of activation energies and frequency factors [18–24].

By the further development of the temperature measuring and recording techniques, the attainable sensitivity of DTA equipment has been increased to such a degree that transformations of $< 10^{-7}$ mole of a substance in a small sample of a 10^{-4} M solution can nowadays be detected with certainty [22–24]. In contrast with conventional isothermal methods, the application of which took several days, the DTA method allows the determination of the enthalpy, activation energy, and entropy of a reaction in a few hours and from a single experiment, though sometimes with a loss of accuracy in the enthalpy. However, these values are often sufficiently accurate for rapidly accessible basic information.

These characteristics of the DTA method make it eminently suitable for the investigation of the thermal stability of chemical compounds even in dilute solutions and open up new possibilities for the detection of intermediates. Photochemical processes are particularly suitable for thermoanalytical investigation, since the energy drop between the starting materials and the final products is very large.

2. Measuring Technique

In differential thermal analysis, the test sample is steadily heated from a temperature at which no reaction occurs. The temperature of the sample is recorded directly, and simultaneously as the difference from the temperature of an inert, thermally equivalent reference sample [10, 11, 25]. By suitable design it is possible to ensure that a DTA apparatus is a serviceable adiabatic calorimeter (ideal case: no heat exchange with the environment), while the system under examination still follows the imposed temperature variation sufficiently quickly (ideal case: best possible heat exchange with the environment). Since the two requirements oppose each other, any instrument must be a compromise.

It seemed to us that what was needed was a design in which the thermal separation of the two systems, *i.e.* the external system whose temperature variation can be predicted and the internal system under investigation, was so decisive that each had its own uniform temperature. An arrangement that has proved its worth is one (Fig. 1) whose operation is formally similar to that of an apparatus for the cryoscopic determination of molecular weights [24]. Its features are:

1. a thermally insulated aluminum heating block having a uniform temperature, with two test tubes for 5 ml of sample and the same amount of reference solution;

2. a poor but definite heat transfer between the test tubes and the block *via* variable PVC, Cr—Ni steel, or Teflon inserts;

3. uniform thermostating of the sample and the reference sample by Teflon stirring disks, which are moved by a pulse-controlled solenoid;

4. very accurate measurement of the temperature difference (to within a few thousandths of a degree, copper-constantan thermocouples, pen recorder with a minimum measurement zone of 50 μV) [24, 26].

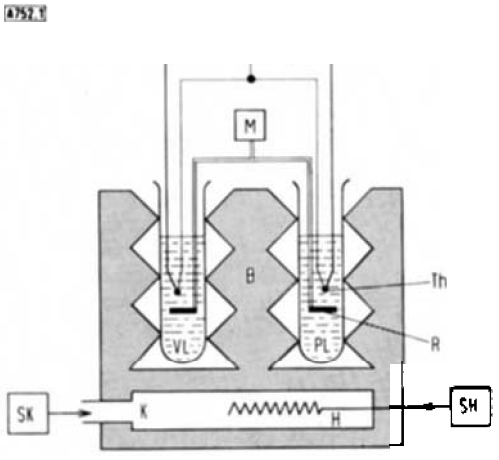


Fig. 1. Apparatus for differential thermal analyses in solution (schematic). B = heating block; H = heater; K = coolant inlet; M = solenoid; PL = sample solution; R = stirrer; SH = heating control unit; SK = cooling control unit; VL = reference solution; T = absolute temperature (°K); ΔT = temperature difference (°C); Th = thermocouple.

The apparatus can be cooled to about —150 °C and thermostated until the start of heating *e.g.* by finely metered injection of liquid nitrogen or of gaseous cold nitrogen.

The heating should be variable over a wide range. Control units ensuring a constant rate of temperature rise facilitate evaluation, since they allow adherence to standard conditions.

3. Evaluation of Recorded Curves

The result of DTA measurements is usually the variation of the temperature difference with time (thermogram).

As soon as the continuously heated system under examination reaches temperatures at which an exothermic (or endothermic) reaction begins, a finite temperature difference appears, rises (or falls) to a maximum (or minimum), and then returns to zero after the reaction (Fig. 2a). This is due to competition between the heat produced (or consumed) by the reaction and the heat exchange with the surroundings. The course

[18] *G. Wada*, J. chem. Soc. Japan, pure chem. Sect. (Nippon Kagaku Zasshi) *81*, 1656 (1960); Chem. Abstr. *55*, 6994 (1961).

[19] *H. J. Borchardt* and *F. Daniels*, J. Amer. chem. Soc. *79*, 41 (1957).

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[22] *C. Eyraud*, C. R. hebd. Séances Acad. Sci. *238*, 1511 (1954).

[23] *R. Charuel* and *Ph. Traynard*, J. Chim. physique *52*, 441 (1955).

[24] *E. Koch*, Chemie-Ing.-Techn. *37*, 1004 (1965)

[25] See ref. [11], p. 117 ff.

[26] *B. Jankowsky*, Silikattechnik (1) *17*, 20 (1966); Chem. Abstr. *65*, 1358f. (1966).

of a DTA curve can thus be used to obtain information about the *kinetics* of the reaction in question, while the *reaction enthalpy* ΔH can be deduced from the overall thermal effect. The quantitative relation is [27–29]:

$$\Delta H = c\, Q_T/n_0 \int_0^\infty \Delta T/\mathrm{d}t \qquad (1)$$

In this equation, ΔT is the temperature difference between the sample container and the reference container, recorded as a function of time t (Fig. 2a), n_0 is the number of moles of reacting substance, Q_T is the heat content of the entire sample system, and c is a cell constant that describes the heat transfer behavior of the system.

Whereas in an adiabatic calorimeter the heat effect is found from the heat content and the temperature difference in relation to the initial state, extrapolated to time $t = 0$, the quantity in which we are interested in DTA is the area between the curve and the abscissa. The heat transfer, which is taken into account only for correction of the enthalpy value in the case of a calorimeter, becomes the principal factor in DTA.

For a constant heating rate (linear temperature rise in the reference container, see Fig. 2b), the reaction order is approximately given by:

$$m \approx 1.26 \sqrt{b/a} \qquad (2)$$

where a and b are fixed by the inflectional tangent of the DTA curve [11, 30, 31] (Fig. 2a).

Finally, for an irreversible reaction, the rate constant can be found for each point of the thermogram, and hence for each temperature in the range under investigation [19, 24, 31–36]:

$$k\,[T(t)] = \left[\frac{V|\Delta H|}{Q_T}\right]^{m-1} \frac{c\,\Delta T + \dfrac{\mathrm{d}\,\Delta T}{\mathrm{d}t}}{\left[c\int_t^\infty \Delta T\,\mathrm{d}t - \Delta T\right]^m} \qquad (3)$$

V = volume of sample solution.

This can be used to find the activation energy ΔE and the reaction entropy ΔS from the Arrhenius equation. A logarithmic plot of k against $1/T$ also provides a check on the reaction orders given by eq. (2), which are only approximate, since a straight line can be obtained only if the order adopted is correct.

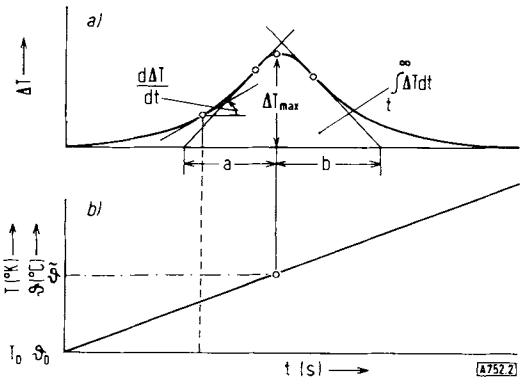


Fig. 2. a) Schematic course of a DTA curve. b) Temperature variation in the reference container.

The heat content Q_T of the sample system is the sum of the water equivalent of the vessel, stirrer, and thermocouple and the heat contents of the sample and reference solutions. The water equivalent is obtained from mixing experiments with liquids at various temperatures or by following a reaction having a known heat effect, *e.g.* a neutralization. Calibration by electric heating is also very simple. The specific heats of dilute solutions are practically the same as that of the pure solvent, which can be found for various temperatures from tables. If the reaction under investigation takes place within a sufficiently narrow temperature range (<30 °C) it can be based on the temperature at the maximum of the DTA curve.

The cell constant c is directly proportional to the effective thermal conductivity between the internal system under investigation and the external temperature-determining system, but inversely proportional to the specific heat (of the internal system) [28, 29]. To determine its value, *e.g.* equal quantities of the solvent to be used are placed in the sample tube and in the reference tube. After equalization of the temperatures, one heats slightly above the temperature of the external system, which is kept constant, and waits until the temperature difference has vanished. The cell constant is now found from the temperature difference extrapolated to time $t = 0$ and the total area above the abscissa [eq. (5a)], or at any point on the curve from its variation with time [eq. (5b)].

$$c = -[\Delta T]_0 / \int_0^\infty \Delta T \mathrm{d}t \qquad (5a)$$

$$c = -\frac{1}{[\Delta T]_t} \cdot \left[\frac{\mathrm{d}\,\Delta T}{\mathrm{d}t}\right]_t \qquad (5b)$$

4. General Notes on Application to Reactions in Solution

Simple information about the course of the reaction under investigation is obtainable merely from the shape of the thermogram (Fig. 3).

A preliminary investigation is often necessary first in order to establish whether the observed effect is due to a chemical or to a physical process. Thus phase transitions, for example, also cause temperature changes (cf. Scheme 1). Interference of this nature can be recognized by repetition of the DTA with the same sample; they usually disappear at sufficiently high dilutions.

[27] *I. L. H. Berkelhamer* and *S. Speil*, Mine Quarry Engng. *10*, 273 (1945); Chem. Abstr. *40*, 2378 (1946).

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[36] *D. S. Thompson*, Ind. Engng. Chem. Fundamentals *5*, 286 (1966).

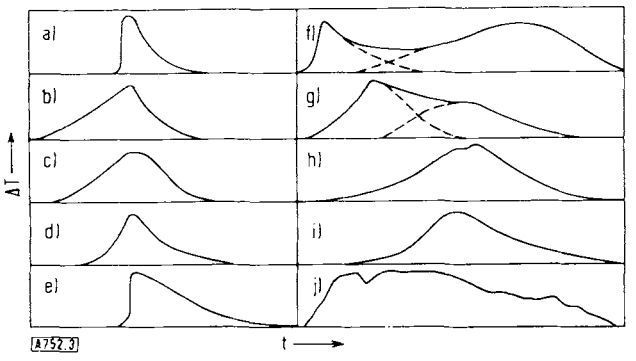


Fig. 3. Examples of DTA curves (with linear temperature variation). a) Immeasurably fast reaction A + B → AB; initiation by second component or catalyst. b) Zero order reaction, *e.g.* with heterogeneous catalysis (initiation by catalyst). c) first order reaction A → B (+C). d) Second order reaction A $\xrightarrow{+A}$ B (+C). e) Polycondensation A $\xrightarrow[(-x_1)]{+A}$ B $\xrightarrow[(-x_2)]{+A}$ C $\xrightarrow[(-x_3)]{+A}$ *etc.* f) Reaction sequence A $\xrightarrow[(-x_1)]{+B}$ C $\xrightarrow[(-x_2)]{}$ D, separable. g) Reaction sequence as f), separable with difficulty. h) Reaction sequence as f), inseparable. i) Parallel first and second order reactions A $\xrightarrow{+A}$ B (+ D). j) Many parallel and consecutive reactions. A → C (+ E).

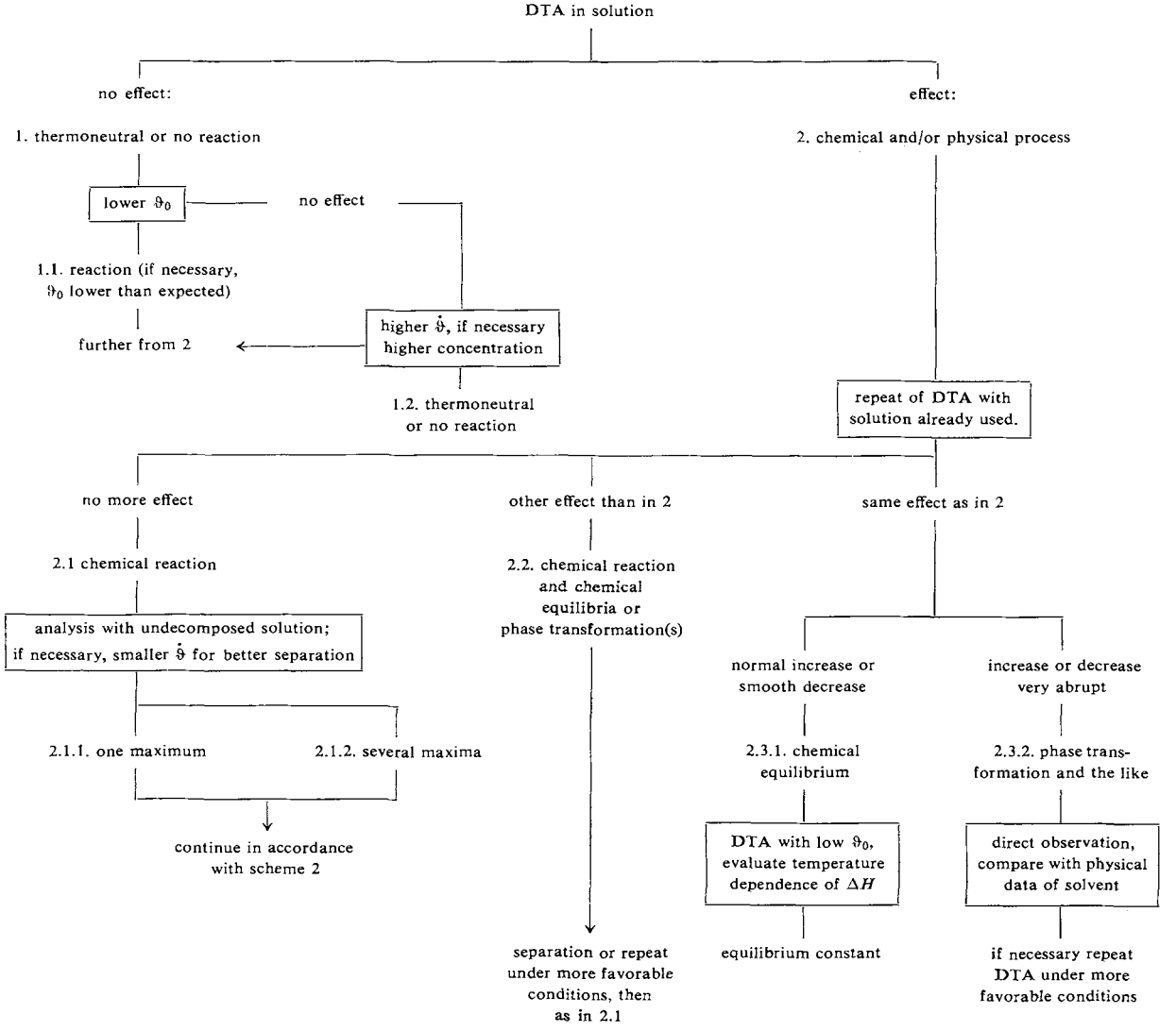
The pure solvent can generally be used as the reference solution for dilute solutions. If higher reactant concentrations are necessary, the appropriate quantity of a substance that corresponds as closely as possible in its physical data (solubility, specific heat, vapor pressure depression) to the mean of the values of the starting materials and of the final products must be added to the reference sample.

If only *one* reaction takes place during the measurement, the DTA curve also contains only one maximum, and the reaction order is found from the inflectional tangents (types a–d in Fig. 3). On the other hand, it cannot always be assumed from the presence of only one maximum that only one reaction occurs.

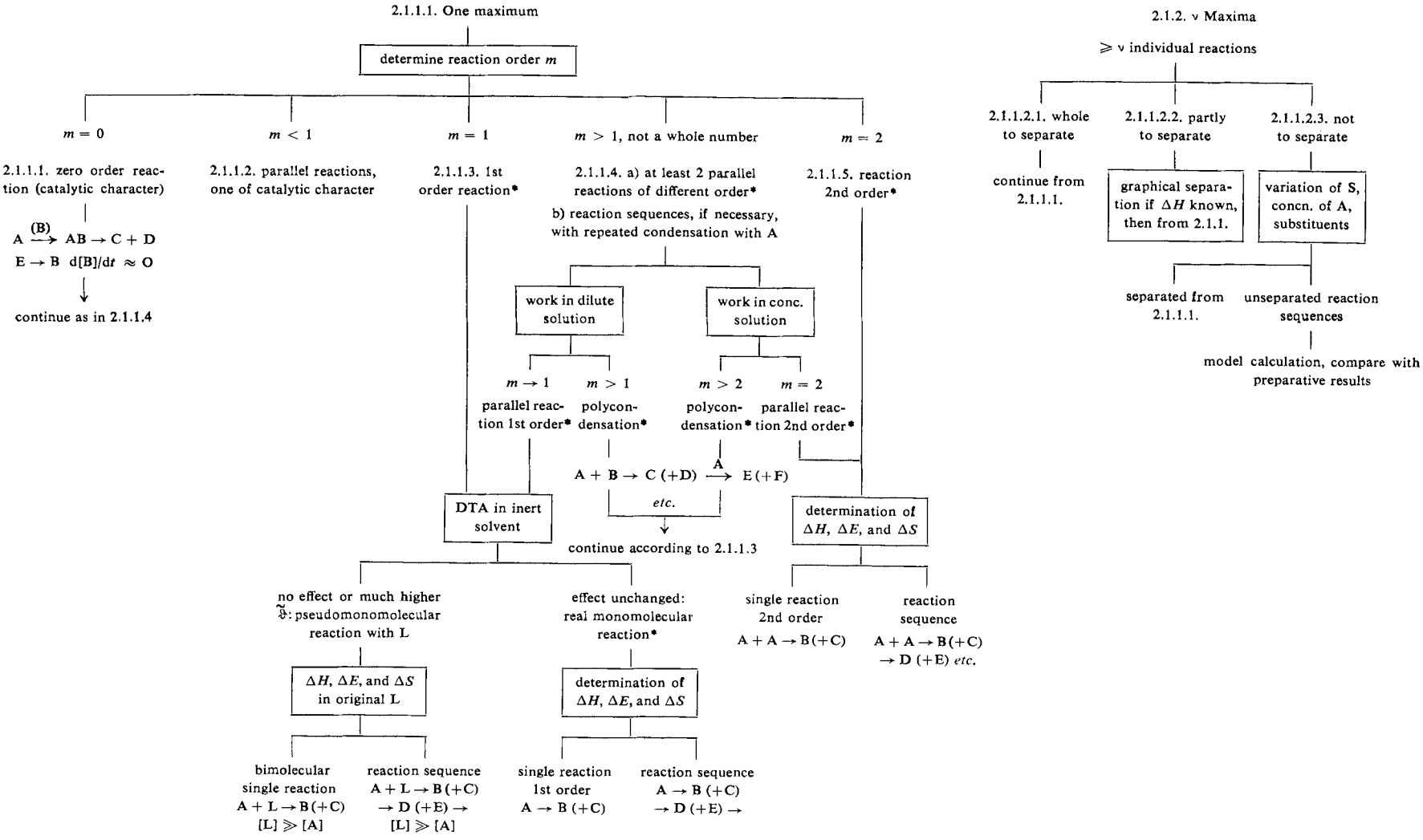
If a whole-number reaction order m is obtained with only one maximum, an exact kinetic evaluation is possible if ln k varies linearly with $1/T$. The first estimate of enthalpies, rate constants, and activation energies is obtained from the height of the ΔT maximum (ΔT_{max}) at a constant heating rate $\dot{\vartheta}$ and the temperature of the reference solution at the time of this maximum ($\tilde{\vartheta}$, referred to in the following discussion as the reaction temperature), which are particularly suitable for fast characterization and for comparison of different thermograms. The enthalpy ΔH of a first order reaction in thoroughly mixed solutions is given [37] by

$$\Delta H \approx 0.034\, c \cdot \Delta T_{max}/(n_0 \dot{\vartheta}^{0.6}) \qquad (6)$$

[37] *E. Koch*, unpublished.



Scheme 1. Preliminary examination of unknown systems by DTA. ϑ = temperature (°C); ϑ_0 = starting temperature (°C); $\dot{\vartheta}$ = heating rate (°C/min).



Scheme 2. Examination of unknown systems by DTA.

A = unstable substance used; L = solvent. * possibly with secondary reaction(s) that is (are) fast in relation to the initiation reaction.

$\tilde{\vartheta}$ temperature of the reference solution at ΔT_{max} (reaction temperature).

It has been shown for many examples[24,37] that rate constants of 10^{-2} to 10^{-3} s^{-1} are found at the maximum for $\dot{\vartheta} = 1.5$ °C/min under the same conditions. For a frequency factor of 10^{13} s^{-1}, such a reaction has a half-life of one hour about 20 °C below $\tilde{\vartheta}$, irrespective of the reaction enthalpy.

Fractional reaction orders point to parallel reactions of different orders or sequences of reactions in which repeated condensation of intermediates with the starting material can occur. In these cases the type of curve must depend on the concentration, and this allows the separation of parallel steps (cf Scheme 2).

Several maxima in the DTA curve are always evidence of at least as many reactions. A reliable quantitative evaluation is possible if the areas corresponding to the various processes overlap only slightly, or if the heat effects and reaction orders of the various processes are known where overlapping is pronounced (cf. Fig. 3, types f and g). A detailed mechanistic study requires a systematic variation of the parameters of the DTA (heating rate $\dot{\vartheta}$[24,30,31,38], starting temperature ϑ_0, and possibly the composition of the reference solution) and of the composition of the sample. Other diagnostic possibilities are offered by interruption of the analyses for a short time to allow intermediates already present to react with added substances at a constant block temperature, after which the temperature is further raised.

An example of the combined application of isothermal and non-isothermal methods is the diazotization of an aromatic amine at 0 °C (determination of ΔH; type a in Fig. 3) and the subsequent loss of nitrogen on continuous heating to form the phenol (determination of ΔH, ΔE, and ΔS; type c in Fig. 3). The thermodynamic quantities found in this way agree well with those obtained by conventional methods[19,24,39].

The non-isothermal methods[40] are preferable for the investigation of unknown systems, since only then is a universal check for secondary reactions possible. Schemes 1 and 2 show that the reaction course can often be recognized by suitable DTA programs without the use of other methods. If the processes can be separated, the reaction enthalpies found in accordance with Hess's law often allow the assignment of the reactions studied to a proposed mechanism. The increments for the energies of formation at temperatures down to −80 °C differ by at most a few kilocalories from the standard values at +20 °C. In photochemical reactions, moreover, the differences in the heats of solvation and vaporization between the starting materials and the final products are relatively small in comparison with the total energy decrease, so that the best results are to be expected here.

If the processes cannot be separated, *e.g.* in a unimolecular reaction sequence in which the initiating reaction is rate-determining, the reaction enthalpy obtained must be assigned to the overall process. However, the activation energy found and the reaction entropy refer only to the first process. The detection of an intermediate and the determination of its activation parameters are then possible only if it can be produced from another unstable starting material that decomposes at a much lower temperature, and even then does so more rapidly than the intermediate.

In the case of complex reactions that are only partly separable can be clarified only by the use of preparative and of other diagnostic methods in conjunction with DTA, and by mathematical analysis of the curves with a computer.

5. Investigation of Photochemical Reactions

If the energy required to initiate a reaction is supplied to the system as light, the first step is the formation of biradical excitation products, which can often undergo fast secondary processes with non-radical components to give other biradical products. In many cases the activation energies of such secondary reactions are so low that the formation of the intermediates is immeasurably fast even at very low temperatures[1].

This behavior is observed in the photosensitized cycloadditions of O_2 to dienes and olefins[2,41–48], and also in the direct photolysis of diazomethane, alkyl azides, and hydrazoic acid[3,7,49,50], and to a lesser degree in the photosensitized synthesis of 1,2-dioxacyclohexanes and cyclobutanes[51–57]. Processes of this type contrast with the much more temperature-dependent photochemical reactions in which monoradical intermediates are formed, such as the photosensitized aut-

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[42] *G. O. Schenck* in: Naturwissenschaften und Medizin in Deutschland 1939–1946 (First Rev. of German Science) *37* (1948); Präparative organische Chemie, Part II: Reaktionen mit molekularem Sauerstoff. Dieterichsche Verlagsbuchhandlung, Wiesbaden 1948, p. 167ff.

[43] *G. O. Schenck*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *56*, 855 (1952).

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[47] *K. Gollnick* and *G. O. Schenck* in *J. Hamer*: 1,4-Cycloaddition Reactions. The Diels-Alder-Reaction in Heterocyclic Syntheses. Academic Press, New York 1967, p. 255.

[48] *K. Gollnick*, Advances *6*, 1 (1968).

[49] See [46], p. 275ff.

[50] See [46], p. 319ff.

[51] *G. O. Schenck* and *R. Steinmetz*, Bull. Soc. chim. belges *71*, 781 (1962).

[52] *G. O. Schenck*, *J. Kuhls*, and *C. H. Krauch*, Liebigs Ann. Chem. *693*, 20 (1966).

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[54] *P. de Mayo*, *S. T. Reid*, and *R. W. Yip*, Canad. J. Chem. *42*, 2828 (1964).

[55] *G. Pfundt* and *G. O. Schenck* [47], there p. 345.

[56] *R. Steinmetz*, Fortschr. chem. Forsch. *7*, 445 (1967).

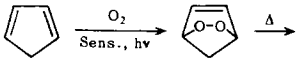
[57] See [46], p. 109ff.

oxidation of alcohols introduced by dehydrogenation [45, 46, 58], sulfochlorination by *Reed*'s method, or light-induced polymerizations [59, 60].

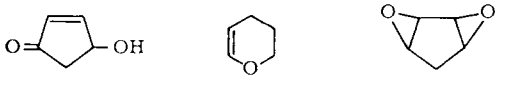
We chose systems of the first type for the investigation of unstable compounds, since intermediates of these reactions can occur even at very low temperatures, and thermograms can be obtained over a wide temperature range. Reactions that proceed with liberation or absorption of gases are favorable, since the quantity of primary product can be readily determined in these cases. Peroxides that are readily obtainable by photosensitized oxygen transfer, and whose preparative study requires extensive safety precautions in view of their tendency to decompose explosively, were very suitable for this purpose, particularly since it is known that oxygen bound in ozonide-like form can in certain circumstances be transferred to cyclic dienes with formation of epidioxides [37, 61–65].

The differential-calorimetric study of solutions that had been irradiated at −60 to −90 °C [6] showed firstly that in all cases where products different from those obtained at +20 °C were formed, thermal effects also occurred. Double maxima (*e.g.* for furfural, furfuryl alcohol), very broad, spread-out maxima (*e.g.* for β-ionone, 2-methylfuran in toluene) or fractional reaction orders (*e.g.* for furfurylamine) point to two or more partly concurrent processes. If heat effects observed are found not to be proportional to the photochemical primary conversion, the intermediates are unstable even during the exposure to light. Thermal secondary reactions will frequently be involved.

Interference due to secondary photochemical reactions can be recognized by further exposure to light after the principal process is complete. Thus in the photosensitized transfer of oxygen to cyclopentadiene *(1)* at



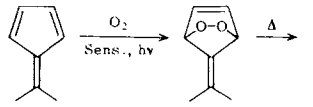
(1) *(2)*



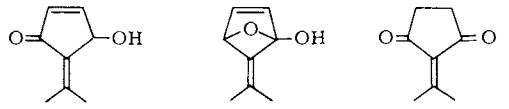
(3) *(4)* *(5)*

20 °C, the compound *(3)* and possibly *(4)* formed *via (5)* are obtained, as well as unknown substances, on concentration and working up, whereas the primary peroxide (5,6-dioxanorbornene) *(2)* can be isolated at −10 °C [4]. This is photoisomerized in a way that is not yet known with Bengal pink as the sensitizer and with polychromatic light. Accordingly, the evolution of heat in differential thermal analysis always decreases further on exposure to light after the uptake of oxygen is complete. However, the photoisomerization (which does not take place when sodium vapor lamps are used in any case) can be eliminated from the energy discussion by extrapolation to exposure time $t = 0$. The agreement of the value of 60 kcal/mole found thermoanalytically for the reaction enthalpy with the difference in the heats of formation of *(3)* and *(2)* and the fact that the reaction order is around unity show that 4-hydroxy-2-cyclopenten-1-one *(3)* is formed here as the primary product of the rearrangement of the peroxide *(2)*. This shows clearly the analogy to 2,5-epidioxydihydrofuran (5,6,7-trioxanorbornene) [*(21)*, $R^1 = R^2 = H$], from which 5-methoxy-2(5*H*)-furanone *(34)* (malealdehydic acid pseudoester) is formed [5, 66–68].

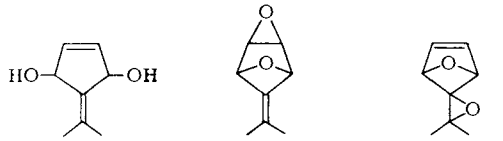
After the photosensitized O_2 transfer to ω-dimethylfulvene *(6)* at +20 °C, only polymeric reaction mixtures, which were assumed to contain the compounds *(8)*–*(17)* of products of further reactions, could be iso-



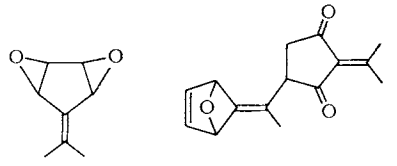
(6) *(7)*



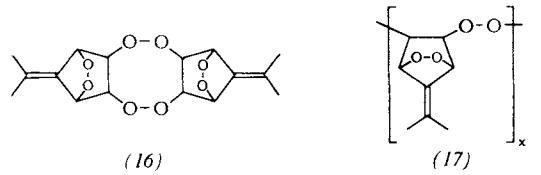
(8) *(9)* *(10)*



(11) *(12)* *(13)*



(14) *(15)*



(16) *(17)*

[58] *G. O. Schenck, H. D. Becker, K.-H. Schulte-Elte*, and *C. H. Krauch*, Chem. Ber. *96*, 509 (1963).

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[65] *P. D. Bartlett* and *G. D. Mendenhall*, J. Amer. chem. Soc. *92*, 211 (1970).

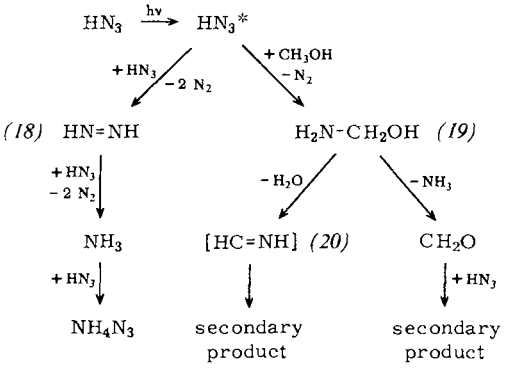
[66] *G. O. Schenck*, Liebigs Ann. Chem. *584*, 156 (1953).

[67] *N. Hellström*, Nature (London) *187*, 146 (1960).

[68] *S. H. Schroeter, R. Appel, R. Brammer*, and *G. O. Schenck*, Liebigs Ann. Chem. *697*, 42 (1966).

lated in some cases[69]. *(8)–(17)* are thought to be formed *via* the peroxide *(7)*. The reaction evidently stops at the peroxide stage at −80 °C. This can be shown thermoanalytically. In a 0.005 M photo-oxidized methanolic solution, 69 kcal/mole are liberated in a first order reaction; this is in agreement with the formation of the compounds *(8)*, *(9)*, and/or *(10)* from *(7)*. Thus seven of the ten formulated compounds can be ruled out on energy grounds in this case. Other processes, some of them endothermic, occur above +50 °C.

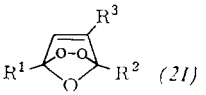
The peroxides formed by sensitized photoadditions at low temperatures liberate very large quantities of energy (up to ≈90 kcal/mole), on decomposing. On the other hand, the products formed in the cold by the photolysis reactions investigated so far, *e.g.* in the elimination of N_2 from diazoacetic ester or azides, exhibit only small energy transformations, if any. Thus the absence of DTA effects in the case of methyl azide solutions photolyzed at −80 °C[3] indicates that the stable final product, hexamethylenetetramine, is formed even at this temperature. In the case of hydrazoic acid, on the other hand, the photolysis of which in methanolic solution leads to ammonium azide, it should be possible to intercept the intermediates, since several exothermic and endothermic rearrangements are observed here, depending on the exposure time and concentration. According to investigations carried out



so far[3,70], excited HN_3 should first give diimide *(18)* in this case, but a side reaction with methanol should also lead by formal insertion of NH to the unstable aminomethanol *(19)*, which would give formaldehyde by loss of ammonia, and methylimine *(20)* by loss of water.

6. Behavior of the Ozonide-Like Epidioxydihydrofurans (5,6,7-Trioxanorbornenes)

A reaction that proceeds rapidly even at very low temperatures in solution is the photosensitized cycloaddition of oxygen to the furan ring[2,5,66,71]. This process, which is of the Diels-Alder type, leads initially to the ozonide-like epidioxydihydrofurans *(21)* with a vanishingly small activation energy. However these are generally no longer stable at 20 °C, and only reaction products or polymeric peroxides are isolated. Only in the case of diphenylisobenzofuran has the oxonide-like peroxide *(22)* (which is explosive above 20 °C)

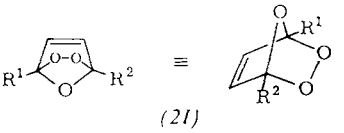


(21)

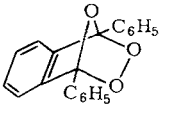
been isolated in the crystalline form[72]. *(21a)*, $R_1 = R_2 = H$, the mono-oxonide of cyclobutadiene, which is the simplest member of this new class of compounds, was isolated at −100 °C[5]. Similar compounds are known in the cyclobutane series[73–75].

On exposure to light in methanol at 20 °C, 2-methyl-, 2,5-dimethyl-, 1,2,3,4,5,6,7,8-octahydrodibenzo-, and 3,6-dimethyl-4,5,6,7-tetrahydrobenzo[b]furan (menthofuran) give the alkoxyhydroperoxydihydrofurans *(25)* and *(26)* as stable products of the addition of methanol to the initially formed ozonides[71].

The malealdehydic acid pseudoester *(34)* is formed as the stable end product from furan in methanol. This product is also formed, after removal of the side chain, from furfural, furfuryl alcohol, furfuryl methyl ether, and *N*-acetylfurfurylamine[5,43,66–68].



(21)



(22)

The peroxide of ethyl furan-2-carboxylate decomposes by a different route. The side chain is again removed, but maleic acid and the monoester of maleic acid *(30)* are formed as well as the cyclic reaction product *(29)* ($R^2 = H$)[76,77].

This tendency to form open-chain decomposition products is also found with furfurylamine, which presumably gives β-glycylacrylic acid [*(27)*, $R^2 = CH_2NH_2$] as the principal product, together with 3-hydroxypyridine[43,76,78]. However, dimeric and polymeric products are also formed.

Reduction of the epidioxide solutions obtained below −30 °C from furan, 2-methylfuran, and 2,5-dimethylfuran with triphenylphosphine in the cold gave 1,4-dicarbonyl compounds[5,66,71] [reaction (2a)].

Various reaction products, some built up from two or more furan rings, have been isolated on conventional working-up of the photo-oxidized solutions. Owing to the many possible reactions of the furan ring[79], the yields of identifiable products were often by no means quantitative, high molecular weight resinification products being obtained instead. A large part of these products was presumably due to the increase in the

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[72] *Ch. Dufraisse* and *S. Ecary*, C. R. hebd. Séances Acad. Sci. *223*, 735 (1946).

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[76] *G. O. Schenck*, Angew. Chem. *64*, 12 (1952).

[77] *R. Brammer*, Dissertation, Universität Göttingen 1953.

[78] *G. O. Schenck* and *G. Stengel*, unpublished.

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contribution of bimolecular processes on concentration. It therefore seemed to us that the fastest and most reliable method of identifying the individual reaction

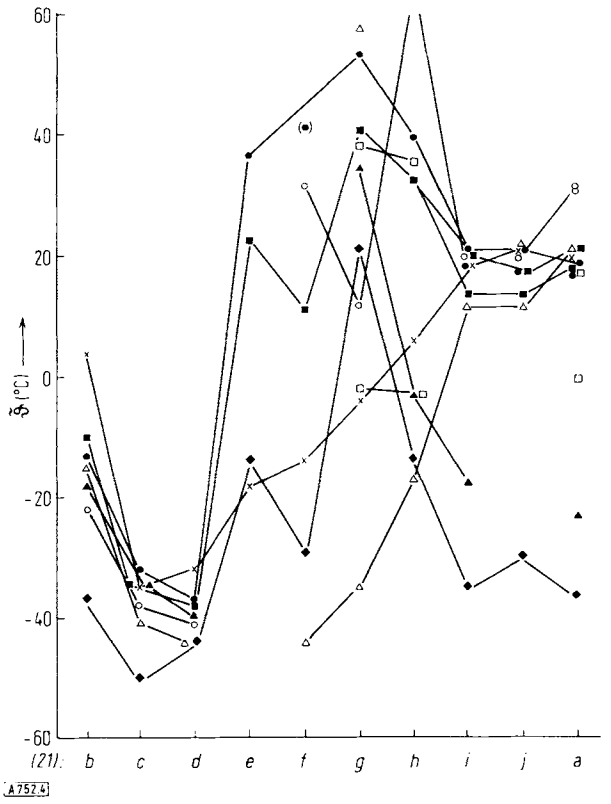


Fig. 4. Reaction temperatures $\tilde{\vartheta}$ of the epidioxydihydrofurans *(21a)* to *(21j)* and influence of added components. Standardized heating rate $\dot{\vartheta}$ = 1.5 °C/min. Several measurement points for one compound and one type of reaction or one solvent means that several reactions take place consecutively and at different temperatures.
● = rearrangement in THF; ■ = rearrangement in THF after addition of 70 moles of CH_3OH/mole of *(21)*; □ = rearrangement in THF after addition of ≈ 70 moles of H_2O/mole of *(21)*; ▲ = reduction in THF with ≈ 1.25 mole of $P(C_6H_5)_3$/mole *(21)*; ● = reduction in THF with ≈ 5 moles of $P(C_6H_5)_3$/mole of *(21)*; × = addition or rearrangement in CH_3OH; o = rearrangement in toluene; △ = rearrangement in toluene after addition of 40 mole of CH_3OH/mole of *(21)* and 1 mole of HCl/mole of *(21)*.

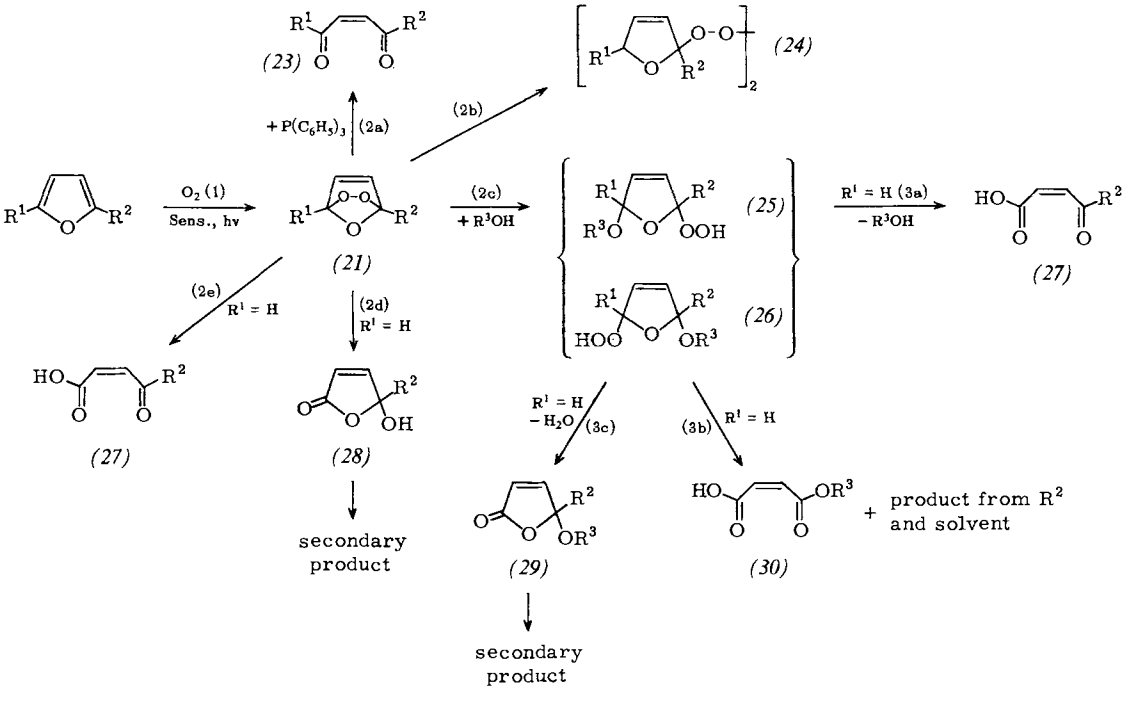
(21)	Group	R^1	R^2	R^3
a	2	H	H	H
b	3	H	CH_2NH_2	H
c	3	H	CH_2NHCH_3	H
d	3	H	$CH_2N(CH_3)_2$	H
e	1	CH_3	H	CH_3
f	1	H	$CH=CH_2$	H
g	1	CH_3	CH_3	H
h	1	H	CH_3	H
i	2	H	CH_2OH	H
j	2	H	CH_2OCH_3	H
k	2	H	CHO	H

steps would be to examine the epidioxydihydrofurans formed in dilute solution and at low temperatures over a wide temperature range by differential calorimetry.

The photochemical synthesis of the oxonide-like peroxides was carried out in methanol, toluene or tetrahydrofuran at −85 °C under pure oxygen (furan: 0.05 to 0.5 mole/l, sensitizer: Bengal pink or diacenaphthyleno [1,2-*b*; 1′,2′-*d*] thiophen (dinaphthylenethiophen), 2×10^{-4} to 3×10^{-4} mole/l). 1 mole of O_2 was taken up per mole of furan with a quantum yield $\varphi \approx 1$.

The thermograms of the solutions kept at −85 °C show three typical behavior patterns between −85 and +50 °C, so that the epidioxides *(21)* investigated here can be divided into three groups (Fig. 4).

Group 1: The epidioxides from 2-alkyl and 2,5-dialkylfurans give a weakly exothermic reaction in methanol at $\tilde{\vartheta}$ = −40 to −10 °C. The heat effects, which are found to be 5–10 kcal/mole, correspond to the addition of methanol to the hydroperoxymethoxydihydrofurans *(25)* and *(26)* (which have already been isolated in some cases) with cleavage of the peroxide bridge [71]. The suggested reaction course [5,71] is thus also confirmed by energy considerations for group 1 [see reaction (2c) and further reactions]. Whereas the hydroperoxides *(25)* and *(26)* generally remain unchanged up to room temperature, the hydroperoxide of 2-vinylfuran, which can be isolated at +20 °C, tends to polymerize [37].



The tendency toward the formation of dimers and polymers [reaction (2b)] is small for the compounds of group 1 in methanol, since the addition (2c) proceeds with first order kinetics. The epidioxide *(21g)* of 2,5-dimethylfuran forms a dimer in apolar solvents such as toluene and petroleum ether [71] [reaction (2b)]. The other epidioxides of group 1 react under these conditions or in tetrahydrofuran only at higher temperatures and in a more complicated manner, in some cases with small heat effects or endothermically.

Group 2: Furan, furfural, furfuryl alcohol, and furfuryl methyl ether behave differently. The reaction in methanol is strongly exothermic (60–70 kcal/mole, formally first order) at $\tilde{\vartheta}$ values of about 10 to 30 °C. 5-Methoxy-2(5*H*)-furanone [*(29)*, R^2=H, R^3=CH_3; reactions (2c) and (3c)] is formed.

Group 3: These compounds are characterized by the formation of open-chain reaction products. Strongly exothermic reactions occur in methanol, toluene, or tetrahydrofuran even at reaction temperatures $\tilde{\vartheta}$ of −40 to −10 °C. In contrast with the reactions of other groups, this reaction has an order of >2 in more concentrated solutions (> 0.2 mole/l). The solutions become dark above about −20 °C, owing to the formation of high molecular weight products or resins. The heats of reaction increase with increasing dilution up to a maximum of ≈85 kcal/mole, while the reaction order falls from ≈3 almost to 1 (Fig. 5a and 5b). These observations are readily reconciled with the assumption

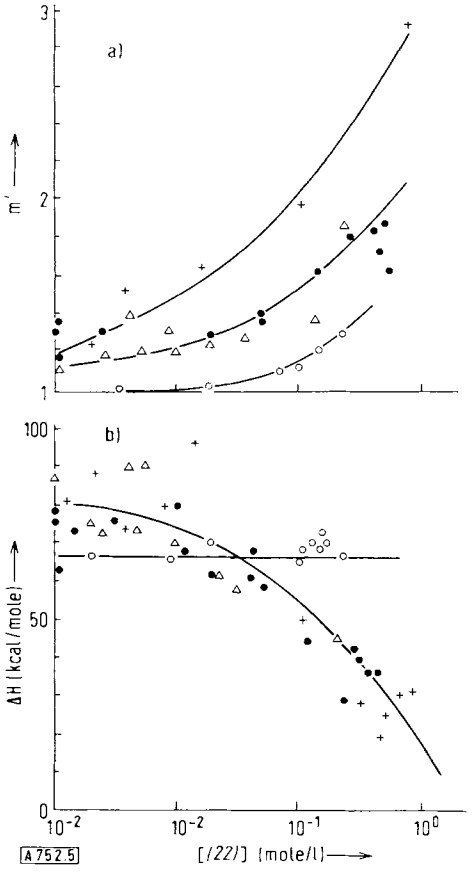


Fig. 5. a) Apparent reaction order m' in the decomposition of the epidioxydihydrofurans at various concentrations. b) Reaction enthalpy for the decomposition of epidioxydihydrofurans at various concentrations. Solvent: methanol. o = *(21a)*; ●: *(21b)*; +: *(21c)*; △: *(21d)*.

of the simultaneous occurrence of a strongly exothermic unimolecular reaction (type c in Fig. 3) and a weakly exothermic bimolecular reaction sequence (type e in Fig. 3) (cf. Section 6.1).

If the reaction mixture is allowed to come slowly to 20 °C and is then carefully worked up, the reaction products contain no methoxy groups. Nevertheless, the question arises whether the cleavage of the peroxide bridge in *(21)* is introduced by addition of methanol and whether the addition and the subsequent reactions, as in the case of furan, take place in practically the same temperature range.

6.1. Formation of the Hydroperoxides

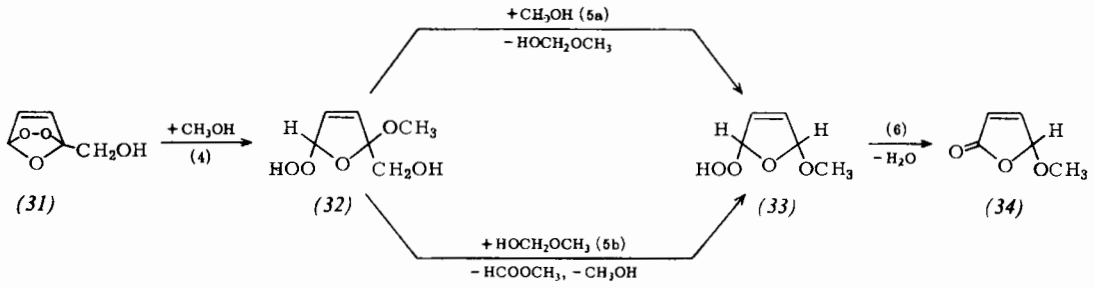
With the block temperature kept constant at −90 °C, we added 0.5 ml of methanol to the epidioxides prepared in 5 ml of toluene or THF at −90 °C and to the reference solution. Distinct heat effects (ΔH = 5–15 kcal/mole) occurred for furfurylamine, *N*-methyl- and *N*,*N*-dimethylfurfurylamines, furfuryl alcohol, and furfuryl methyl ether. These point to a reaction between the methanol and the epidioxides with formation of the methoxy hydroperoxides *(25)* and *(26)*.

The homogeneity of the solutions in THF allows the reactions to be followed kinetically. Their rate constants are between 3×10^{-3} and 10×10^{-3} mole·l^{-1}·s^{-1}; with a plausible A factor of 5×10^{10} mole·l^{-1}·s^{-1} this would correspond to activation energies of only 10–15 kcal/mole. Compounds of group 1 undergo appreciable addition of methanol only above −40 °C. The ease of cleavage of the peroxide bridge is evidently greatly increased in 2-substituted epidioxydihydrofurans by functional groups in the substituent.

On preparative low-temperature working-up of epidioxide solutions of furfuryl alcohol and furfuryl methyl ether, removal of the methanol by distillation below −30 °C and high-vacuum sublimation at 0 °C gave unstable colorless oils, which were identified as hydroperoxides [37]. However, differential thermal analyses showed conclusively that the hydroperoxide of furfuryl alcohol (5-hydroperoxy-2-furanylmethanol) undergoes a change at −20 °C, with loss of the side chain, to reach the energy stage of malealdehydic acid [reactions (5a) and (6)].

The formaldehyde hemiacetal formed in reaction (5a) evidently reacts with further hydroperoxide to give the furanone *(34)* and methyl formate, which is also detected [reactions (5b) and (6)].

The thermograms of 5-hydroperoxy-2-furanylmethanol in THF, both in the presence and in the absence of methanol, have a double maximum at $\tilde{\vartheta}$ = +22 °C (heating rate $\dot{\vartheta}$ = 1.5 °C/min) that is practically inseparable (type h in Fig. 3). This suggests on the one hand that the loss of the side chain may occur even without methanol by formaldehyde formation shortly before the loss of water, and on the other that the 2-hydroperoxy-5-methoxy-2,5-dihydrofuran *(33)* formed above −20 °C in reactions (5a) and (5b) exists for a short time.

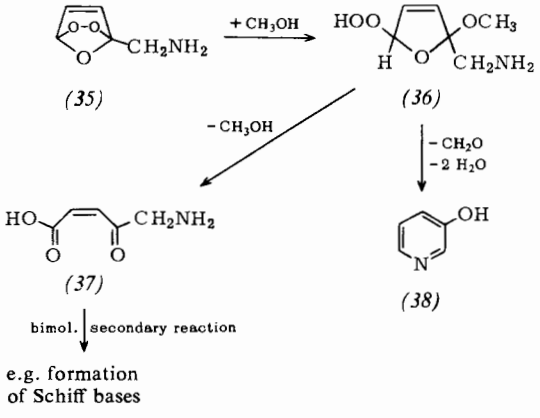


The epidioxydihydrofuran *(21a)* in methanol also gives two maxima situated close together at roughly equal reaction temperatures. However, since methanol adds to *(21a)* only at $\vartheta = 20\,^{\circ}C$ (cf. above and Fig. 4), the first maximum in this case must be assigned to the formation of the hydroperoxide, and the second to its fragmentation to give the furanone *(34)*.

If water is added instead of 10 % of methanol to a solution of *(21a)* in THF, the analogous reaction takes place at $\approx 2\,^{\circ}C$. The difference between the reaction temperatures of the two maxima increases from 2 to 20 °C, and the reaction enthalpy for the addition of water is about 5 kcal/mole.

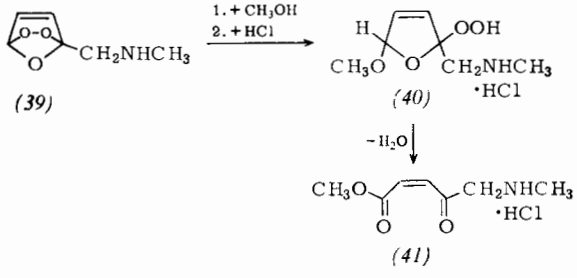
The epidioxide of furfuryl methyl ether behaves in a similar manner to that of furfuryl alcohol. Methanol is added at −90 °C, but the loss of the side chain occurs only above −20 °C, and is immediately followed by that of water to give the furanone *(34)*, as can again be seen from the presence of a double maximum. The last two reactions take place at roughly the same temperature as the reactions of the epidioxide of furan and furfuryl alcohol, since *(33)* again occurs as an intermediate. Two similar reactions also occur in the case of furfural.

Different behavior is found for furfurylamine. Methanol addition products are formed at −85 °C; these products are stable up to $\approx$ −40 °C, and must consist mainly of 2-(aminomethyl)-5-hydroperoxy-2-methoxydihydrofuran *(36)*, since the final product formed above −20 °C, *i.e.* β-glycylacrylic acid *(37)*, is obtained unesterified, though in dimerized and more highly condensed forms [37].



3-Hydroxypyridine *(38)*, which has also been found on low-temperature working-up of photo-oxidized methanolic furfurylamine solutions [37], could also be formed from the hydroperoxide *(36)* in a side reaction [76, 78]. Unlike the removal of the side chain in the cases of furfural, furfuryl alcohol, *etc.* this rearrangement would have to begin with a ring cleavage before the pyridine ring can be closed by the still bound methanol.

The epidioxide of *N*-methylfurfurylamine *(39)* also adds methanol at −90 °C to give a methoxyhydroperoxide that is partly precipitated as the hydrochloride *(40)* on addition of methanolic HCl at this temperature [37]. *(40)* decomposes slowly (half life $\approx$ 1 h) even at −50 °C, so that a rapidly recorded IR spectrum (the sample temperature rises to at most −20 °C during the recording) contains bands due to the decomposition product *(41)*.



It is surprising to find that the arrangement of the OCH_3 and OOH groups here is evidently opposite to that in the product from furfurylamine; the isomeric product may be too soluble to be precipitated as the salt from methanol, or the isomer ratio may depend on the pH value.

In the case of epidioxides of group 3, the concentration dependence of the heat of reaction and reaction order show particularly clearly that the pure unimolecular formation of the β-glycylacrylic acids, which makes the greatest energy contribution, occurs preferentially only in very dilute solution. In more concentrated solutions, *i.e.* on working up *e.g.* by evaporation of the solvent, different, bimolecular processes become predominant. Owing to the reaction orders of much more than 2 in some cases in the thermograms, repeated reactions with the starting material (type e in Fig. 3) must occur in this case.

The much more inert epidioxides of the 2- and 5-substituted alkylfurans are appreciably more reactive in the presence of HCl, as is shown by the depression of the reaction temperatures by 20 to 40 °C (Fig. 4). In the case of 2,5-dimethylfuran, the methoxy hydroperoxide [*(25)*, $R^1=R^2=CH_3$], which is normally stable at $\approx$ 50 °C, decomposes at this temperature.

Water is also added much more rapidly than methanol by the alkylfurans (Fig. 4). The reaction enthalpy also

indicates that the 5-hydroperoxydihydrofuran-2-ols are to be expected here. The thermogram (type *f* in Fig. 3) allows an approximate separation of the double maximum. However, the kinetics of the reaction with water have not yet been fully elucidated, since the reaction order cannot be determined directly owing to the overlap. Unrealistically high frequency factors result if a bimolecular reaction is assumed. It is nevertheless found that the intermediates are stable below −10 °C.

6.2. Enthalpies of Formation of the Epidioxydihydrofurans

Further confirmation of the views developed is provided by the calculation of the enthalpies of formation of the ozonides *(21)* from the enthalpies of formation of the final products and the reaction enthalpies ΔH. These quantities cannot be determined by conventional methods, since the explosive pure ozonides can be handled only at very low temperatures (below −80 °C), and even then not without danger.

However, the heat effects in dilute solutions can be determined by DTA. Despite the diversity of the final products, the heats of formation found for the epidioxides *(21a)* and *(21e)—(21k)* (groups 1 and 2) differ only slightly from those estimated from the bond increments[80] if −50 kcal/mole is used in the calculation for the peroxide bridge (Table 1)[81].

The deviations are partly explained by the fact that the same increment is used in every case, since the peroxide bridge should be weakened with increasing polarization by asymmetric substitution in position 2. Moreover, side reactions may lead to polymeric peroxides, which should give much lower energy values than the isomerization to give the malealdehydic acid.

Table 1. Enthalpies of formation of unstable epidioxydihydrofurans and kinetic parameters of their cleavage. Solvent: methanol. A = action constant (s^{-1}).

Epidioxide *(21)*	Enthalpy of formation (kcal/mole) calc.	meas.	Activation energy (kcal/mole)	log *A*
Group 1				
e	− 81.7	− 77.0	17.0	7.5
f	− 47.2	− 53.4	≈16	10.8
g	− 80.6	− 89.0	20.2	10.1
h	− 71.7	− 82.5	20.0	10.2
Group 2				
a	− 62.8	− 63.6	20.0 [a]	10.2
i	−106.7	−101.7	12.7	(11)
j	−121.7	−117.4	13.1	(11)
k	− 94.5	−101.4	—	—
Group 3				
b	− 63.8	− 17.4	12.5	(11)
c	− 64.7	− 17.5	13.1	(11)
d	− 67.7	− 20.5	13.8	(11)

[a] Practically the same value is found with ethanol, propanol, and butanol as solvents, while the action constants decrease.

It is clear in the case of the epidioxide *(21j)* of furfuryl methyl ether that here, in contrast with that of furfuryl alcohol *(21i)*, the formaldehyde acetal formed no longer reacts further with the hydroperoxide; this is supported by preparative results. The enthalpy of formation of *(21a)* (≈ −60 kcal/mole) has recently been verified by compensation of the energy liberated during the photo-oxidation with a calibrated Peltier element[82].

Thus the validity of reactions (1), (2a), (2c), and (3a)—(3c) for the examples described here is also demonstrated on energy grounds (see also Section 6.3).

The measured heats of formation of the nitrogenous epidioxides *(21b)—(21d)* of group 3 differ by 46 to 48 kcal/mole from the expected values. However, the final products, being amino acids, exist partly in the form of zwitterions in solution; much more positive values must therefore evidently be used for their energies of formation than those calculated from the increments.

6.3. Reduction of the Epidioxydihydrofurans with Triphenylphosphine

The epidioxides examined differ in their reactivity to triphenylphosphine (Fig. 4)[83,84]. Whereas the compounds of groups 2 and 3 react even below −60 °C ($\tilde{\vartheta}$ = −50 to −30 °C), the reaction temperatures for group 1 are much higher (−30 to +21 °C). The reactivity of the epidioxydihydrofuran *(21a)* is thus increased by the *N*-methylaminomethyl or aminomethyl group in position 2, but greatly decreased by an alkyl group. The epidioxide *(21g)* of 2,5-dimethylfuran reacts only at $\tilde{\vartheta}$ = +21 °C, and is thus the least reactive.

This cannot be due to the absence of polarization of the peroxide bridge, since furan itself reacts very readily ($\tilde{\vartheta}$ = −36 °C); it is probably caused by steric factors.

By comparison of the heats of formation ΔH_f of compounds such as Br_3P, Br_3PO, Cl_3P, and Cl_3PO[60], a heat effect $-\Delta H_{PO}$ of about 70–80 kcal is found for

$$(C_6H_5)_3P + 1/2\ O_2 \xrightarrow{+\Delta H_{PO}} (C_6H_5)_3PO$$

Approximately the same values are obtained from the thermoanalytically determined heat effects if it is assumed that vicinal diacylethylenes such as *(23)* are formed. Occasional deviations are explained by a different reaction course, *e.g.* by partial loss of side chains in the cases of furfuryl alcohol and furfuryl methyl ether, by bimolecular competing reactions in the case of *N,N*-dimethylfurfurylamine, or by solvation effects in general. The initial step is almost conclusively the formation of the unsaturated 1,4-dicarbonyl compound such as *(23)*. However, it is difficult to obtain[71] in good yields because of its sometimes considerable reactivity.

6.4. Comparison of the Kinetic and Energetic Results

The formally different processes of bimolecular addition [reaction (2c)] and monomolecular decomposition of the hydroperoxides [(reactions (3a)/(3c)] and the re-

[80] *d'Ans-Lax*: Taschenbuch für Chemiker und Physiker. Vol. II: Organische Verbindungen, 3. Edit., Springer, Berlin 1964, p. 1047.

[81] *W. Pritzkow* and *K. A. Müller*, Chem. Ber. *89*, 2318 (1956).

[82] *E. Koch*, Angew. Chem. *79*, 998 (1967); Angew. Chem. internat. Edit. *6*, 978 (1967).

[83] *L. Horner* and *W. Jurgeleit*, Liebigs Ann. Chem. *591*, 138 (1953).

[84] *L. Horner* and *H. Hoffmann*, Angew. Chem. *68*, 473 (1956).

arrangement of the epidioxydihydrofurans [reactions (2d)/(2e)] can proceed only with cleavage of an O–O bond. Similar activation energies (around 20 kcal/mole) are often found for the addition to furans and alkylfurans (Table 1). The ease of cleavage of the O–O bond does not appear to be strongly influenced either by alkyl substituents on the furan ring or by the nature of the alcohol added. The activation energy, and hence also the reaction temperature (Fig. 4), of the alkylfurans is distinctly increased only in the absence of polar addends when the process is carried out in tetrahydrofuran or toluene.

Asymmetrical substitution with functional groups strongly reduces the activation energies for addition and decomposition. The hydroperoxides of groups 2 and 3 are formed even at −90 °C and decompose well below 0 °C and below −20 °C respectively. In the cases of *N*-methylfurfurylamine and *N*,*N*-dimethylfurfurylamine, the epidioxides and hydroperoxides are so unstable that bimolecular reactions can no longer occur (Fig. 4).

The frequency factors are of the expected order of magnitude of $10^{14} - 10^{15}$ s^{-1} for the decomposition of the hydroperoxides [85], and much lower in some cases for the epidioxides (Table 1).

The energy diagram (Fig. 6) shows the sums of the heats of formation of all the compounds and transition states involved in the reaction sequence (1) → (2c) → (3c) for furan, as found from the measured enthalpies and activation energies. After the absorption of a photon by the sensitizer, the oxygen is first brought into the $^1\Delta g$ state [2, 48, 86], which lies 22.6 kcal/mole above the ground state. Practically no further activation energy is required for the cycloaddition to the acceptor [2, 45], and 50 kcal/mole are in fact immediately liberated. The hydroperoxide can be formed if a further 20 kcal/mole are supplied; this is so only above

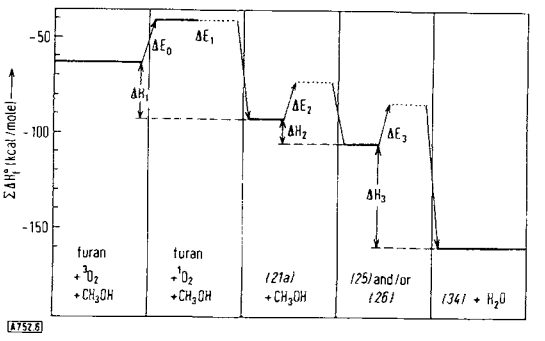


Fig. 6. Arrhenius activation energies and reaction enthalpies for the photosensitized cycloaddition of O_2 to furan (schematic). (All values in kcal/mole).

$\Delta E_0 = 22.6$
$\Delta E_1 = 0.2$ $\quad \Delta H_1 = -30$(g) -26(liq.)
$\Delta E_2 = 20.0$ $\quad \Delta H_2 = -13$(g) $- 2.4$(liq.)
$\Delta E_3 = 21$ $\quad \Delta H_3 = -54$(g) -67(liq.)

−20 °C. At this temperature, however, water is eliminated with an activation energy that is also around 20 kcal/mole [reaction (3c)]. The final product is immediately formed with liberation of a further 55–60 kcal/mole.

The activation energies of the hydroperoxide formation for all the substituted furans examined are much lower than those of the decomposition reactions. The hydroperoxides can therefore be isolated in favorable temperature ranges in these cases.

The stimulus for instrumental development in the field of low-temperature photochemistry came from Professor G. O. Schenck. I am grateful to him and to Prof. Dr. O. E. Polansky, G. von Bünau, F. Schaller, M. Barthels, G. Lindner, and H. Siepmann for their support, valuable advice, and stimulating discussions.

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COMMUNICATIONS

Ethyl 2-Oxazoline-5-carboxylate from Ethyl Isocyanoacetate and Carbonyl Compounds[1]

By *Dieter Hoppe* and *Ulrich Schöllkopf*[*]

Ethyl 2-oxazoline-4-carboxylates *(6)* are readily hydrolyzed to serines [2, 3] and are of particular interest as model substances for the study of base-induced electrocyclic ring-opening [4].

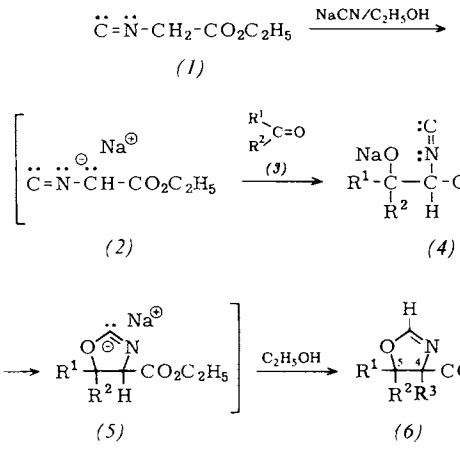
The esters *(6)*, R^3 = H, cannot be prepared by a method given previously in the literature [5] for the synthesis of oxazolines, since, under the conditions mentioned, they are converted by ring scission into the β-substituted ethyl α-formylaminoacrylates [4]. They can be prepared in good yields, however, by treating ethyl isocyanoacetate [6] *(1)* in ethanol with carbonyl compounds *(3)* in presence of a small amount of (suspended) sodium cyanide. The catalyst undergoes partial alcoholysis and thus provides a weakly basic medium in which *(1)* is partially converted into its sodium derivative *(2)*, the (alkali-labile) oxazolines *(6)*, R^3 = H, on the other hand, not undergoing any further decomposition. Presumably, in addition to *(2)*, the carbonyl adducts *(4)* and the metalated oxazolines *(5)* are present as intermediates.

Reaction with aldehydes leads almost exclusively to formation of the *trans* compounds, which on hydrolysis afford the *threo* forms of the β-substituted serines.

As experiments with ethyl α-isocyanopropionate and formaldehyde, acetone, or benzaldehyde have shown, the method is also applicable to α-substituted ethyl isocyanoacetates.

Ethyl trans-5-phenyl-2-oxazoline-4-carboxylate (6c):

A solution of ethyl isocyanoacetate [6] (4.52 g, 0.04 mole) and benzaldehyde (4.26 g, 0.04 mole) in dry ethanol (15 ml) is added dropwise with vigorous stirring at 15 °C to a suspension of sodium cyanide (0.25 g) in dry ethanol (10 ml). The mixture is stirred for one hour and the solvent is then removed (water-jet vacuum, bath temp. 50–80 °C). The residue is taken up in carbon tetrachloride (50 ml) and the



(1) (2) (4) (5) (6)

Ethyl-2-oxazoline-4-carboxylates *(6)* prepared.

	R^1	R^2	R^3	*T* (°C)	*t* (h)	*trans* : *cis*	Yield (%)
(a)	H	H [a]	H	30	0.5		53
(b)	CH_3	H	H	40	0.5	>10 : 1	55
(c)	C_6H_5	H	H	15	1	>20 : 1	72
(d)	CH_3–CH=CH	H	H	−10	0.5	>10 : 1	15 [d]
(e)	$(CH_3)_2CH$	H	H	0	0.5	>10 : 1	71
(f)	CH_3	CH_3	H	reflux	1		47
(g)	$-(CH_2)_5-$		H	30	0.5		75
(h)	H	H [a]	CH_3 [b]	30	1		67
(i)	CH_3	CH_3	CH_3 [b]	reflux	1		70
(j)	C_6H_5	H	CH_3 [b]	25	0.5	0.4 : 1 [c]	86

[a] HCHO used as paraformaldehyde. [b] With ethyl α-isocyanopropionate. [c] *cis* and *trans* refer to ethoxycarbonyl and phenyl. [d] Polymerizes on distillation; crude yield higher.

resulting solution allowed to stand for 30 mins at 0 °C, filtered, and the filtrate fractionated. 6.3 g (72%) of *(6c)*, b.p. 112 °C/0.2 torr (according to the NMR spectrum > 95% *trans* form), is obtained [NMR spectrum (CCl_4): =CH, τ = 3.1 (d, *J* = 2 Hz); IR spectrum (film): 1620 cm^{-1} (νC=N), 1735 cm^{-1} (νCO)].

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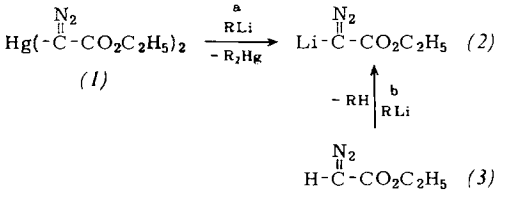
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Ethyl Lithiodiazoacetate[1]

By *Ulrich Schöllkopf* and *Hubert Frasnelli* [*]

In spite of the extensive work that has been carried out in diazo chemistry[2] there is still a lack of methods available for exchange of ligands attached to the carbon atom of readily accessible diazomethyl compounds. Since a *C*-lithium atom is replaceable by a variety of other substituents[3], we have directed our attention toward possible routes leading from diazo compounds to *C*-lithium derivatives[4].

We have now found that ethyl lithiodiazoacetate *(2)* is obtained when a) diethyl mercuriobis(diazoacetate)[5] *(1)* in tetrahydrofuran is allowed to react at *ca.* −70 °C with phenyl- or butyllithium or with lithium thiolates, or b) ethyl diazoacetate *(3)* is metalated at −110 °C in ether or ether/tetrahydrofuran. The lithium compound *(2)* is stable only below −50 °C[6]; it can be intercepted, *e.g.*, by trialkylstannyl or trialkylsilyl chlorides, by carbonyl compounds, or by alkyl halides and thus be utilized in preparative work. Since method a) is relatively involved and not without attendant danger, owing to the poisonous nature of the mercury compounds formed, metalation according to b) is probably the more suitable method for preparative purposes.



(1) (2) (3)

Preparation and reactions of *(2)*.

R	Intercepting reagent	Interception product	Yield (%) in method a	b
C_4H_9	$(CH_3)_3SiCl$	ethyl trimethylsilyl-diazoacetate	15	52
C_6H_5	$(CH_3)_3SiCl$	ethyl trimethylsilyl-diazoacetate	47	
$(CH_3)_3CS$	$(CH_3)_3SiCl$	ethyl trimethylsilyl-diazoacetate	40	
C_2H_5S	$(CH_3)_3SiCl$	ethyl trimethylsilyl-diazoacetate	25	
C_4H_9	$(C_4H_9)_3SnCl$	ethyl tributylstannyl-diazoacetate	61	50
C_4H_9	C_6H_5COCl	ethyl benzoyldiazo-acetate	20	45
C_4H_9	CH_3I	ethyl 2-diazo-propionate	35	
C_4H_9	CH_2=CH–CH_2I	ethyl 2-diazo-4-pentenoate	45	
C_4H_9	C_6H_5CHO	ethyl 2-diazo-3-hydroxy-3-phenyl-propionate		41
C_4H_9	cyclohexanone	ethyl 2-diazo-2-(1-hydroxycyclo-hexyl)acetate		62
C_4H_9	C_6H_5–CO–CH_3	ethyl 2-diazo-3-hydroxy-3-phenyl-butyrate		50

Ethyl 2-diazo-3-hydroxy-3-phenylpropionate

A solution containing 47 mmoles of butyllithium (21.5 ml of a 2.2 M solution in pentane) precooled to −70 °C is added dropwise at −110 °C to a solution of ethyl diazoacetate (5.47 g, 47 mmoles) in ether (150 ml) and tetrahydrofuran (50 ml) over a period of 30 min. A solution of benzaldehyde (5 g, 47 mmoles) in tetrahydrofuran (30 ml) which has been cooled to −70 °C is then added dropwise at −110 °C and the reaction mixture is allowed to warm to −25 °C, whereupon a solution of glacial acetic acid (2.85 g, 47 mmoles) in tetrahydrofuran (30 ml) that has been cooled to −70 °C is also added. On reaching room temperature, the solution is filtered and the solvent removed under water-pump vacuum (rotary evaporator, 30 °C). The residue is taken up in 500 ml of light petroleum (b.p. 40–50 °C) and shaken with *ca.* 1 g of active charcoal. After filtration the solvent is removed under water-pump vacuum. There remained 4.3 g (41%) of crude ethyl 2-diazo-3-hydroxy-3-phenylpropionate [IR spectrum (film): 3500 (νOH), 2100 (νN_2), 1680 (νCO) cm^{-1}; NMR spectrum

(CCl_4): τ = 2.52 (m), 4.24 (s), 5.82 (s), 5.4 (q), 8.77 (t)]. — A part of the residue was purified by chromatography on aluminum oxide (neutral, activity grade 3), elution with light petroleum first affording a little benzaldehyde and subsequent elution with ether yielding the diazo compound.

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[1] Metal-Substituted Carbenes and *C*-Metalated Diazoalkanes, Part 4. — Part 3: *U. Schöllkopf, D. Hoppe, N. Rieber,* and *V. Jacobi*, Liebigs Ann. Chem. *730*, 1 (1969).

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1-*tert*-Butylvinyl Trifluoromethanesulfonate: Solvolysis and Rearrangement *via* a Vinyl Cation[**]

By *Antonio Garcia Martinez, Michael Hanack, Richard H. Summerville, Paul von Ragué Schleyer,* and *Peter J. Stang*[*]

Solvolysis of simple acyclic and cyclic vinyl halides and vinyl sulfonates could proceed *via* vinyl cations as intermediates[1]. Formation of rearranged solvolysis products would indicate such a reaction course.

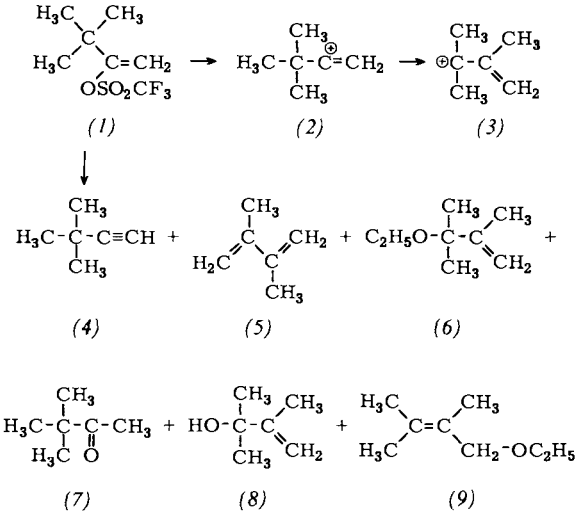
Rearrangements of vinyl cations generated by protonation of alkynes are known[2]; in contrast, occurrence of isomerizations of this kind during the solvolysis of simple acyclic vinyl derivatives has not hitherto been described[3].

For the generation of vinyl cations by solvolysis of vinyl sulfonates the fast-reacting trifluoromethanesulfonates[4] prove particularly suitable[5]. We now report on the solvolysis of 1-*tert*-butylvinyl trifluoromethanesulfonate *(1)* which gives rise to rearranged products.

Compound *(1)* was prepared by slow dropwise addition of trifluoromethanesulfonic acid[6] at —20 °C to 3,3-dimethyl-1-butyne *(4)*. After 30 min the reaction mixture was neutralized by addition of a solution of $NaHCO_3$ and extracted with ether. The extract was dried, and after evaporation of the ether, compound *(1)* could be isolated by distillation [yield 40–60%, b.p. 45–50 °C/15 torr; NMR spectrum: τ = 4.95 (2H/q, J = 4 Hz); 8.80 (9H/s)]. *(1)* was found to be homogeneous on gas chromatography (3 m polyethylene glycol 20000, 10%, column, 100 °C); no rearrangement products were formed during the addition.

Compound *(1)* was solvolyzed in pyridine-buffered 80% aqueous ethanol for three days at 80 °C. There were formed: 27% of 3,3-dimethyl-1-butyne *(4)*; 13% of 2,3-dimethylbutadiene *(5)*; 24% of 3-ethoxy-2,3-dimethyl-1-butene *(6)*; 1% of pinacolone *(7)*; 10% of 2,3-dimethyl-3-buten-2-ol *(8)*; and 25% of higher boiling substances (mean values from five experiments). After separation by gas chromatography the products were identified, *inter alia*, by their NMR, IR, and mass spectra, and by comparison with authentic samples (except for *(6)*).

On solvolysis of *(1)* in non-buffered 50% aqueous ethanol (75 °C, 4 h) we obtained 76% of *(4)*, 14% of *(5)*, 1.5% of *(6)*, 2% of *(7)*, 1.5% of *(8)*, and 5% of 1-ethoxy-2,3-dimethyl-2-butene *(9)*.



(1) *(2)* *(3)* *(4)* *(5)* *(6)* *(7)* *(8)* *(9)*

The formation of the rearranged products *(5)*, *(6)*, *(8)*, and *(9)* proves the intermediacy of a vinyl cation *(2)*, which is converted into the more stable ion *(3)* by migration of a methyl group. *(3)* yields the butadiene *(5)* by elimination, and the ethers *(6)* and *(9)*, as well as the alcohol *(8)*, by substitution. The major product *(4)* can, in principle, also arise from the vinyl cation *(2)*; however, a concerted elimination reaction of *(1)* with the solvent as base cannot be ruled out[7].

The reaction of the trifluoromethanesulfonate *(1)* in 50% aqueous ethanol was characterized by a rate constant k = 9.14×10^{-4} s^{-1} (at 75.4 °C) and k = 6.03×10^{-5} s^{-1} (at 50.4 °C); $\Delta H^{\neq}$ = 23.7 kcal/mole; $\Delta S^{\neq}$ = —4.8 e.u. Thus *(1)* reacts three times as fast as isopropenyl trifluoromethanesulfonate, which was solvolyzed by *Stang* and *Summerville*[5b] under the same conditions (k = 1.95×10^{-5} s^{-1} at 50 °C).

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[5] a) *W. M. Jones* and *D. D. Maness*, J. Amer. chem. Soc. *91*, 4314 (1969); b) *P. J. Stang* and *R. Summerville, ibid. 91*, 4600 (1969).

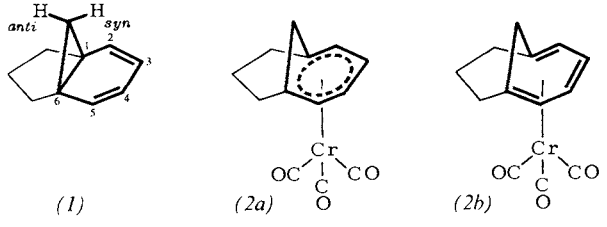
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Tricyclo[4.3.1.0^{1,6}]deca-2,4-dienetricarbonylchromium, a Homoaromatic Transition Metal Complex

By *Wolf-Eckhard Bleck*, *Wolfram Grimme*, *Harald Günther*, and *Emanuel Vogel*[*]

Classification of the norcaradiene hydrocarbon tricyclo-[4.3.1.0^{1,6}]deca-2,4-diene[1] *(1)*, which owes its existence to the bracketing effect of the trimethylene group, as a homoaromatic compound[2], *i.e.* a derivative of the hypothetical species homobenzene, appears unjustifiable on the basis of its chemical and spectral properties[1,3]. However, if *(1)* assumes the role of a ligand in a transition metal complex whose central atom bonds preferentially to a 6π-system, the electrons of the double bonds and the three-membered ring might reorganize to give a homoaromatic structure [as in *(2a)*] or, alternatively, a cycloheptatriene structure [as in *(2b)*]. Synthesis and structure of a carbonylchromium complex of *(1)* warrant attention in this respect.



(1) *(2a)* *(2b)*

Reaction of the hydrocarbon *(1)* with triamminetricarbonylchromium [$(NH_3)_3Cr(CO)_3$][4] in boiling *n*-hexane (48 h) leads to a dark red solution which, after filtration, affords red-violet crystals of a complex $C_{10}H_{12} \cdot Cr(CO)_3$ *(2)* (*m/e* 268) on cooling to −15 °C. The complex, which is stable on exposure to air, was obtained in analytically pure form (sinters above 95 °C with decomposition) by sublimation (90 °C, 10^{-4} torr) and subsequent recrystallization from *n*-hexane; yield 67% (based on $(NH_3)_3Cr(CO)_3$). Since *(2)* contains three CO groups, six electrons of the $C_{10}H_{12}$ ligand must be involved in bonding with the chromium atom. This finding, together with the observation that *(2)* regenerates the starting hydrocarbon on treatment with 2,2'-diaminodiethylamine[5] restricts the possible structures to the two alternatives *(2a)* and *(2b)* given above.

The IR spectrum (in CS_2) of *(2)* contains three strong CO bands at 1967, 1900, and 1868 cm^{-1}. The UV spectrum [maximum at 412 (ε = 3500) with shoulders at 300 (4500) and 540 nm (650); in *n*-hexane] differs markedly from that of the complex 1,6-dimethylcycloheptatrienetricarbonylchromium[6] *(3)* [maxima at 352 (ε = 3900) and 490 nm (570), and shoulders at 272 (8100) and 400 nm (3000); in *n*-hexane)] and is similar to the spectrum of 1,6-methano-[10]annulenetricarbonylchromium *(4)* [maxima at 253 (ε = 23600) and 402 nm (8200), and shoulders at 300 (5600) and 550 nm (710); in *n*-hexane].

A clearer insight into the π-electron structure of *(2)* is provided by the ^{1}H-NMR spectrum (in C_6D_6). Thus the four olefinic protons give rise to an AA'XX' system with $\tau_{2,5}$ = 4.29 and $\tau_{3,4}$ = 5.51, the two bridge protons to an AB systems with τ = 10.82 and 12.43 (J = 3.4 Hz), and the six protons of the $(CH_2)_3$ bracket to a multiplet between τ = 8.2 and 9.7. Analysis of the AA'XX' system gave the following coupling constants: $J_{2,3} = J_{4,5}$ = 6.73 Hz, $J_{3,4}$ = 6.18 Hz, $J_{2,4} = J_{3,5}$ = 0.69 Hz, and $J_{2,5}$ = 1.09 Hz. Another important NMR parameter is the ^{13}C—H coupling constant obtained for one of the bridge protons (H_{syn}), which was found to have the value 164 ± 2 Hz. The relatively high value of this constant parallels the small geminal coupling of the bridge protons.

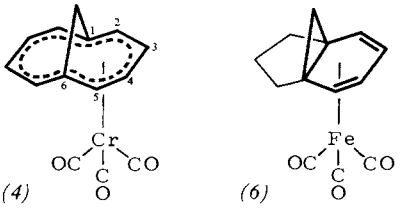
Table 1. H,H coupling constants J (in Hz) of the olefinic protons in *(2)*, *(3)*, *(4)*, and *(6)*.

	$J_{2,3} = J_{4,5}$	$J_{3,4}$	$J_{2,4} = J_{3,5}$	$J_{2,5}$
(2)	6.73	6.18	0.69	1.09
(4)	7.05	7.31	0.37	1.18
(3)	6.83	8.49	0.71	0.29
(6)	6.77	4.06	1.51	~0

On the basis of the coupling constants, the possibility that the complex possesses the cycloheptatriene structure *(2b)* seems to be ruled out. As can be seen from Table 1, *(2)* shows more similarity to *(4)* than to *(3)* as regards the coupling of the olefinic protons. This is particularly true of the relative magnitudes of $J_{2,3}$ and $J_{3,4}$ and of $J_{2,4}$ and $J_{2,5}$. Whereas the relationships $J_{2,3} \approx J_{3,4}$ and $J_{2,4} < J_{2,5}$ are valid for *(2)* and *(4)*, in the case of *(3)* $J_{2,3} < J_{3,4}$ and $J_{2,4} > J_{2,5}$. The finding that, in the case of *(2)*, the geminal coupling and the ^{13}C—H coupling of the bridge protons have hardly changed from the corresponding constants in the free ligand *(1)* [1] is even more informative. The interatomic distance C-1—C-6 in *(2)* is therefore unlikely to be much larger than that in *(1)*.

The question whether *(2)* may be regarded as homoaromatic should prove most readily answerable on the basis of the chemical shifts. As shown in Table 2, the transition of *(1)* into the tricarbonylchromium complex *(2)* has the effect of shifting the resonances of the bridge protons upfield by 2.13 (H_{syn}) and 2.18 ppm (H_{anti}), respectively, and those of the olefinic protons upfield by 1.33 (H-3, H-4) and 0.44 ppm (H-2, H-5). In order to judge to what extent these changes in the chemical shifts are caused by complex formation as such, a comparison may be made with the ligand-complex pair 1,6-methano-[10]annulene *(5)* — 1,6-methano-[10]annulenetricarbonylchromium *(4)* in which the geometrical conditions should resemble those in the present system. According to the results of NMR analyses[7] and X-ray structural studies[8,9], both ligand and complex are aromatic in this case, so that it is justifiable to assign the resonance shifts observed mainly to complex formation.

The data in Table 2 reveal that in *(2)* the resonance frequencies of the bridge protons H_{syn} and H_{anti} lie surprisingly far upfield and those of the olefinic protons unexpectedly far



(4) *(6)*

Table 2. Chemical shifts (τ values in ppm; in C_6D_6) of the protons in *(1)*, *(2)*, *(4)*, *(5)*, and *(6)*.

	$H_{2,5}$	Δτ	$H_{3,4}$	Δτ	H_{syn}	Δτ	H_{anti}	Δτ	Ref.
(1)	3.85		4.18		10.30 [a]		8.64 [a]		[b]
		0.44		1.33		2.13		2.18	
(2)	4.29		5.51		12.43 [a]		10.82 [a]		[b]
(5)	2.79		3.08		10.40		10.40		[7]
		1.01		2.59		0.74		1.37	
(4)	3.80		5.67		11.14		11.77		[7]
(6)	6.62		5.10		9.10 [a]		8.89 [a]		[b]

[a] This assignment is based on the observed long-range coupling of H_{syn} with the methylene protons of the five-membered ring; it was confirmed for *(1)* and *(2)* by complete deuteration in the five-membered ring. [b] This communication.

downfield. Thus on complex formation of *(1)*, additional shielding and deshielding effects occur which can be explained in terms of a diamagnetic ring current in complex *(2)*. We therefore propose the homoaromatic structure *(2a)* for the complex. Further support for this assignment comes from the fact that tricyclo[4.3.1.0^{1,6}]deca-2,4-dienetricarbonyliron[10] *(6)* [m.p. 49 °C; UV spectrum: maxima 247 (ε = 17500) and 305 (3500) with a shoulder at 390 nm (350); in *n*-hexane], whose central atom bonds only with the four π-electrons of the ligand, is shown by its NMR parameters[11] (cf. Tables 1 and 2) and by its UV spectrum[12] to be a normal diene complex.

The interatomic distances in *(2)*, especially the distance C-1—C-6 = 1.65 Å (*d* C-1—C-6 in 2,5-dimethyl-7,7-dicyanonorcaradiene = 1.50 Å[14]), which have recently been determined in an X-ray structure analysis by *Mills et al.*[13], may be regarded as further confirmation of the homoaromatic structure *(2a)*[15].

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[10] Compound *(6)* was prepared by reaction of *(1)* with dodecacarbonyltriiron in boiling benzene (6 h).

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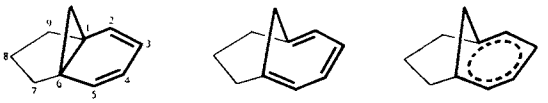
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[15] A complex analogous to *(2)* was obtained on reaction of bicyclo[4.4.1]undeca-1,3,5-triene [1] with triamminetricarbonylchromium [6, 13].

Crystal Structure of Tricarbonyl Complexes of Chromium(0) and Iron(0) with Tricyclo[4.3.1.0^{1,6}]-deca-2,4-diene

By *R. L. Beddoes, P. F. Lindley*, and *O. S. Mills*[*]

Unsaturated hydrocarbons only infrequently form stable complexes with both the dienophile $Fe(CO)_3$ and the trienophile $Cr(CO)_3$. Such behavior can be associated with valence isomerism of the ligand. Recently it has been shown that tricyclo[4.3.1.0^{1,6}]deca-2,4-diene[1] forms such complexes[2]. Whilst all the physical and chemical evidence supports structure *(1a)* for the free ligand, nevertheless structures based on *(1b)* and *(1c)* may have to be considered for the metal complexes.



(1a) *(1b)* *(1c)*

The 4 π-electron system in *(1a)* could well be used for bonding in the tricarbonyliron complex *(2)*, which would then be comparable with cyclohexadienetricarbonyliron[3] and, by analogy with the determined structure of 1,3-butadienetricarbonyliron[4], the tricarbonylmetal group would be expected to take the orientation shown in (A).



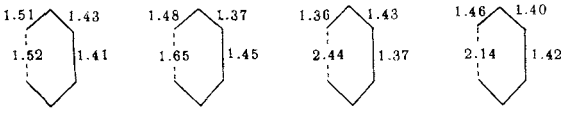
(A) (B)

The tricarbonylchromium complex *(3)* of the cycloheptatriene ligand *(1b)* would, by comparison with *exo*-7-phenylcycloheptatrienetricarbonylchromium[5] *(4)*, also take the form (A) unless prevented from so doing through the steric interference between the trimethylene chain and the nearest CO group attached to the metal atom. In 1,6-methano-[10]-annulenetricarbonylchromium *(5)* on the other hand[6], the orientation of the $M(CO)_3$ group corresponds to (B) although the bond lengths of the ligand are non-alternating and resonance persists through participation of the uncomplexed ring. By contrast, conjugation with a second ring is not possible in *(1)*. A comparison of the NMR spectra[2] of the free ligand $C_{10}H_{12}$ and both complexes suggests that the ligand in *(2)* may more closely resemble *(1a)* than that in *(3)*. Thus whilst *(2)* may contain the norcaradiene arrangement, the chromium complex may favor lengthening the bond between C-1 and C-6 either to the value found in *(5)*, 2.1 Å, or to some intermediate value.

Complex *(2)*, $C_{10}H_{12}Fe(CO)_3$, has the structure (A) expected for a substituted cyclohexadienetricarbonyliron. The molecule possesses crystallographic mirror symmetry (as does butadienetricarbonyliron)[4] with Fe—C-2 = 2.17 and Fe—C-3 = 2.05 Å [$C_4H_6Fe(CO)_3$: Fe—C = 2.14 and 2.06 Å]. The C—C distances in the "butadiene" portion do not differ significantly (1.43 (2×) and 1.41 Å). The C-1—C-6 distance is 1.52 Å which shows that the ligand is in the tricyclic norcaradiene arrangement in the complex. This form has previously been found[7] in 2,5-dimethyl-7,7-dicyanonorcaradiene where the corresponding distance is 1.50 Å which does not differ significantly from our value, bearing in mind the standard deviation of a C—C bond length, 0.02 Å, in our analyses.

Complex *(3)*, $C_{10}H_{12}Cr(CO)_3$, also contains a crystallographic plane of symmetry on which the metal atom and one CO group must lie. We find that the $M(CO)_3$ group is oriented according to (B). As is the case with *(5)*, the chromium atom makes four contacts $\approx$ 2.18 Å to C-2 to C-5 and longer ones, $\approx$ 2.50 Å, to C-1 and C-6. The C-1—C-6 distance has increased to 1.65 Å, which indicates that the ligand apparently no longer has the tricyclic form. However, this distance is 0.5 Å shorter than that found in *(5)*. Such a shortened bond length could be examined from two standpoints; (i) the atoms C-1 and C-6 repel each other but are prevented from moving farther apart by the steric requirements of the trimethylene chain, (ii) there may be bonding in a homoaromatic sense [as in *(1c)*] between these atoms. The former argument is unconvincing since the C-1—C-6 distance could increase to 2.01 Å if the C—C—C bond angles at the methylene carbons were to open out to 113 °, the usual value.

Confirmation of independence from chain length could be provided by the completed analysis of tricarbonylbicyclo[4.4.1]-undeca-1,3,5-trienechromium currently under investigation. A comparison of the bond lengths (Å) found in the systems bound to the metal atom is given for *(2)*–*(5)*:



(2) *(3)* *(4)* *(5)*

The Figure, which is a superposition of the projections of the two structures *(2)* and *(3)* onto their respective mirror planes, shows that, relative to the iron complex in which the metal atom makes only four contacts with the ligand, the chromium atom is moved sideways thus participating more with the ligand as a whole. These relative positions are in accord with the ideas of 4- and 6 π-electron involvement, respectively, by the $M(CO)_3$ groups.

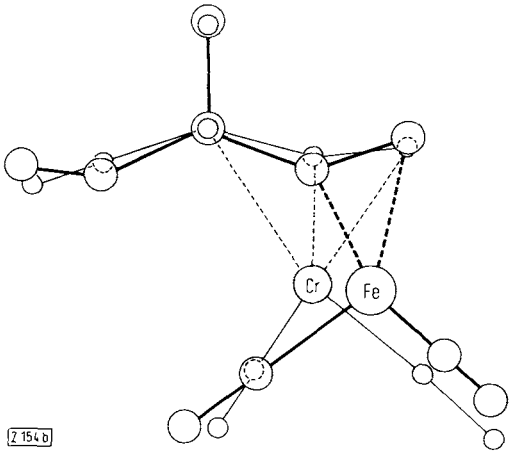


Figure: Superposition of the tricarbonyl complexes of iron(0) and chromium(0) with tricyclo[4.3.1.$0^{1,6}$]deca-2,4-diene, *(2)* and *(3)*, respectively. The molecules are made to coincide in the projection along the direction C-1—C-6. The larger circles refer to complex *(2)*.

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n-Ionization Potentials of Alkyl Bromides[1]

By *Joseph A. Hashmall* and *Edgar Heilbronner*[*]

The lone pairs (n) of the σ-bonded bromine atom of an alkyl bromide RBr occupy the atomic orbitals 4 $p\pi_+$ and 4 $p\pi_-$, and, to a first approximation, 4 pσ. In the present communication we wish to demonstrate that the photoelectron (PE) spectroscopic determination of the ionization potential $I(n)$ of those processes $RBr \rightarrow RBr^+ + e$, in which the electron e comes from the atomic orbital 4 $p\pi_+$ or 4 $p\pi_-$, is a convenient and sensitive tool for the investigation of inductive and (hyper)conjugative effects. σ-Bonded bromine atoms represent an ideal probe for the measurement of such effects for the following reasons:

1. The n-ionization potential of their 4 pπ electrons lies between 9.5 and 11 eV, *i.e.* in a range between the normal ionization potentials of the C=C π electrons (≈9 eV) and the C—C σ- and C—H σ-electrons (≈ > 10.5 eV).

2. Owing to the nonbonding character of the 4 pπ atomic orbitals of the bromine atom, the n-ionization bands observed in the PE spectrum of RBr exhibit sharp 0—0 transitions (cf. Fig. 1) which are clearly distinguishable from the other broad bands. They are easy to locate and can be measured with high precision (cf. ref. [2]).

3. With few exceptions (see below), the PE spectrum of RBr shows two sharp bands separated by 0.30 ± 0.01 eV and which correspond to n-ionization (cf. Fig. 1). This makes their identification even easier and increases the accuracy of the measurement of the ionization potential.

4. Alkyl bromides are more readily accessible, more stable, and more suitable for PE spectroscopy than the corresponding iodides.

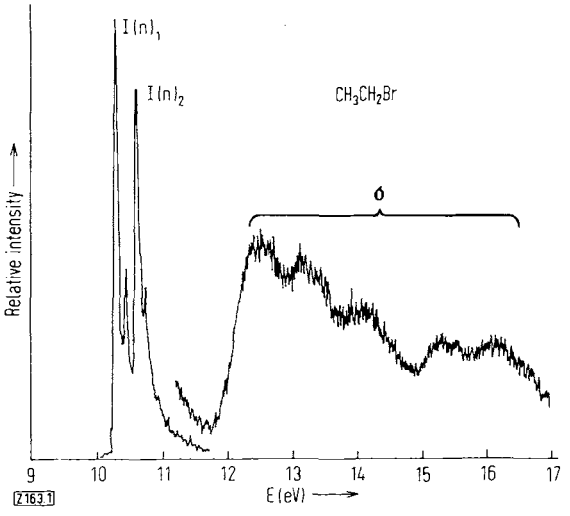


Figure 1. Photoelectron spectrum of ethyl bromide (recorded with a modified spectrometer [7] manufactured by Perkin-Elmer Ltd. (Beaconsfield, England). The n band is recorded at reduced sensitivity. The decrease in intensity with increasing energy is in part due to the instrument.

The method is illustrated by the following Table of ionization potentials $I(n)_1$, $I(n)_2$ of a series of alkyl bromides RBr, their mean values $\overline{I(n)} = (I(n)_1 + I(n)_2)/2$, and their differences $\Delta(n) = I(n)_1 - I(n)_2$.

Table: n-Ionization potentials of alkyl bromides RBr (in eV). Mean error *ca.* ±0.01$_5$ eV. $I(n)_1$ and $I(n)_2$ correspond to the 0-0 transition.

R	$I(n)_1$	$I(n)_2$	$\overline{I(n)}$	$-\Delta(n)$
CH_3	10.53	10.85	10.69	0.32
CH_3CH_2	10.30	10.61	10.45$_5$	0.31
$CH_3CH_2CH_2$	10.18	10.49	10.33$_5$	0.31
$CH_3CH_2CH_2CH_2$	10.13	10.44	10.28$_5$	0.31
$(CH_3)_2CH$	10.12	10.41	10.26$_5$	0.29
$(CH_3)_3C$	9.95	10.24	10.09$_5$	0.29
$(CH_3)_2CHCH_2$	10.10	10.41	10.25$_5$	0.31
$(CH_3)_3CCH_2$	10.04	10.34	10.19	0.30

Remarks:

1. In the case of the radical cations RBr^+ with R = methyl or *tert*-butyl, in which the bromine atom is situated on a threefold axis, $I(n)_1$ and $I(n)_2$ correspond to the states $^2\Pi_{3/2}$ and

$^2\Pi_{1/2}$, which show a —0.31 eV splitting due to spin-orbit coupling[3]. This splitting is still observed even when RBr no longer possesses a threefold axis of symmetry. Apparently, the local cylindrical symmetry at the bromine atom is disturbed to a negligible extent by an alkyl group of low symmetry. This is shown by the fact that the splitting Δ(n) remains constant within the limits of experimental error.

2. Figure 2 shows the dependence of the mean ionization potential $\overline{I(n)}$ on R. On the average, $\overline{I(n)}$ is shifted by —0.2 eV per α-methyl substituent and by —0.09 eV per β-methyl substituent.

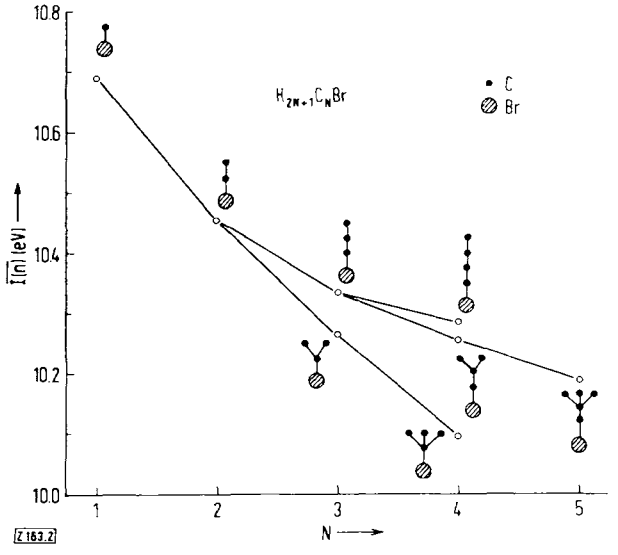
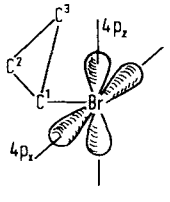


Fig. 2. Variation of the mean n-ionization potential of the alkyl bromides RBr as a function of the alkyl group R.

3. With reference to the first band in the PE spectrum of RH[4], the corresponding band of the series of σ bands in the PE spectrum of the alkyl bromide RBr is shifted by 0.4 eV towards higher energies if we confine our attention to the adiabatic ionization potentials.

4. While the results for cycloalkyl bromides (*e.g.*, cyclohexyl bromide, $\overline{I(n)}$ = 10.02 eV; Δ(n) = —0.29 eV) are in line with the predicted values, the group R = cyclopropyl represents a special case. The PE spectrum of cyclopropyl bromide contains only one clear n-ionization band with a sharp 0—0 transition at 10.41 eV, which can be ascribed to the 4 p_z lone pair.



The 4 p_x orbital, which is oriented parallel to the C^2—C^3 bond of the cyclopropyl group, conjugates with one of the Walsh orbitals[5] of this group and thus gives rise to a fine-structured, broad band at 9.53 (adiabatic) and 9.66 eV (vertical) (cf. ref.[6]).

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[1] Applications of Photoelectron Spectroscopy, Part 11. This work is part of Project No. 2.120.69SR of the Schweizerischer Nationalfonds. — Part 10: *E. Heilbronner* and *K. A. Muszkat*, J. Amer. chem. Soc., in press.

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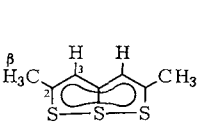
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ESR Spectra of Radical Anions of Some 6a-Thiathiophthene Derivatives[1]

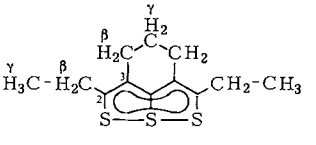
By *Fabian Gerson, Rolf Gleiter, Josef Heinzer*, and *Hans Behringer*[*]

The results of the ESR studies reported in this communication present an opportunity for testing the MO models proposed[2,3] for 6a-thiathiophthene. The experimental data allow conclusions to be drawn regarding the symmetry of the system in general and the form of the lowest vacant orbital in particular.

Tables 1 and 2 list the coupling constants of the magnetic nuclei for the radical anions of the 6a-thiathiophthene derivatives *(1)* to *(4)*[4]. The experimental values were refined with the aid of a computer program[5]; thus the relative experimental error should not exceed 1%. Wherever the assignment could not be deduced directly from the ESR spectrum it was made on the basis of analogy with the corresponding data for known radical anions. (The number of



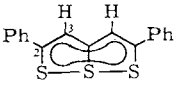
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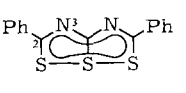


(2)

Table 1. Coupling constants (in gauss) for $(1)^{\ominus}$ and $(2)^{\ominus}$.

radical anion	T (°C)	a_{H3}	methyl or ethyl a_H^{β}	methyl or ethyl a_H^{γ}	trimethylene a_H^{δ}	trimethylene a_H^{γ}
$(1)^{\ominus}$	+25	2.17 (two)	6.35 (six)	—	—	—
$(2)^{\ominus}$	+25	—	4.10 (four)	≤0.15 (six)	2.05 (four)	0.31 (two)
	−40	—	4.08 (two) 3.54 (two)	≤0.15 (six)	2.98 (two) 1.19 (two)	0.51 (one) ≤0.15 (one)





Ph = Phenyl

(3) *(4)*

Table 2. Coupling constants (in gauss) for $(3)^{\ominus}$ and $(4)^{\ominus}$.

radical anion	T (°C)	a_{H3}	a_{N3}	phenyl a_H^{ortho}	phenyl a_H^{meta}	phenyl a_H^{para}
$(3)^{\ominus}$	+25 to −40	1.58 (two)	—	1.37 (four)	0.45 (four)	1.58 (two)
$(4)^{\ominus}$		—	2.29 (two)	1.33 (four)	0.44 (four)	1.49 (two)

equivalent nuclei, which are responsible for the coupling constant, is given in parentheses.)

The radical anions were generated either by electrolytic reduction in *N,N*-dimethylformamide ($(1)^{\ominus}$ and $(2)^{\ominus}$) or by reaction with potassium in 1,2-dimethoxyethane ($(3)^{\ominus}$ and $(4)^{\ominus}$).

In anticipation of a more detailed discussion of the experimental results, the following remarks can be made:

1. With respect to the ESR time scale and in the temperature range investigated (+25 to −40 °C), the results are consistent with a plane of symmetry passing through the central S atom and vertical to the plane of the molecule.

2. The π-spin population at atom 2 is relatively large (0.2 to 0.3), whereas at atom 3 it has a smaller value (0.06 to 0.08). A spin distribution of this kind is in accord with the form of the relevant orbital in the MO model [2].

3. As expected [6], the trimethylene chain in $(2)^{\ominus}$ can occur in two equivalent conformations which undergo rapid interconversion (frequency $>10^7\ s^{-1}$) at room temperature. Cooling of the solution reduces the frequency of interconversion: the spectrum recorded at −40 °C is already typical of a "frozen" conformation. The decrease in temperature also causes one of the two methylene protons in the 2-ethyl substituent to assume a position in which — on time average and relative to the freely rotating methyl group — hyperconjugation is still less favored [7] (compare data for $(2)^{\ominus}$ with those for $(1)^{\ominus}$).

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Chemiluminescence on Oxidative Formation of Triplet States of Anthrasemiquinone- and Anthraquinone-2-sulfonate

By *Joachim Stauff* and *Peter Bartolmes* [*]

Hydroquinones that reduce O_2 to H_2O_2 emit a weak light while doing so; this light can be registered with a sensitive photodetector. Emission of this kind is also observed when *e.g.* anthraquinone-2-sulfonate is reduced to the semiquinone under argon at a Pt cathode at pH 12.5 and is then exposed to the action of O_2. Although the hydroquinone is also present under these conditions, owing to the equilibrium $Q + HQ \rightleftharpoons 2\,SQ$ (Q = quinone, SQ = semiquinone, HQ = hydroquinone), the possible formation of O_2^- radical anions according to $SQ + O_2 \rightarrow O_2^-$ cannot be immediately ruled out. In such a case, the chemiluminescence could be due to singlet oxygen [1] formed by recombination of O_2H radicals which are produced by O_2^- and H^+. A chemiluminescence of the same kind is also observed, however, on oxidation of HQ or SQ with $K_3[Fe(CN)_6]$ in the complete absence of oxygen (Ar atmosphere); the excited states that emit the photons must therefore arise from the participating organic molecules and not from oxygen species. The quantum yield of the reaction is about 10^{-10} Einstein/mole. The fact that the reaction appears to number among the exceptional cases in which chemiluminescence can be produced without the participation of oxygen or peroxides [2] makes it all the more interesting.

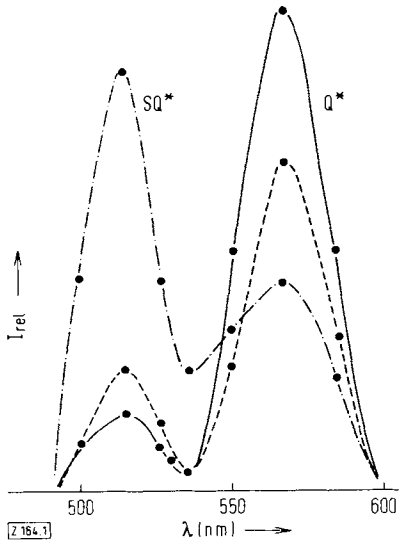


Figure. Chemiluminescence spectra of the reactions: anthrasemiquinone-2-sulfonate + hexacyanoferrate(III) (——); anthrahydroquinone-2-sulfonate + hexacyanoferrate(III) (— — —); and anthrahydroquinone-2-sulfonate + O_2 (—·—·—).

Since oxidation with hexacyanoferrate(III) can only proceed in a series of one-electron steps, variation of the ratio $q = Fe(CN)_6^{3-}$/reductant should reveal which of the reactions

$$HQ + [Fe(CN)_6]^{3-} \rightarrow SQ^*;\ SQ^* \rightarrow SQ + h\nu_1 \qquad (1)$$

and

$$SQ + [Fe(CN)_6]^{3-} \rightarrow Q^*;\ Q^* \rightarrow Q + h\nu_2 \qquad (2)$$

is responsible for the emission. It was found that with HQ as reductant the maximum intensity of luminescence occurs at $q = 2$, and for SQ, on the other hand, at $q = 1$; moreover, the luminescence yield in the former case was double that in the latter. Thus light is emitted during both reaction (1) and reaction (2). The only possible explanation is that removal of an electron and formation of a $>C=O$ group each lead to an excited state of the reaction product which releases part of its energy in the form of light. Whereas SQ can yield only one $>C=O$ group, HQ can form two and thus initiate twice as many emission processes.

This hypothesis derived further support from an approximate plot of the emission spectra recorded with the aid of filters. The figure shows that both oxidation of HQ and SQ with $[Fe(CN)_6]^{3-}$ or O_2 invariably gives rise to two bands that can be attributed to the emission of SQ* and Q*. Owing to the equilibrium between HQ, Q, and SQ, both reactions (1) and (2) must occur together; it was, however, to be expected that the relative intensity of one of the two bands, corresponding to SQ* or Q*, would be higher than that of the other, depending upon which starting material was used. In fact, with HQ as starting material the band at 515 nm is the stronger one, and the converse is true in the case of SQ. The band at 515 nm is therefore ascribed to the excited semiquinone and that at 568 nm to the excited quinone. This assignment is consistent with the concept that reaction (1), as a processes involving doubly and trebly charged anions, must be slower than reaction (2) between singly and trebly charged anions, and that the intensity of the quinone band must be greater than that of the semiquinone band. More-

over, in the spectrum of the reaction HQ + O_2, the 515-nm band is twice as strong as the 568-nm band. Since the rate of reaction of O_2 with HQ, having two $-O^-$ groups, must statistically be twice as high as that of O_2 with SQ, having one $-O^-$ group, the same relationship is to be expected between the intensities of the emission bands.

Since the singlet states of anthraquinonesulfonate lie at 260 ($\pi \rightarrow \pi^*$) and 320 nm ($n \rightarrow \pi^*$), SQ* and Q* must be triplet states. This means that removal of an electron from a group like $\rangle \dot{C}-\ddot{O}:^{\ominus}$ leaves the $\rangle C=O$ group not in the bonding π state but initially in the antibonding π^* state. Owing to the considerably lower energy required for its formation (49 instead of 88 kcal/mole), the antibonding state should be a triplet state which undergoes transition into the singlet ground state in a subsequent step, thereby emitting a very small portion of its energy as light.

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Reactions of Tritolylphosphines

By *S. I. A. El Sheikh, B. C. Smith,* and *M. E. Sobeir* [*]

Tri-*p*- *(1a)* and tri-*m*-tolylphosphine *(1b)* resemble triphenylphosphine in their oxidation behavior, whereas tri-*o*-tolylphosphine *(1c)* differs in its reactions with several oxidizing agents. Thus *(1a)* and *(1b)* react with thionyl chloride in boiling benzene to give the phosphine oxide and disulfur dichloride [1].

$$3\ R_3P + 2\ SOCl_2 \rightarrow 2\ R_3PO + S_2Cl_2 + (R_3PCl_2) \downarrow R_3PO$$

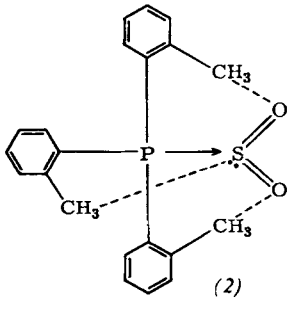
(1a), R = *p*-$CH_3C_6H_4$
(1b), R = *m*-$CH_3C_6H_4$

The initially formed triaryldichlorophosphorane undergoes subsequent conversion into the phosphine oxide. Under similar conditions *(1c)* gives a mixture of the phosphine oxide and phosphine sulfide.

(1a) and *(1b)* recrystallize unchanged from liquid sulfur dioxide, but undergo oxidation when the yellow solutions are heated in sealed tubes (185 °C/2 days):

$$3\ (1a, b) + SO_2 \rightarrow 2\ R_3PO + R_3PS$$

In contrast, the isomer *(1c)* reacts with liquid SO_2 to give an orange precipitate of the complex [(*o*-$CH_3C_6H_4)_3P \cdot SO_2$] *(2)*, which is stabilized by specific attractions between *o*-methyl groups and ligands. The phosphine oxide and phosphine sulfide are not formed, even on heating with an excess of SO_2 at 185 °C for 8 days.



(2)

Compounds *(1a)* and *(1b)* react with SeO_2 in boiling benzene to give the phosphine oxide and either selenium or the phosphine selenide, depending on the relative proportions of the reagents.

$$2\ (1a, b) + SeO_2 \rightarrow 2\ R_3PO + Se$$

$$3\ (1a, b) + SeO_2 \rightarrow 2\ R_3PO + R_3PSe$$

The phosphine *(1c)* does not react under these conditions.

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[1] *M. E. Sobeir, B. C. Smith, A. N. Swamy,* and *M. Woods*, unpublished results.

Ionization Isomerism of Sulfinato Complexes of Transition Metals

By *Ekkehard Lindner* and *Günter Vitzthum* [*]

Sulfinato complexes are eminently suitable subjects for the detection of various isomerism phenomena: alongside stereo- [1] and valence isomers [2] we have now observed, for the first time, ionization isomers.

Reaction of the potentially bidentate ligand ethylenediamine (en) with the sulfinato-*O,O'* complex (*p*-$CH_3C_6H_4SO_2)_2Mn(OH_2)_2$ [3] in ethanol at room temperature affords the ionic compound [*p*-$CH_3C_6H_4SO_2Mn\ en_2$] [*p*-$CH_3C_6H_4SO_2$] *(1)* (yield about 70%). Compound *(1)* exhibits conductivity in ethanol and its cation could be characterized in the form of [*p*-$CH_3C_6H_4SO_2Mn\ en_2$] [$B(C_6H_5)_4$] *(2)*.

On repeated recrystallization from ethanol with tetrahydrofuran the metastable compound *(1)* is converted irreversibly into the non-polar isomer (*p*-$CH_3C_6H_4SO_2)_2Mn\ en_2$ *(3)*, which is insoluble in all organic solvents. Composition and structure of the almost colorless sulfinato-*O,O'* derivatives *(1)*—*(3)* were established by complete elemental analysis and by the electronic and IR spectra, which indicate a pseudo-octahedral environment of the Mn^{2+} ion (see Table).

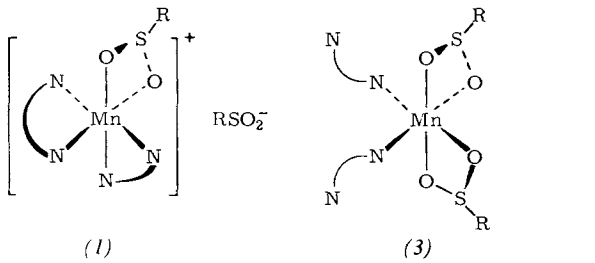
In every case, the *coordinated* *p*-$CH_3C_6H_4SO_2^-$ ligand is bonded to the central ion *via* both oxygen atoms (*O,O'* type) [4].

Table: SO_2 stretching vibrations (in cm^{-1}) of complexes *(1)*—*(3)* and of *p*-$CH_3C_6H_4SO_2Na$ *(4)*.

	$\nu_s(SO_2)$	$\nu_{as}(SO_2)$
(1)	979 s	1027 vs (anion) 1009 vs
(2)	970 vs	1000 vs, b
(3)	977 s	1012 vs
(4)	979 m	1027 m

The IR spectrum of *(1)* also contains the SO_2 stretching vibrations of the *anion* *p*-$CH_3C_6H_4SO_2^-$ (cf. spectrum of *(4)*), which are absent from that of *(2)*. Thus ethylenediamine is *bidentate* in *(1)* and *(2)*, but *monodentate* in *(3)*.

Possible stereoisomerism (*cis-trans*) in *(3)* cannot be detected owing to the insufficient frequency splitting of $\nu_{as}(SO_2)$ and $\nu_s(SO_2)$.



(1) (3)

R = p-$CH_3C_6H_4$

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[2] *E. Lindner*, *G. Vitzthum*, *D. Langner*, and *I.-P. Lorenz*, Angew. Chem. *82*, 133 (1970); Angew. Chem. internat. Edit. *9*, 160 (1970).

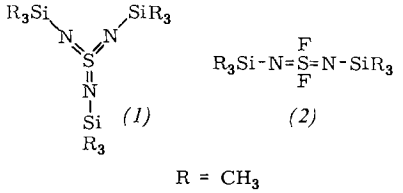
[3] *E. Lindner* and *G. Vitzthum*, Z. anorg. allg. Chem., in press.

[4] *E. Lindner* and *G. Vitzthum*, Chem. Ber. *102*, 4053, 4062 (1969).

Tris(*N*-trimethylsilylimido)sulfur and Bis(*N*-trimethylsilylimido)sulfur Difluoride

By *Oskar Glemser* and *Joachim Wegener*[*]

We have now succeeded in synthesizing, for the first time, a derivative of the hitherto unknown sulfur triimide, namely tris(*N*-trimethylsilylimido)sulfur *(1)*, by reaction of sulfur nitride trifluoride with lithium bis(trimethylsilyl)amide in light petroleum at 0 °C; the reaction also affords bis(*N*-trimethylsilylimido)sulfur difluoride *(2)*. *(1)* is the only compound to have been discovered so far that contains 3-coordinate sulfur in the oxidation state +6 and yet does not polymerize[1].



(1) (2)

R = CH_3

Compound *(1)* is a stable colorless liquid (b.p. 204 °C/748 torr), whose composition has been confirmed by elemental analysis and cryoscopic molecular-weight determination (calc. 293.67; found 304) in benzene. The ^{1}H-NMR spectrum contains only one signal at δ = −0.15 ppm (TMS as external standard).

Mass spectrum (relative intensities): molecular ion $S[NSi(CH_3)_3]_3^+$ (3), $Si(CH_3)_3^+$ (100), $S[NSi(CH_3)_3]_2NSi(CH_3)_2^+$ (25), $S[NSi(CH_3)_3]_2NSiHCH_3^+$ (14), $S[NSi(CH_3)_3]NSi(CH_3)_2^+$ (6), NSN^+ (5), NS^+ (5).

IR (cm^{-1}): 72 w, 175 w, 228 s, 272 s, 430 w, 619 s, 696 s, 738 w, 758 w, 840 vs, 1260 vs, 1290 vs, 3000 vs.

Raman (cm^{-1}): 97.5 dp, 130 pp, 175 dp, 212 dp, 230 dp, 257 pp, 280 p, 306 dp, 533 p, 644 p, 697 p, 760 p, 1005 p, 1127 p, 1262 p, 1290 p.

If the SN_3 group is assumed to have a planar-trigonal structure (symmetry D_{3h}), as is most probably the case, the double bands at 1290 and 1260 cm^{-1} in the IR and at 1290 and 1262 cm^{-1} in the Raman can be assigned to a ν_3 mode, and the strong, IR-inactive band at 1127 cm^{-1} to a ν_1 mode.

The product *(2)* is also a stable, colorless liquid (b.p. 158 °C/749 torr); m.wt.: calc. 244.47, found 243, in benzene. ^{1}H-NMR: singlet at δ = −0.15 ppm (TMS as external standard); ^{19}F-NMR: singlet at δ = −77.4 ppm ($CFCl_3$ as external standard).

Mass spectrum (relative intensities): molecular ion $SF_2[NSi(CH_3)_3]_2^+$ (8), $Si(CH_3)_3^+$ (100), $SF_2N_2Si_2(CH_3)_5^+$ (72), $SN_2Si(CH_3)_3^+$ (28), $SiCH_3^+$ (25), SN_2^+ (14), SN^+ (14), $SFNSi(CH_3)_3^+$ (7.5), $NSF_2[NSi(CH_3)_3]^+$ (3), $SF_2NSi(CH_3)_3^+$ (3), $SF[NSi(CH_3)_3]_2^+$ (2), $SF_2N_2Si_2(CH_3)_3^+$ (2).

IR (cm^{-1}): 580 w, 620 s, 638 s, 700 w, 710 w, 735 w, 760 w, 787 w, 840 w, 889 w, 1258 s, 1302 s, 1430 vs, 2200 s, 3000 vs.

Raman (cm^{-1}): 182, 195, 255, 338, 350, 582, 595, 620, 640, 698, 765, 790, 888, 1265, 1307, 1416, 1425.

Procedure:

NSF_3 (30 g, 0.29 mole) is added dropwise to a stirred solution of $LiN[Si(CH_3)_3]_2$ (110 g, 0.66 mole) in light petroleum (b.p. 40–60 °C) (150 ml) at 0 °C over a period of 1 h. After removal of solvent under reduced pressure, the products are fractionated in a high vacuum; yield of *(1)* about 10 g, of *(2)*, 15 g.

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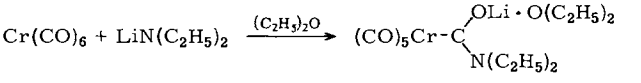
[1] Cf. *R. Appel* and *B. Ross*, Chem. Ber. *102*, 1020 (1969); Angew. Chem. *80*, 561 (1968); Angew. Chem. internat. Edit. *7*, 546 (1968).

Ethoxydiethylaminocarbenepentacarbonylchromium(0)[1]

By *Ernst O. Fischer* and *Hans J. Kollmeier*[*]

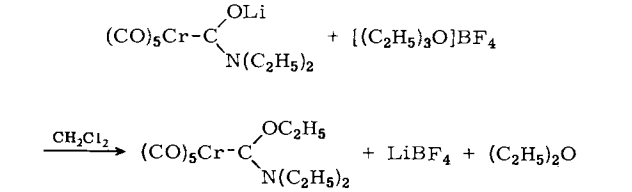
Alkyl- and aryllithium compounds react with transition metal carbonyls to give lithium acylcarbonylmetalates, which can be converted into alkoxyalkyl- or alkoxyaryl complexes by alkylation[2]. We have now investigated whether lithium amides can be made to react in the same manner.

Reaction of lithium diethylamide and hexacarbonylchromium in ether affords a colorless, crystalline product which we regard as a 1 : 1 adduct and which, according to its ^{1}H-NMR spectrum, is coordinated to approximately one molecule of ether.



(1)

The IR spectrum (THF, LiF optics) of *(1)* contains four $\nu_{C\equiv O}$ bands at 2034 m, 1939 w, 1897 vs, and 1870 s cm^{-1}. In the ^{1}H-NMR spectrum ([D_6]-acetone), the signals due to the OC_2H_5 protons appear at τ = 6.6 (q) and 8.9 (t), and those of the NC_2H_5 protons at τ = 7.45 (q) and 9.0 (t) in the intensity ratio of approximately 1 : 1. The lithium salt *(1)* was ethylated with triethyloxonium tetrafluoroborate in methylene chloride to give ethoxydiethylaminocarbenepentacarbonylchromium(0) *(2)* as pale yellow crystals (m.p. 29 °C).



(2)

The structure of *(2)* was determined from the mode of preparation, complete elemental analysis, and spectroscopic findings. The IR spectrum (*n*-hexane, LiF optics) reveals two CO stretching vibrations at 2057 m (A_1) and 1927 cm^{-1} vs (A_1, E).

For an octahedral configuration of the complex, the $Cr(CO)_5$ group should have approximately C_{4v} symmetry and exhibit three IR-active fundamental vibrations: two of class A_1 and one of class E. Since only two bands are actually observed, it must be assumed that the E vibration and the second A_1 vibration coincide[3].

The ^{1}H-NMR spectrum (benzene) recorded at 25 °C contains signals due to three different ethyl groups in the intensity ratio 1 : 1 : 1. The two quartets at τ = 6.29 and 7.10 are slightly broadened as a result of quadrupole coupling with the nitrogen atom and are therefore assigned to the NCH_2 protons; the quartet corresponding to the OCH_2 protons appears at τ = 5.49. The triplets due to the CH_3 protons of the three ethyl groups are seen at τ = 8.96, 9.07, 9.25.

The positions of the $\nu_{C\equiv O}$ bands show that the (d→p)π back-donation Cr→$C_{carbene}$ in *(2)* can only be weak. The electron deficiency at the $C_{carbene}$ atom must therefore be cancelled mainly by way of π-electron interactions with the lone pairs of the two hetero atoms. The non-equivalence of the *N*-ethyl groups further supports the high bond order of the $C_{carbene}$–N bond; that of the $C_{carbene}$–O bond, however, must by considerably lower since the occurrence of only one group of signals for the C_2H_5 group rules out the existence of stable *cis-trans* isomers.

A marked double-bond character of the C–N bond in alkoxyaminocarbenes bonded to a metal was previously suspected in the Hg^{2+} complexes, also on the basis of non-equivalent *N*-alkyl groups (^{1}H-NMR)[4], and recently confirmed by an X-ray structure determination of *cis*-$Cl_2P(C_2H_5)_3$–$PtC(OC_2H_5)NHC_6H_5$[5] (the $C_{carbene}$–O bonds in this complex were also found to be considerably shorter than expected for a C–O single bond). The dipole moment of *(2)* was determined as μ_{20} = 5.75 ± 0.1 D in cyclohexane.

The mass spectrum of *(2)* provides independent proof of its structure[6]: molecular ion at *m/e* 321; there follow five peaks corresponding to the stepwise loss of five CO groups: the most intense peak at *m/e* 181 is due to the fragment $CrC(OC_2H_5)N(C_2H_5)_2^+$.

Procedure:

All operations must be carried out in the absence of air and in N_2-saturated, anhydrous solvents.

$LiN(C_2H_5)_2$ (10.0 mmoles) in ether (100 ml) is slowly added dropwise to an ice-cooled, stirred suspension of $Cr(CO)_6$ (2.2 g, 10.0 mmoles) in ether (200 ml). The yellow solution is concentrated to a volume of about 50 ml and filtered, and *(1)* is precipitated by addition of *n*-hexane. To a stirred, ice-cooled suspension of *(1)* (1.86 g, 5.0 mmoles) in methylene chloride (25 ml) is added portionwise a solution of $[(C_2H_5)_3O]BF_4$ (0.95 g, 5.0 mmoles) in methylene chloride (25 ml). After removal of solvent the yellowish-brown, oily residue is extracted with two 20-ml portions of *n*-hexane, the extract is concentrated to a volume of 10 ml and filtered, and *(2)* is precipitated by cooling to –50 °C. The crystals can be sublimed at 30 °C in a high vacuum; yield about 20% [based on $Cr(CO)_6$].

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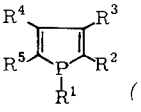
[5] *E. M. Badley*, *J. Chatt*, *R. L. Richards*, and *G. A. Sim*, Chem. Commun. *1969*, 1322.

[6] Atlas CH 4; ion source TO 4. Measurements performed by Dr. *J. Müller*, München.

Novel Radicals from the Reaction of Phospholes with Potassium

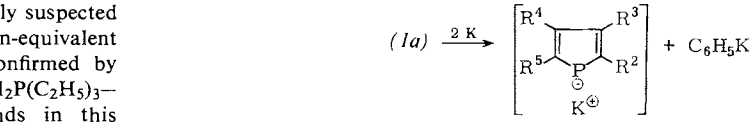
By *Colin Thomson* and *D. Kilcast*[*]

During the investigation of the room temperature and low temperature reactions of various substituted phospholes *(1)* with potassium in dimethoxyethane (DME) and tetrahydrofuran (THF), anomalous ESR signals have been observed, similar to those found in the reduction of benzene with Na–K alloy in DME/THF[1–3].



(1)

The reaction of *(1a)* (with R^1 = phenyl) with potassium in DME at room temperature has been found to proceed as follows[4]:



We have observed three strong, distinct and interconvertible signals during the reduction of 1,2,5-triphenylphosphole *(1b)*, and of pentaphenylphosphole *(1c)* with potassium, both in DME and in THF.

Signal A consists of a 1 : 2 : 1 triplet (a_H = 6.1 gauss) split into a 1 : 4 : 6 : 4 : 1 quintet (a_H = 1.7 gauss); the signal contour corresponds to a 15 line spectrum already mentioned several times in the literature[1–3]. Under high resolution and low microwave power level, each line is split further into approximately 12 lines (separation about 0.13 gauss; cf.[3]).

Signal B consists of a doublet (a_H = 6.3 gauss) split into seven or nine lines (a_H = 1.7 gauss; cf. Fig. 1). As with A, further resolution is observed at low powers, but varying linewidths make the number of additional lines uncertain, although the separation is about 0.14 gauss.

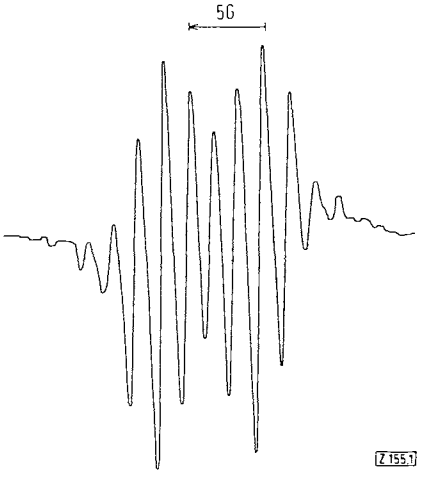


Fig. 1. ESR spectrum "B", from pentaphenylphosphole with potassium in THF at 25 °C. (Moderate resolution.)

Signal C consists of nine lines (a_H = 1.7 gauss), which have further structure at low power levels, the separation being about 0.3 gauss (Fig. 2).

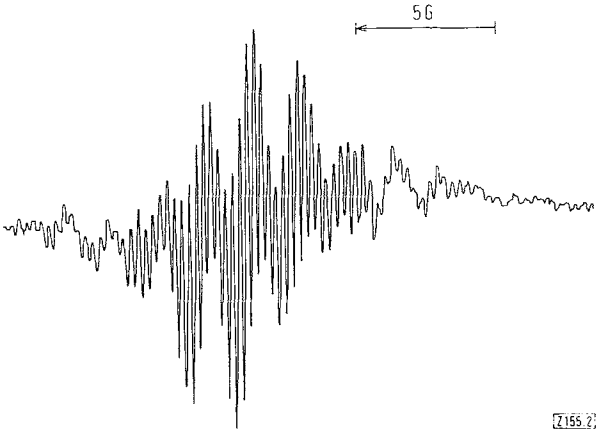


Fig. 2. ESR spectrum "C", from pentaphenylphosphole with potassium in DME at 25 °C. (High resolution.)

The g-values of all three signals, measured with respect to Frémy's salt (g = 2.0055) are g = 2.0027.

All three signals have been observed from each phosphole in both DME and THF, in no particular sequence, although signal C is usually the ultimate signal. We consider signal A to be identical to that reported in references [1–3].

That these signals are associated with the phenyl group is confirmed by the fact that no such signals are observed when R^1 = alkyl. We consider that whichever radical is produced initially, whether A, B, or C, this is a result of a radical polymerization of the cleaved phenyl group; this could occur *via* a dehydrobenzene type of intermediate, which has already been postulated for the reaction of benzene with alkali metal in hexamethylphosphoric triamide [5]. A high polymer is indicated by the large number of hyperfine lines. Since our solvent drying procedure also involved the use of $LiAlH_4$ (cf. [1–3]), the reaction would seem to be catalyzed by some impurity derived from the use of this compound. We do not consider the initial radical to undergo further polymerization, as this should change the g-values and the spin distributions. In fact, the coupling constants of the major splittings remain the same, and only the number of lines change (the largest and smallest splittings are lost in Spectrum C). This could arise from some form of rearrangement of the initial radical to one with a closely related structure.

The radicals are not the anions of the phospholes, as the spectra of these show a large phosphorus doublet [6].

No such radicals have been observed on reaction with Na or Li, the former not cleaving the phosphole, the latter reacting too slowly to give any observable radicals.

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[**] We thank Dr. *E. H. Braye* (Union Carbide, Brussels) for the phosphole samples and the Carnegie Trust for a maintenance grant to D.K.

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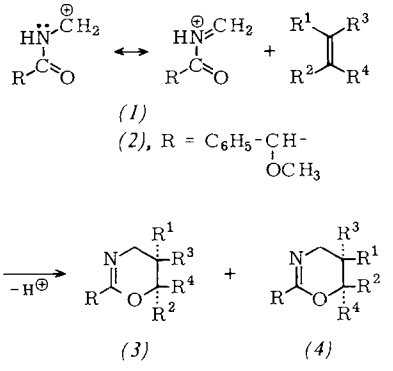
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Geometry of the Transition State in Polar Cycloadditions[1] [**]

By *Richard R. Schmidt* and *Rudolf Machat* [*]

The specific *cis*-addition of amidomethylium ions *(1)* to olefins [2] is a prerequisite for, but no proof of, a synchronous process [3]. Polar cycloadditions, however, may possibly proceed in two steps, even though orbital symmetry considerations formally suggest a synchronous formation of the two new σ bonds. In order to make a decision between these two possibilities we have carried out investigations on the geometry of the transition state.



(1)

(2), R = C_6H_5-CH(OCH$_3$)-

(3) *(4)*

The reactions of *(2)* with olefins confirmed the regio- and stereospecific *cis*-addition [2]. Since R is chiral, the two diastereoisomeric oxazine derivatives *(3)* and *(4)* were obtained in varying amounts [5] (see Table 1) as a result of asymmetric induction [4].

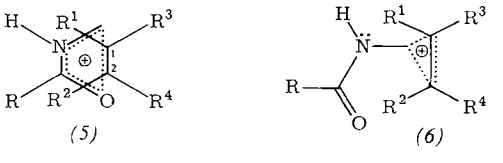
Table 1. Diastereomeric 2-(α-methoxybenzyl)-5,6-dihydro-4*H*-1,3-oxazines *(3)* and *(4)* synthesized from *(2)* and olefins.

	R^1	R^2	R^3	R^4	Yield *(3)* + *(4)* (%)	$J_{a,b}$ (Hz)	*(3)*/*(4)* [a]
(a)	H	Ha	Hb	H_5C_6	78	8.9	1.8 : 1
(b)	H	CH_3	H	H_5C_6	82	—	1.1 : 1
(c)	CH_3	Ha	Hb	H_5C_6	69	9.2	1.8 : 1
(d)	C_2H_5	Ha	Hb	H_5C_6	78	8.4	1.8 : 1
(e)	*n*-C_3H_7	Ha	Hb	H_5C_6	63	8.0	1.7 : 1
(f)	H	H	$-(CH_2)_3-$		69	—	1.4 : 1
(g)	H	H	$-(CH_2)_4-$		72	—	1.6 : 1
(h)	Hb	Ha	1,3-cyclopentylene		70	7.9 [8]	6.7 : 1

[a] Determined by NMR spectroscopy.

The ratio of diastereoisomers ought to depend upon the substituents of the olefin which are adjacent to the chiral center R. If the sizes of R^1 and R^2, and R^3 and R^4, are comparable or equal, the geometry of the transition state can readily be established. The ratio *(3a)*/*(4a)* can be used as a reference in the addition of styrene; the ratio *(3)*/*(4)* in the adducts of the styrene derivatives *(b)*—*(e)* is influenced mainly by the nature of R^2 and practically not by the nature of R^1. In the transition state of this reaction, therefore, R^2 is very much nearer to R than is R^1.

This finding is consistent only with the transition state *(5)* previously discussed for synchronous cycloadditions [6] and not with the typical transition state [7] *(6)* for the primary electrophilic attack of *(2)* on olefins, since the ratio R^1—R/R^2—R (R^1 = R^2 = CH_3) is 2.6 : 1 in the case of *(5)* and 1.1 : 1 in



(5) *(6)*

the case of *(6)*. The large increase in the ratio *(3)*/*(4)* in the series of cycloolefin derivatives *(f)*—*(h)* supports the cyclic transition state *(5)*. This and the strong influence of the methyl group in *(b)* provide evidence for the C-2 atom being situated about two bond lengths distant from the asymmetric C atom in R; such is the case only in *(5)*.

Experimental:

A mixture of *(2)* (0.01 mole) and olefin (0.015 mole) in glacial acetic acid (20 ml) was treated with a solution of conc. sulfuric acid (1.25 g) in glacial acetic acid (5 ml) (added over a period of 5 minutes). After 4 hours the reaction mixture was added with stirring to a mixture of 8 N NaOH (100 ml) and chloroform (100 ml) at 0 °C. The chloroform phase was separated off, dried over potash, and the compounds *(3)* and *(4)* isolated by distillation.

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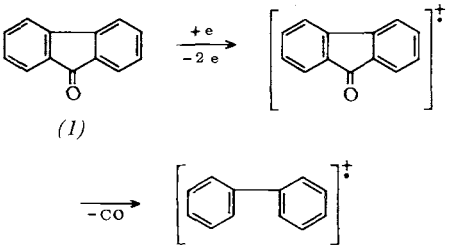
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Single-Step Synthesis of Biphenylene from 9-Fluorenone in a Discharge Plasma

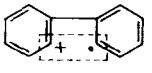
By *Harald Suhr* and *Rudolf I. Weiss* [*]

Decarbonylations by electron impact are well known in mass spectroscopy; thus, *e.g.*, 9-fluorenone *(1)*, which is very stable towards the action of light and heat, decomposes into CO and a $C_{12}H_8$ fragment,



(1) (1)

which has been formulated by *Beynon et al.* [1] as containing a one-electron bond:



Since the primary processes in mass spectroscopy and in plasmas are very similar [2] — particularly at high electron temperatures and low gas temperatures (cold plasmas) — reaction (1) should also take place on a preparative scale in a glow-discharge plasma. When compound *(1)* was fed as vapor through a high-frequency glow discharge at reduced pressure (≈ 1 torr), the main product formed was biphenylene *(2)* (see Table).

Yields of biphenylene in a glow-discharge plasma; composition of reaction products formed from 9-fluorenone (in wt.-%) at various RF energies.

Energy consumption of emitter (VA)	*(1)*	*(2)*	Naphthalene	Biphenyl	Polymer
30	90	10	≈0.1	≈0.1	—
41	82.5	17.5	≈0.1	≈0.1	—
60	79.5	20.5	≈0.1	≈0.1	—
93	16	1.8	0.8	1.4	80

When the vapor pressure of *(1)* is kept constant, the amount of *(2)* in the condensed reaction mixture increases to about 20 wt.-% on increasing the emission energy. A further increase in energy results in decomposition of *(1)* and *(2)* with formation of black, insoluble polymers.

Most of the compound *(2)* that is formed can be separated from unreacted *(1)* by vacuum distillation and then purified chromatographically. The reaction probably proceeds *via* cleavage of CO from the molecular ion of *(1)* with subsequent stabilization by electron capture (three-body collision or wall reaction) to give *(2)*.

A discharge apparatus having the oscillation coil of a push-pull LC oscillator (25—27 Hz) wound around it proved suitable for the experiments [3]. Both the chamber used for vaporization of the fluorenone and the reaction tube were double-walled and were thermostated at 130—131 °C by recirculating oil. In each of the experiments, 10 g of compound *(1)* was passed through the reaction tube in a period of 60—70 minutes; the reaction products were collected in a cold trap at −78 °C. After gas chromatographic analysis of the reaction products [FM 5750, 2 m, 20% silicone oil MS 710; 220 °C; 37 ml N_2/min] the fraction distilling at temperatures up to 120 °C (2×10^{-3} torr) was separated off for identification and subsequent isolation of the biphenylene. This was achieved by chromatographic separation with petroleum ether on an 80 cm Al_2O_3 column (Woelm, basic) semisaturated with picric acid [4]. After repeated recrystallization the biphenylene thus obtained had m.p. 110.9 to 111.2 °C. The UV spectrum agreed with that given in the literature [5].

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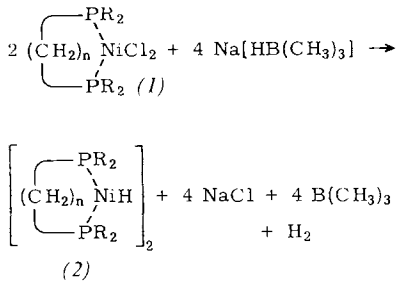
Hydrogen Bonds in a Ni–Ni System

By *Klaus Jonas* and *Günther Wilke* [*]

The Ni^0 complex $(L_2Ni)_2N_2$ (L = $(C_6H_{11})_3P$) [1], in which two nickel atoms are bound to one nitrogen molecule can be used as starting material for the preparation of hydridonickel complexes having the composition L_2NiHX (where X, for example, is Cl, CH_3COO, C_6H_5O or CH_3, C_6H_5) [2]. In the following paper we report on hydridonickel complexes,

which contain only chelating α,ω-alkanediphosphines and hydrogen as ligands.

If Ni^{II} complexes of type *(1)*, which can be prepared from $NiCl_2 \cdot 6\,H_2O$ and the corresponding phosphines[3] in alcohol, are allowed to react with $Na[HB(CH_3)_3]$ deep red crystals of the complex *(2)* are obtained.



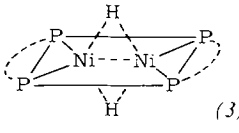
$R = C_6H_{11}$

(2a), n = 2; *(2b)*, n = 3; *(2c)*, n = 4

According to their mass spectra — and also cryoscopic measurements in benzene in the case of *(2a)* — the compounds *(2)* are dimeric. While the IR spectra of the monomeric complexes L_2NiHX[2] show intense bands (νNiH) between 1800 and 1950 cm^{-1}, the IR spectra of the dimeric hydridonickel complexes *(2)* are void of bands in this region.

In the ^{1}H-NMR spectrum[4] of *(2)*, the signal of the hydrogen atom bound to nickel shows splitting of first order into quintets with $J_{P-H} = 23.5$ Hz, $\tau = 21.4$ for *(2a)* and $J_{P-H} = 15$ Hz, $\tau = 20.4$ for *(2c)*, *i.e.* two equivalent H atoms and four equivalent P atoms are present.

Thus, the IR and ^{1}H-NMR spectra suggest a structure in which the two nickel atoms and four phosphorus atoms lie in one plane, the two bridging hydrogen atoms, however, are situated symmetrically above and below the plane:



(3)

The complex of type *(2)* formally comprises two paramagnetic Ni units $\{R_2P(CH_2)_nPR_2\}NiH$ but is diamagnetic (NMR spectra). We presume, therefore, that *(2)* contains a Ni—Ni bond superposed by hydrogen bridge bonds in the sense of multicenter bonds as are characteristic for boranes and higher alkylboranes. That *(2)* could also occur by interation of two $\{R_2P(CH_2)_nPR_2\}Ni^0$ units with a hydrogen molecule cannot be ruled out.

The complexes *(2a)* and *(2b)* are thermally very stable. Thus *(2a)* decomposes in mesitylene solution, with evolution of H_2, only at the boiling temperature. Hydrogen is replaced even at room temperature by triphenylphosphine, olefins such as ethylene, propylene, and *cis*-butene as well as by benzonitrile or tolan; in each case the calculated amount of H_2 and the corresponding Ni^0 complexes, which have not as yet been examined closely, are formed. Compound *(2a)* reacts with *(1a)*, undergoing comproportionation to give $\{R_2P(CH_2)_2PR_2\}NiCl$ and a stoichiometric amount of H_2; reaction of *(2a)* and I_2 likewise leads to formation of H_2 and the Ni^I compound $\{R_2P(CH_2)_2PR_2\}NiI$.

Experimental:

A suspension of *(1a)* (15 g, 27 mmoles) in toluene (600 ml) is added dropwise with stirring at room temperature to a solution of $Na[HB(CH_3)_3]$ (4.8 g, 60 mmoles) in toluene (100 ml). After three hours' stirring the NaCl formed is separated off by filtration and the filtrate is evaporated to dryness under reduced pressure. The residue is dissolved in hot toluene (50 ml at about 80 °C); after addition of ether (50 ml) pure *(2a)* (10 g, 75% yield) crystallizes out.

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X-Ray Structure Analysis of a 1,2,3,6,7,8-Hexathiecane[1]

By *Friedhelm Lemmer* and *Franz Fehér*[*], and *Alfred Gieren*, *Siegfried Hechtfischer*, and *Walter Hoppe*[**]

Perhydrodibenzo[1,2,3,6,7,8]hexathiecin $(C_{12}H_{20}S_6)$[2] *(1)* contains a ten-membered ring in which there are six sulfur atoms. The structure of this compound is of interest because the conformation of sulfur analogs of cyclodecane has not as yet been established[3].

We have used monoclinic single crystals (from bromobenzene) for the three-dimensional X-ray structure analysis. Crystallographic data: $a = 10.76_8$, $b = 9.10_4$, $c = 8.34_2$ Å; $\beta = 99.6_5°$; $d_{exp} = 1.48$ g/cm³; space group $P2_1/n$. The asymmetric unit cell consists of half a formula unit of *(1)* ($d_{calc} = 1.47$ g/cm³). All reflections having $\theta \leq 26°$ were measured with $Mo_{K\alpha}$-radiation on a Siemens single crystal diffractometer ($\theta/2\theta$ scan, 5-point measurement). Of 1573 independent reflections, only 271 were unobserved ($I < 2\sigma_I$).

Signs for the 300 largest unitary structural factors were determined by means of the triple product method using a program previously developed by us[4]. All sulfur and carbon atoms were visible in a successive Fourier synthesis of the phased U-values. Refinement was carried out by the method of least squares (full matrix), at first isotropically and finally anisotropically (R = 6.5%). In a difference Fourier synthesis the ten largest maxima could be assigned to the hydrogen atoms. Further refinement with the hydrogen atoms (S and C anisotropic, H isotropic) closed with an R value of 4.8% (for the observed reflections). In the last cycle the change in the parameters was on average 0.27 of the respective standard deviation.

The molecular structure is shown in Figure 1. The molecule has a crystallographic center of symmetry; deviations from the higher 2/m symmetry are not significant. The ten-membered ring has a conformation analogous to that of cyclodecane[5] with eight synclinal and two antiperiplanar partial conformations; the ring in *(1)* is, however, less strained. Replacement of the carbon atoms by sulfur atoms increases the distance between the interannular hydrogen atoms (H12—H22* and H12*—H22) from 1.8 ± 0.1 to 2.3 ± 0.1 Å. The dihedral angles in hexathiecane differ markedly from those in cyclodecane; the C—S—S—S and S—S—C—C dihedral angles are 81 and 52° respectively, the S—C—C—S dihedral angle is 164°.

The position of the sulfur atoms bound to C1 and C2 is transdiaxial with respect to the cyclohexane ring. The incorporation of the atoms C1 and C2 in the hexathiecane ring leads to a flattening of the chair conformation of the cyclohexane ring the change being most prominent at C1 and C2. The deviation of the dihedral angle of the antiperiplanar conformation of the S1—C1—C2—S2 fragment from the ideal value (180°) is −16°, in contrast to −27° in the corresponding partial con-

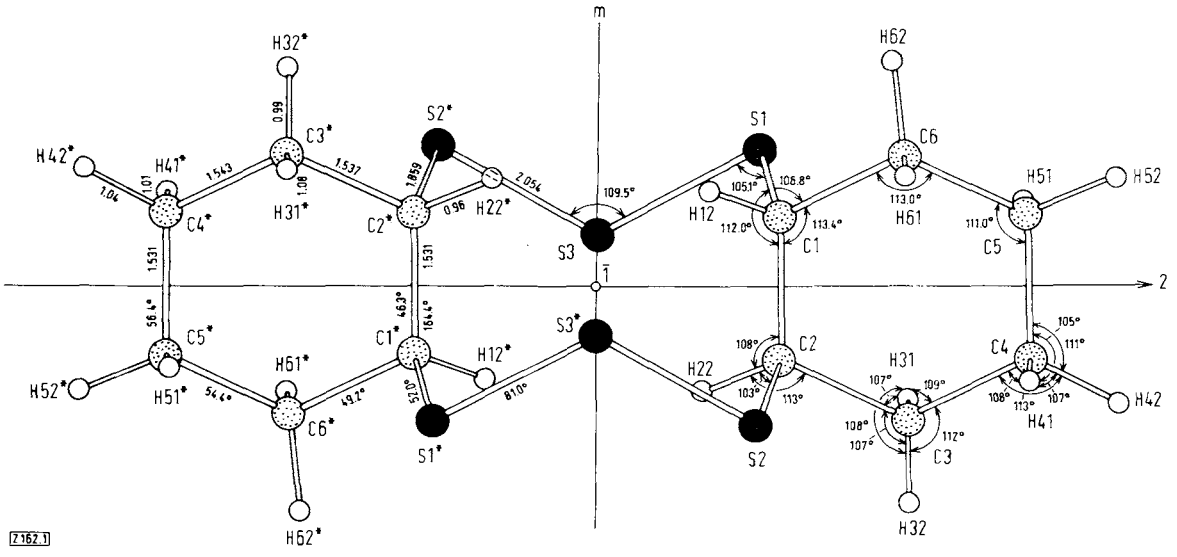


Fig. 1. Perhydrodibenzo[1,2,3,6,7,8]hexathiecin *(1)*: Projection on the C1-C2-C1* (C2*) plane.
The atoms marked with an asterisk are symmetry-equivalent to the unmarked ($\bar{1}$). The bond lengths (Å) and angles (°) were averaged according to the full symmetry of the molecule (2/m). Standard deviations of the bond lengths and angles (without averaging): σ_{S-S}, σ_{S-C}: 0.001–0.004 Å; σ_{C-C}: 0.005–0.007 Å; σ_{C-H}: 0.04–0.06 Å; σ_{S-S-S}, σ_{S-S-C}, σ_{S-C-C}: 0.1–0.3 °; σ_{C-C-C}: 0.3–0.4 °; σ_{S-C-H}, σ_{C-C-H}: 3 °; σ_{H-C-H}: 4 °. The dihedral angles in the ten-membered ring and in the six-membered ring are also given.

formation in the cyclodecane skeleton. A larger deviation from the ideal value would have led to a greater degree of flattening of the cyclohexane ring.

The C–S (1.86 Å) and S–S–S (2.05 Å) bond lengths are indicative of single bonding. The S–S–S angle (109.5 °) corresponds to a tetrahedral angle while the angle at S1 is about 4.5 ° smaller. All intermolecular distances are equal to (or greater than) the sum of the van der Waals radii. It can be concluded, therefore, that crystal packing has little influence on the conformation of the molecule.

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CONFERENCE REPORTS

Kinetics of Fast Thermal Reactions in Bituminous Coal

By *Werner Peters*[*]

The by-product oven, grate firing, and fixed bed generators are used in the traditional processes for the utilization of coal. Recent developments initiated by the introduction of fluidized-bed gasification by *Winkler* in the early 1920's had the aim of improving reactor performance by increasing the reaction rates. This aim is still pursued nowadays in projects at the Bergbau-Forschung, Essen, that are just starting or are already in progress on, *e.g.* continuous coking processes, magnetohydrodynamic energy conversion, and dust gasification with process heat from nuclear reactors.

The starting point for the study of the kinetics of fast thermal reactions is based on the fact that a pyrolysis reaction, whose rate depends primarily on the temperature and thus on the heat and mass transfer, precedes heterogeneous reactions of gasification and combustion. If the physical conditions remain constant it is possible to analyze the kinetics due only to the chemical processes in specifically designed apparatus. Since the duration of a reaction is only a few hundredths of a second at heating rates of up to 10^5 °C/min the instruments must have a high resolving power with regard to time. High speed photography (40000 frames/s) and time-of-flight mass spectrometry (10000 analyses/s) have proved effective in such work.

The curves for gas evolution which were recorded at linear heating rates afford activation energies and frequency factors for the products of individual components which are valid for the relevant pyrolysis reactions. The kinetic data recorded for coals at very different heating rates (10^{-3} to 10^5 °C/min) show that the same decomposition reactions take place both during carbonification on the geological time scale and during the very fast reactions occurring in a dust flame. The experimentally determined kinetic results for pyrolysis permit deduction of the combination of pyrolysis and reaction with the gasification agent. Measurements confirm the calculated data.

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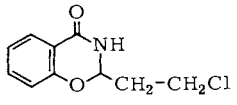
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Recent Lines of Development in the Field of Antiinflammatory Agents

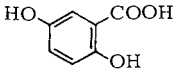
By *Alfred Kreutzberger* [*]

The term "antiinflammatory agents" is to be considered as a collective name for substances used in the treatment of local reactions of the vascular and supporting tissue system to local tissue damage. The discovery of very different types of active substances and numerous investigations on structural modifications (with the aim of increasing the activity and decreasing undesirable side effects) have led to a very heterogeneous class of drugs.

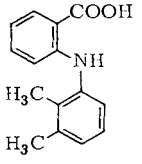
Well known fundamental types often serve as leitmotiv of such developments; *e.g.* the antiinflammatory chlorothenoxazine *(1)* [1] contains essential structural elements of the



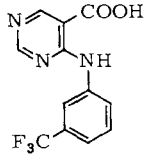
(1)



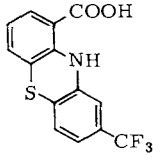
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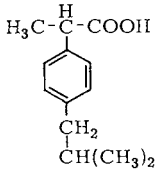
(3)



(4)



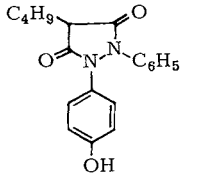
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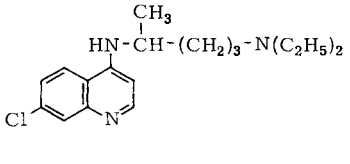
(6)

salicylic acid skeleton. Investigations on metabolism are another major source of information about substances having an improved spectrum of action. Thus the introduction of gentisic acid *(2)* into therapy followed the discovery that this substance occurs as a metabolite of salicylic acid [2]. The discovery of the highly active [3] compound mefenamic acid *(3)* resulted in the development of numerous structurally related agents such as *(4)* [4] and *(5)* [5]. Studies on the arylacetic acid systems have led to ibuprofen *(6)*, which proved to be 20 times as effective as acetylsalicylic acid in the UV erythema test [6]. Arylacetic acids can also act as antiinflammatory agents when present as part of a heterocyclic system [7].

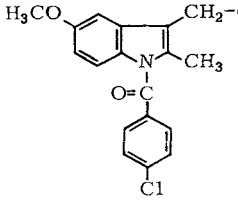
Investigations on the metabolism of phenylbutazone inspired the introduction of oxyphenbutazone *(7)* into chemotherapy [8]. Chloroquine *(8)*, which was originally developed for the chemotherapy of malaria, is being used today in the treatment of rheumatic illnesses. Several derivatives of hydrogenated isoquinoline, which are readily accessible by reaction of carbonium ions with nitriles, have also proved to exhibit strong antiinflammatory properties [9]. An annelated heterocyclic ring is the common structural feature of another group of antiinflammatory agents, which are derived from indole, *e.g.* indometacin *(9)* [10], from indazole, like benzydamine *(10)* [11], from benzimidazole [12] or from benzotriazole [13].



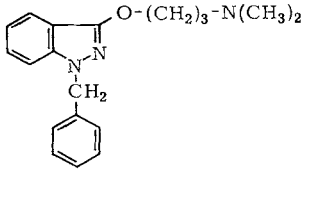
(7)



(8)



(9)



(10)

Lecture at Bielefeld, January 16, 1970 [VB 230 IE]
German version: Angew. Chem. *82*, 296 (1970)

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[1] *G. Ohnacker*, DBP 1028999 (1958); Chem. Abstr. *54*, 18561 b (1960).

[2] *K. Meyer* and *C. Ragan*, Science (New York) *108*, 281 (1948).

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[13] *A. Kreutzberger* and *E. Dietz*, unpublished.

Syntheses in the Cyclopeptide Series

By *Theodor Wieland* [*]

Cyclopeptides, which are produced by higher and lower organisms, have recently acquired significance as antibiotics, uncouplers of oxidative phosphorylation, toxins, and antitoxins. In the author's laboratory, analytical and synthetic studies on the cyclic peptides of the green death cup fungus (*Amanita phalloides*) have been in progress for some time.

The phallotoxins and amatoxins are respectively hepta- and octacyclopeptides whose ring is divided by a thioether or a sulfoxide bridge to position 2 of the indole ring of the tryptophan lying in the opposite position of the ring. They contain, *inter alia*, γ-hydroxylated leucine or isoleucine as an important structural unit. While the γ-OH of phallotoxins can be replaced by H without any loss of toxicity [norphalloin (LD_{50} = 1.5 mg/g white mouse) is even more toxic than phalloidin (LD_{50} = 2.5 mg)], its absence from amatoxins leads to loss of toxicity. Both the naturally occurring amanullin — having isoleucine in place of γ-hydroxyleucine — and an "aldoamanitin", prepared oxidatively and containing an aldehyde function in the γ-position, are non-toxic. Whereas α-amanitin clearly inhibits [1] the function of an RNA polymerase of mammalian cell nuclei at a concentration of 0.02 μg/ml, aldoamanitin again has no toxic action.

Norphalloin has been obtained by total synthesis[2]. Such a preparation of amatoxins remains to be accomplished. However, several syntheses of the antitoxin antamanide[3] are known, including one based on a Merrifield synthesis which gives a linear decapeptide that is subsequently cyclized. Suitable processes are the mixed anhydride method or the use of dicyclohexylcarbodiimide with addition of *N*-hydroxysuccinimide.

Antamanide, an antagonist of phalloidin, lowers the vapor pressure of an alcoholic NaBr solution and reduces the electrochemical activity of an alcoholic NaBr solution at the Na^+ sensitive glass electrode; further, its ORD spectrum shows a marked change in the presence of Na^+ ions and to a much lesser degree in the presence of K^+ ions. Since phalloidin leads to liberation of K^+ ions in an isolated perfused rat-liver preparation[4], a biological action *via* alkali metal ions cannot be ruled out.

Lecture at Tübingen on February 6, 1970 [VB 232 IE]
German version: Angew. Chem. *82*, 327 (1970)

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69 Heidelberg, Jahnstrasse 29 (Germany)

[1] *F. Stirpe* and *L. Fiume*, Biochem. J. *103*, 67 P (1967).

[2] Nachr. Chem. Techn. *18*, 5 (1968).

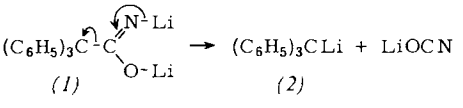
[3] *Th. Wieland et al.*, Angew. Chem. *80*, 209 (1970); Angew. Chem. internat. Edit. *7*, 204 (1968).

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SELECTED ABSTRACTS

Liquid ethyl azide can explode. A brief communication dealing with the explosion of azides in the laboratory reports on a recent observation by *E. Koch* of a 300 ml stoppered flask containing 70 g ethyl azide exploding, without any outside influence, 3—4 minutes after having been transferred from storage at −55 °C to the laboratory bench. It is assumed that the explosion was not due to the presence of contaminants but rather the gradual increase in pressure in the flask that was stoppered with an ungreased glass stopper. Either the stopper became loose as a result of shaking or the flask cracked, so that the ethyl azide could have been brought to the point of explosion mechanically. — Ethyl azide is known as a distillable liquid that explodes only at temperatures above 200 °C or when subject to mechanical stress. / Nachr. Chem. Techn. *18*, 26 (1970) / —Kr. [Rd 154 IE]

***n*-Butyllithium cleaves carboxamides,** as has been established by *H. A. Smith* and *C. R. Hauser* for 2,2,2-triphenyl- and 2,2-biphenylacetamide. 2,2-Triphenylacetamide in THF was heated for 6 h with 1.2 mol. equiv. of *n*-butyllithium in hexane and, after work-up, afforded triphenylmethane (65 %)

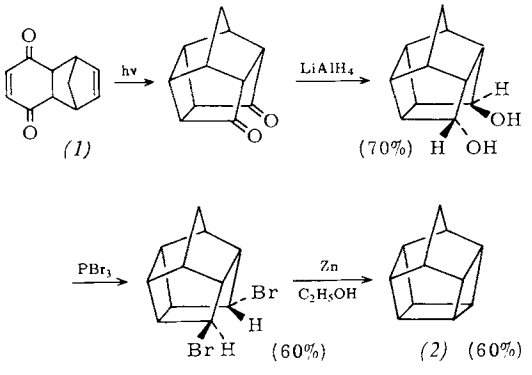


(1) *(2)*

alongside starting material (21 %). It is assumed that the reaction proceeds *via* the dilithium compound *(1)* and leads initially to tritylllithium *(2)* and lithium cyanate. / J. Amer. chem. Soc. *91*, 7774 (1969) / —Kr. [Rd 159 IE]

A method for analysis of the surface layer of solids is described by *A. Benninghoven*. The surface is bombarded with argon ions of suitable energy (a few keV) at a very low current density (of the order of 10^{-9} Å cm^{-2}); the secondary ions liberated are analyzed by mass spectrometry. The energy of the primary ions is chosen such that the secondary ions are emitted almost exclusively from the first surface layer. The time required for degradation of a monolayer is of the order of 10^4 s. The variation in the intensity of the mass peaks of a particular ionic species with time permits an unequivocal decision whether the species arises only in the first layer or also in deeper layers. The facts that sufficiently stable surface compounds can be detected and that isotopes can be separated represent advantages of the present method over the other technique of surface layer analysis, Auger electron spectroscopy. / Z. Physik *230*, 403 (1970) / —Hz. [Rd 162 IE]

Homopentaprismane, hexacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]undecane *(2)*, a new cage compound, has been synthesized by *G. R. Underwood* and *B. Ramamoorthy* from the *p*-benzoquinone/cyclopentadiene adduct *(1)* *via* the following simple route:



(2) is a white, volatile compound, m.p. 98—100 °C, which is resistant to attack by Br_2 in CCl_4. / Chem. Commun. *1970*, 12 / —Ma. [Rd 160 IE]

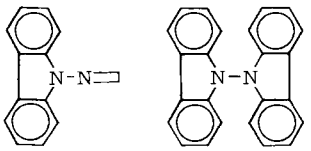
The existence and the oxidation potential of heptavalent neptunium was investigated by *A. J. Zielen* and *D. Cohen*. In sodium hydroxide solutions, Np^{VII} and Np^{VI} form a reversible redox couple; the potential determining reaction was shown to be

$$e^- + NpO_5^{3-} + H_2O \rightleftharpoons NPO_4^{2-} + 2\ OH^-.$$

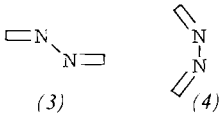
The formal potential of the system in 1 N NaOH at 25 °C is 582.1 ± 0.45 mV *vs.* the normal hydrogen electrode. Besides ozone oxidation of neptunium(V) hydroxide, electrolysis was found to be a good preparative method for heptavalent neptunium. In its infrared spectrum in aqueous alkaline solution, Np^{VII} exhibits a single band at about 1100 cm^{-1}, as does Np^{VI}. / J. physic. Chem. *74*, 394 (1970) / —Hz. [Rd 165 IE]

Magnetophotoselection was used by *G. P. Rabold* and *J. M. Gaidis* to distinguish between several possible structures *(1)*—*(4)* of 9,9′-bicarbazole. If a rigid solution of bicarbazole is irradiated at 77 °K with polarized light only those molecules will be excited that have a transition moment, for the wavelength used, closely parallel to the direction of polarization of the exciting light. The triplet states generated by

subsequent intersystem crossing can be identified by ESR measurements. With the aid of Hückel MO theory, ESR spectra were calculated for *(1)*—*(4)* and compared with the



(1) *(2)*



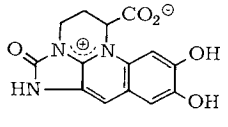
(3) *(4)*

experimental spectra taking into account the relative orientation of magnetic field and plarization plane of the exciting light. The agreement between prediction and experiment strongly favors structure *(1)* with sp^2 hybridization of the nitrogen atoms. / J. physic. Chem. *74*, 227 (1970) / —Hz.

[Rd 166 IE]

The Mössbauer spectra of hexaammineiron(II) chloride are reported by *L. Asch, J. P. Adloff, J. M. Friedt*, and *J. Danon*. At room temperature, the salt exhibits a single line, characteristic of a perfectly octahedral environment. Upon cooling, two other lines, symmetrical about the former, appear at 109.5 °K; at 107 °K, the single line has disappeared. Upon heating, the single line reappears at 110 °K, the doublet has vanished at 116 °K. The splitting at low temperature can be explained in terms of frozen rotation of the NH_3 ligands around the Fe—N axes. At high temperature, however, the rotation is free and fast enough to produce an octahedral average symmetry around the iron ion. The hysteresis is also known from ESR investigations on nickel(II) hexaamines and is characteristic for order-disorder transitions with cooperative interaction between neighboring complexes. / Chem. Physics Letters *5*, 105 (1970) / —Hz. [Rd 167 IE]

The crystal structure of the chromophore from the yellow-green fluorescent peptide produced by iron-deficient *Azotobacter vinelandii* has been determined by *J. L. Corbin, I. L. Karle*, and *J. Karle* by X-ray crystallographic examination of a methylated derivative. The structure is that shown in *(1)*. The



(1)

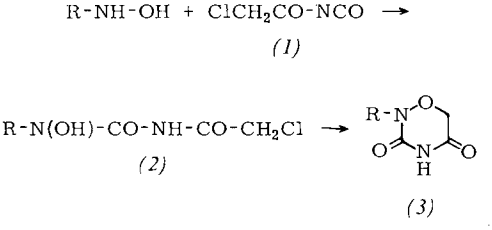
unusual heterocyclic structure of the chromophore has not heretofore been observed in any naturally occurring system. Chem. Commun. *1970*, 186 / —Ma. [Rd 171 IE]

A new separation method for gas molecules of different mass is discussed by *R. Campargue*. The shock wave system of a supersonic gas jet in the pressure range 10^{-2}—1 torr tends to aspirate gas molecules from its surroundings. When a gas mixture is introduced into the nozzle chamber outside the jet boundary, the light molecules are selectively carried away by the jet and can be enriched by "skimming" the jet. The separation efficiency is superior to that of gas diffusion: the separation factor defined by

$$S = f_2(1-f_0)/f_0(1-f_2)$$

(f is the mole fraction of the light component, the subscripts 0 and 2 refer to starting and final mixture, respectively) for example, reaches, with optimum conditions, 1.01 for $^{32}SF_6$ $^{34}SF_6$ with N_2 as the carrier gas, as compared to the diffusion separation factor of 1.0068. / J. chem. Physics *52*, 1795 (1970) —Hz. [Rd 169 IE]

A new method for the synthesis of the 1,2,4-oxadiazine ring system is described by *P. Rajagopalan* and *B. G. Advani*. Chloroacetyl isocyanate *(1)*, which can easily be prepared from chloroacetamide, reacts with *N*-monosubstituted hydroxylamines in anhydrous benzene medium to yield the *N*-chloroacetyl-*N'*-hydroxyureas *(2)*. Compounds *(2)* readily



undergo cyclization in 2 % aqueous NaOH to afford, upon acidification, 2-substituted 2*H*-1,2,4-oxadiazine-3,5(4*H*,6*H*)-diones *(3)* (overall yield 30—60 %). / Chem. Commun. *1970*, 167 / —Ma. [Rd 172 IE]

R = isopropyl, phenyl, 4-chlorophenyl, 4-methoxyphenyl, 3-nitrophenyl, 2,5-dichlorophenyl

Formamides from carbon dioxide, amines, and hydrogen in the presence of transition metal complexes is the subject of a report by *P. Haynes, L. S. Slaugh*, and *J. F. Kohnle*.

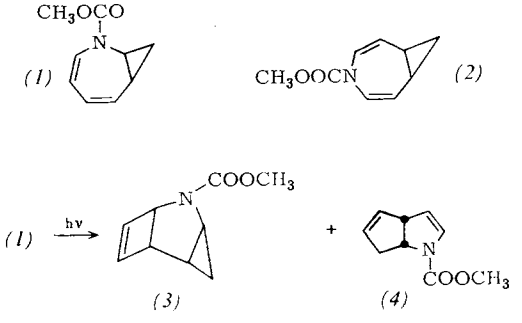
$$R_2NH + CO_2 + H_2 \rightarrow R_2NCHO + H_2O$$

The amines employed included, *inter alia*, dimethylamine, di-*n*-propylamine, and piperidine. Typical catalysts were $[(C_6H_5)_2P{-}CH_2{-}CH_2{-}P(C_6H_5)_2]_2CoH$, $[(C_6H_5)_3P]_3RhCl$, and $[(C_6H_5)_3P]_2(CO)IrCl$. Although the reaction is not fast at 100—125 °C, it is clearly catalyzed. In the DMF synthesis, tetramethylurea does not occur as intermediate. The following reactions are — at least for the irdium system — consistent with the results obtained.

$$LxMH + CO_2 \rightarrow LxMOCHO \xrightarrow{HN(CH_3)_2} LxMOH + DMF$$
$$LxMOH + H_2 \rightarrow LxMH + H_2O$$

Tetrahedron Letters *1970*, 365 / —Kr. [Rd 175 IE]

The synthesis and photoisomerization of homo-1*H*-azepine derivatives is described by *L. A. Paquette* and *R. J. Haluska*. On heating a solution of methyl azidoformate in cyclohepta-



(1) *(2)*

(3) *(4)*

triene (4 h, 127–128 °C) a mixture of the homo-1*H*-azepines *(1)* and *(2)* was formed (total yield 35 %) which was separated by preparative gas chromatography. Presumably the compounds are formed by valence isomerization of initially formed methoxycarbonylaziridines. The NMR spectra of *(1)* and *(2)* are not temperature dependent, *i.e.* valence isomerization does not now take place. *(1)* and *(2)* do not enter into cycloadditions. Irradiation of *(1)* gives a mixture of *(3)* and *(4)* while *(2)* is virtually unaffected. / J. org. Chemistry *35*, 132 (1970) / —Kr. [Rd 176 IE]

Tetrakis(acetatomercurio)methane, $C(HgOCOCH_3)_4$, a crystalline, stable, water soluble substance has been prepared in good yields by *D. S. Matteson, R. B. Castle,* and *G. L. Larson* by heating a mixture of $C[B(OCH_3)_2]_4$ and $Hg(OCOCH_3)_2$ under reflux. Pure $C(HgOCOCH_3)_4$, m.p. 265–285 °C (dec), gives a white precipitate with NaOH and with $SnCl_2$. An iodine compound $C(HgI)_4$, m.p. > 300 °C, can also be formed. The stability of the C—Hg bond may be explained by the shielding of the carbon atom by the four Hg atoms. / J. Amer. chem. Soc. *92*, 231 (1970) / —Kr. [Rd 178 IE]

BOOK REVIEWS

Inverse Polarographie und Voltammetrie Inverse Polarography and Voltammetry). By *R. Neeb*. Verlag Chemie GmbH, Weinheim/Bergstr. 1969. 1st Edit., xii + 256 pp., 139 figures, 33 tables, plastic, DM 48.—.

The high detection sensitivity of electrochemical analytical methods has contributed to the widespread use of polarography. The sensitivity of any analytical method can be substantially increased by integrating processes. Inverse polarography constitutes such a process, in which substances present in an electrolyte solution are collected by deposition on a stationary mercury drop or mercury pool or on other electrodes made of suitable materials with simultaneous selection by the applied potential. The process is therefore particularly suitable for trace analysis.

The present work gives the first really comprehensive and up-to-date treatment of this process. The first section contains a concise and very lucid review of the principles of the enrichment process. The second section deals with the electrochemical methods used for the quantitative determination of the collected substances. A detailed experimental section follows, in which emphasis is given to the description of the electrodes and the apparatus employed. This section also contains a discussion of the sources of error. The second part of the work deals with the methods used to determine particular elements and includes the relevant literature data. The highly informative book can be recommended without reservation to everyone interested in this field.

Heinz Gerischer [NB 855 IE]

Terminologie Chimique Franco-Anglaise. French-English Chemical Terminology. An Introduction to Chemistry in French and English. By *H. Fromherz* and *A. King*. Translated by *J. Jousset*. Verlag Chemie GmbH, Weinheim/Bergstr. and Gauthier-Villors, Paris 1968, 1st Edit., xix + 561 pp., linen, DM 66.—.

As far as the average chemist is concerned, technical dictionaries are often unsatisfactory. Despite the fact that he is perfectly capable of understanding "Keton", "ketone", or "cétone" without their help, they nevertheless burden the luckless reader with pages of translations for terms that are obvious to anyone expert in the subject. Certain dictionaries in the chemical field omit these terms; such dictionaries simplify the problem for the chemist who is trying to read a paper in his own subject[1]. If, however, a paper is to be translated into the foreign language, there still remains the problem of the correct usage of words, the problem, in short, of terminology.

The present book is not a dictionary but a series of parallel texts, the French and the English versions being printed on facing pages. In this way, in the guise of a very simple but comprehensive introduction to chemistry, it actually provides a comparison of the terminology used. A wide range of topics in physical, inorganic, organic and analytical chemistry is covered. It must be admitted that in places the material is rather outdated. (In 1934, when the original German-English version of the book was published[2], it may well have been true to say that "Sugden's parachor method is much used in Britain!") As an introduction to chemistry, however, the book is surprisingly clear and free from errors. The presentation is in general limited to facts and to theories that have stood the test of time. With a few exceptions, the French translation faithfully reproduces current usage, and should provide a quick way for the English-speaking reader to get to grips with this terminology; in the same way, French-speaking readers will be able to acquaint themselves with contemporary English usage. I am convinced that both groups will learn to value this book, and in many cases will make use of it as a chemically-orientated dictionary and language textbook.

In a book like this errors are particularly dangerous though possibly, in view of the breadth of coverage, unavoidable. Thus "Cardiac glycosides" are not "les glycosides du coeur"; "ribose" is "le" and not "la"; DNA has a "structure en double hélice", not "à double filet"; adrenalin is "une hydroxy-amine", not "une hydroxylamine"; ESR is "RPE", never "RPM"; chemical displacements are "déplacements chimiques", not "transferts chimiques". Fortunately mistranslations such as these occur in only a few chapters, and these are generally more up-to-date than the rest of the book and thus offer the reader fewer difficulties in other respects.

Guy Ourisson [NB 857 IE]

[1] *R. Cornubert:* Dictionnaire Chimique Allemand-Français. Chemisches Wörterbuch Deutsch-Französisch, Dunod, Paris 1967, 3rd Edit..

Dispersions of Powders in Liquids, with Special Reference to Pigments. By *G. D. Parfitt*. Elsevier Publishing Company, Amsterdam-London-New York 1969. 1st Edit., xiii + 354 pp., numerous figures and tables, bound, Dfl. 52.—.

Nine contributions from eleven eminent authors, including the editor, have been effectively combined into one homogeneous work. The subject is approached from various points of view. The book has been written for scientists in whose work highly dispersed solids play a role. Particular attention is given to problems of interest to manufacturers and users of pigments wishing to keep up with the latest developments. One should not be dismayed by the fact that the dispersion process is influenced by numerous factors that are difficult or impossible to define in practice. The editor lays stress on the fact that the sensible use of certain guidelines can lead to better dispersions and a better understanding of the dispersion process. This alone is a good enough reason for "students" of all ages to peruse this book.

The first two chapters (I: *M. J. Jaycock*; II: *A. L. Smith*) deal with the scientific principles concerned in solid-liquid interfaces. Starting with the forces between atoms, ions, and molecules, the authors go on to discuss boundary surface energy, wetting, adsorption, and, finally, electric double layers and zeta potentials, covering innumerable surface properties and

[2] Cf. Angew. Chem. *75*, 696 (1963).

concepts. The principles of the dispersion process, dispersibility, and stability or flocculation of dispersion form the subject of the next chapter (*G. D. Parfitt*). Obviously, in the given context consideration must be given to agglomerates and aggregates. After all, these structural formations of powdered substances are the reason why dispersion is necessary. These processes are mentioned in the fourth chapter (*A. G. Walton*), which gives a general survey of the formation and growth of nuclei in precipitation reactions. The few facts on the problem of agglomeration in precipitation for which space could be found suggest that further research is needed.

The fifth chapter (*S. H. Bell* and *V. T. Crowl*) is devoted to industrial applications of dispersions and the relevant methods of measurement. It is followed by a chapter (*W. Black*) on the effects of surface-active agents. The industrial aspects of dispersion classified according to dispersion machines and products are summarized in the seventh chapter (*R. Sheppard*). The book ends with chapters on inorganic (*H. D. Jefferies*) and organic (*H. D. Brearley* and *F. M. Smith*) pigments giving information on pigment-specific dispersion and other application problems.

The references are given at the end of each chapter, and the book contains about 500 in all. A short but adequate index is provided. The presentation of the material is good, the photographic reproductions being of satisfactory quality and the schematic drawings clear and distinct. The book deserves every success.

B. Honigmann [NB 865 IE]

Introduction to Quantum Chemistry. By *J. M. Anderson*. W. A. Benjamin, Inc., New York 1969. 1st. Edit., xiv, 445 pp., numerous Figs. and Tables, bound $ 14.95.

Since quantum mechanics or quantum chemistry became one of standard courses in chemistry departments about fifteen years ago, numerous and varied textbooks on this subject have been published. Although many excellent quantum mechanics textbooks are available today (*Messiah:* Quantum Mechanics; *Dike* and *Wittke*: Introduction to Quantum Mechanics; *Saxon*: Elementary Quantum Mechanics; *Merzbacher*: Quantum Mechanics, *Gotterfied*: Quantum Mechanics, *etc.*), it is still quite difficult to find a suitable text for a one-semester introductory quantum mechanics or quantum chemistry course for chemists. The reason for this is that most excellent quantum mechanics textbooks are primarily written for physicists and some good quantum chemistry books (*Pauling* and *Wilson*: Quantum Mechanics; *Eyring, Walter*, and *Kimball*: Quantum Chemistry: *Kanzman*: Quantum Chemistry, *etc.*), are out of date. In the reviewer's opinion this book can fill in the gap and can serve very well as a textbook for a one-semester introductory quantum chemistry course. This book has four striking features: (1) The *Heisenberg* and *Schrödinger* viewpoints are developed and used simultaneously throughout and the emphasis is on the formulation of quantum mechanics. In doing so, students can get a more general and more rigorous view of quantum mechanics. (2) The notation used is in line with that found in the current literature. This enables students to follow the papers on quantum chemistry which appear in modern chemical and physical journals. (3) Some problems in the book are solved by computer. This makes students able to appreciate the importance of the computer in modern quantum chemistry. (4) Topics chosen in the book are important and useful to chemists. However, the book also has some shortcomings, namely: (1) Some presentations are too sloppy or unclear. (2) There are quite a few typographical errors.

The author begins his presentation with the discussions on some intuitions and some experiments in quantum mechanics; then follows a postulational introduction to quantum mechanics. Both matrix mechanics viewpoint and wave mechanics viewpoint are introduced and developed simultaneously by a very fresh approach – one which differs from most competing texts of quantum chemistry. Constant potential problems such as the free particle, the particle in a box, the motion of a particle in region of several constant potentials *etc.* are discussed. The quantum mechanical concepts of these problems are emphasized. After briefly describing the many-body, many-coordinate systems, angular momentum is introduced. Following this the harmonic oscillator and the hydrogen atom are treated in quite an elegant manner.

The second part of the book considers the approximation methods in quantum chemistry. Variational method and perturbation theory are explained in detail. The applications of variational method and perturbation theory to atomic and molecular systems are illustrated very well. The molecular orbital theory, valence bond theory, Hartree-Fock SCF and LCAO are discussed. Time-dependent theory and spectroscopic theory are also presented. The author concludes the book with a descriptive treatment of scattering theory.

Overall, the presentations are good and the approaches are fresh. However, in some places, I think that there would be a more effective way to convince readers, but the author just throws up his hands by asking readers to believe him (*e.g.* p. 27 lines 6 and 7). For a textbook of this level (intended for seniors and first year graduate students), in some places the presentations should be more detailed. For example, on p. 37, the derivation of Eq. (1—41) is presented poorly. On p. 347, without discussing properties of Dirac Delta function or mentioning it, the author just states: "now $\int_{-\infty}^{\infty} e^{i(k'-k)} = 0$; ..." (Readers have to believe it!) Despite these minor shortcomings, I still highly recommend this book to be used as a textbook for the one-semester introductory quantum chemistry course.

Yuh Kang Pan [NB 869 IE]

Amino Acids Determination – Methods and Techniques. By *S. Blackburn*. Marcel Dekker, Inc., New York-London 1968, 1st Edit., xi + 271 pp., numerous figures, bound, approx. DM 52.—.

This book is intended for the man at the bench in amino acid analytical laboratories, research institutes, and in industry. The title theme is the unifying thread that holds the whole volume together. The concise and practical nature of the work is lost sight of only in the opening chapter on the history and importance of amino acids analysis, and the chapter might well have been shortened to make room for more operating instructions and recommendations. This would have been to the advantage of the more important first half of the book, which deals with ion-exchange chromatography and the associated technology and use of modern automatic analyzers, highlighting the author's knowledge and experience of the subject. The very latest developments in theory and practice have been covered, as far as this is possible in a widely ramified field characterized by continuous improvements in equipment. The plentiful literature references in each section are treated only briefly and in review fashion in the text; occasionally a definite evaluation would perhaps be preferable.

The second half of the book deals, with acceptable brevity, with such vital methods and techniques as paper and gas chromatography, infrared and mass spectrometry, and the proven high-voltage electrophoresis. All things considered, the treatment of the analysis of physiological fluids is definitely too short. Despite this, the book is highly recommended to anyone who uses or runs an amino-acid analyzer.

Christian Birr [NB 870 IE]

Mineralöle und verwandte Produkte. (Mineral Oils and Related Products). A handbook for laboratory and industrial use, in two volumes. Edited by *C. Zerbe*. Springer-Verlag, Berlin-Heidelberg-New York 1969, 2nd Edit., 1834 pp., 582 figures, bound DM 348.—.

This work contains more than would be expected from the title. Written by 42 well-known specialists, it is first and foremost a laboratory handbook for the testing and evaluation

of mineral oils in the widest sense. The first chapter, "General Methods of Testing", reviews methods of determining physical properties and describes various chemical tests, including the methods for the statistical determination of constitution. In addition, it includes a section by *H. Luther* on physicochemical tests, which in its 260 pages provides a comprehensive handbook on modern physicochemical methods of analysis in organic chemistry, going far beyond the analysis of hydrocarbon mixtures. There are 10 chapters on specific analytical methods. Each chapter is preceded by a state of the art review, which deals with the processes concerned and gives statistical data.

Almost all sections of the book have been rewritten for the second edition. It is a pity that the division into chapters is still the same as in the first edition, since this division has a confusing effect. In the chapter "Petroleum and petroleum products" we find as subsections "Gasoline", "Fuel oil", and "Bitumen"; these are not really comparable, since the sections on "Fuel oil" and "Bitumen" are principally concerned with test methods, while the section on "Gasoline" is primarily concerned with process descriptions. To find test methods for gasolines it is necessary to consult another chapter on "Fuels". Although it is justifiable to have a chapter on "Fuels" and another on "Lubricants", I find it difficult to understand why a chapter is devoted to the Fischer-Tropsch synthesis. It does not seem likely that any user of this book will be working in a Fischer-Tropsch plant. The inclusion of a chapter on "Fuller's earth" is also puzzling, since this is not a mineral oil product, and in any case other materials used in petroleum processing (*e.g.* catalysts) are of greater significance. The appearance of sections such as "Natural gas" or "Town gas from mineral oils" in the chapter on "Fuels" is not an aid to clear understanding.

The literature has been carefully sifted, and an ample (though alas not uniform) selection of references is provided. The wealth of information supplied is sufficient recompense even for the somewhat high price. In any mineral oil laboratory this book is indispensable and irreplaceable by any other book, so that it really needs no recommendation. Every oil chemist should have a copy. *H. J. Neumann* [NB 867 IE]

Mathematics for Quantum Chemistry. By *J. M. Anderson*. W. A. Benjamin, Inc., New York 1966. 1st Edit., x, 154 pp., numerous Figs. and Tables, bound $ 3.95.

This is a readable but somewhat superficial (monograph) booklet on physical and mathematical preparation for quantum chemistry. The author begins with a brief discussion of eigenvalue problems in quantum mechanics and classical mechanics, then introduces the concepts of orthogonality and normalization, expansion in terms of orthonormal functions, the Fourier series, construction of orthonormal functions, the Legendre polynomials, associated Legendre polynomials, Laguerre polynomials, and Hermite polynomials. After the chapter on orthogonal functions, the essential topics of linear algebra such as matrices, determinants, linear transformations, and linear operators are discussed. Following these the conservation laws, generalized coordinates, Lagrange's equations, Hamilton's equations, vibrations of a mechanical system, and rotations of a rigid mechanical system are presented. Finally, the bridge between classical and quantum mechanics, the synthesis of matrix and wave mechanics is discussed. Overall, the presentations are quite clear even for the average junior or senior. The topics chosen in the book are useful to students of chemistry who intend to take quantum chemistry course(s) in the future. The author does not exhaust all important mathematical background topics of quantum chemistry as he states in his preface; in the reviewer's opinion, at least the Dirac delta function and elementary integral transforms should be introduced or briefly described. In the chapter on linear algebra, pieces of information are loosely put together without the beauty of logic. The beautiful logical structure of linear algebra and its implications to the formation of quantum mechanics are not fully explored. In some places the presentations are too brief to be consistent with overall development of the book (*e.g.* on p. 29 the derivations of Eqs. (2—56) and (2—57), on p. 81 the derivation of Eq. (3—60), on p. 90 to 91 the example of the projection operator *etc.*). Besides these, there are a few typographical errors in the text and some mistakes in the answers to problems. For example, p. 36 line 10, a_0 should be a_1; p. 37, line 7 from the bottom, $(n+1)$ should be $(l+1)$; p. 37 line 5 from the bottom the last term $2 \times n \frac{d^{l+1}y}{d\chi^{l+1}}$ should be $2 \times l \frac{d^{l+1}y}{d\chi^{l+1}}$; p. 37 line 4 from the bottom, $2n\,(n+1) \frac{d^l y}{d\chi^l}$ should be $2l\,(l+1) \frac{d^l y}{d\chi^l}$; p. 38 right hand side of Eq. (2—97) should be $-\frac{1}{2^l l!} \frac{d^l}{d\chi^l}(1-\chi^2)^l$ or $\frac{1}{2l!} \frac{d^l}{d\chi^l}(\chi^2-1)^l$ p. 72 line 8, —4 should be +4 *etc.* Despite these shortcomings, it is still a very good supplementary reading for quantum chemistry course(s) and a mathematical course for chemists. Because the scope of the book is not sufficiently broad nor its degree of sophistication sufficiently deep, I do not recommend this book to be used as the main textbook for an "Applied Mathematics for Chemists" course for seniors or first year graduate students. *Yuh Kang Pan* [NB 868 IE]

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Modern Steroid Problems

By Rudolf Wiechert[*]

Dedicated to Professor R. Tschesche on the occasion of his 65th birthday

The present article is concerned primarily with the latest developments in the fields of steroids exhibiting contraceptive, antiandrogenic, or cardiac activity and of steroid metamorphosis hormones. Both the biological action and the current sources of raw materials are considered.

1. Introduction

Of all the natural products, no group has had more time and work devoted to it by a variety of scientists than the steroids.

The history of the steroids is rich in scientific climaxes, such as the isolation, structural elucidation, and synthesis of the sex hormones in the 1930's, and the beneficial discovery of the antiarthritic and antiinflammatory effects of the adrenocortical hormones.

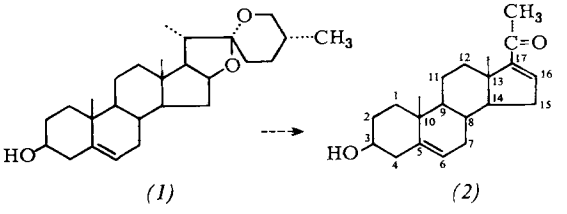
The diversity of the biological effects of steroids and their potentiation and variation by chemical modification are unequalled among the natural products.

As an extreme example of the versatility of these substances, the male sex hormone testosterone[1] and several pregnane derivatives[2–4] have been found in surprising quantities as active substances in the prothoracic defensive gland secretions of some water beetles.

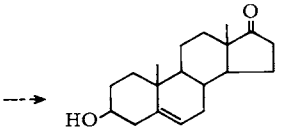
The purpose of the present article is to provide a picture of the latest developments and of some of the problems that await solution. The evaluation and selection of the topics are naturally subjective. Thus no mention is made, for example, of the use of steroids in mechanistic and steric studies or in the development of new physical methods.

2. Sources of Raw Materials

The raw material for by far most of the steroids produced at present is diosgenin *(1)*. The development of this natural product, which occurs in the roots of several types of Dioscorea, is due to the work of *R. E. Marker*[5]. The dried roots of the plants, which grow wild, *e.g.* in Mexico, Guatemala, India, China, and South Africa, contain about 5–6% of diosgenin.



(1) *(2)*



(3)

[*] Dr. R. Wiechert
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1 Berlin 65, Müllerstrasse 170–172 (Germany)

[1] *H. Schildknecht, H. Birringer*, and *U. Maschwitz*, Angew. Chem. *79*, 579 (1967); Angew. Chem. internat. Edit. *6*, 558 (1967).

[2] *H. Schildknecht* and *H. Dotz*, Angew. Chem. *79*, 902 (1967); Angew. Chem. internat. Edit. *6*, 881 (1967).

[3] *H. Schildknecht* and *W. König*, Angew. Chem. *80*, 45 (1968); Angew. Chem. internat. Edit. *7*, 62 (1968).

[4] *H. Schildknecht, H. Tacheci*, and *U. Maschwitz*, Naturwissenschaften *56*, 37 (1969).

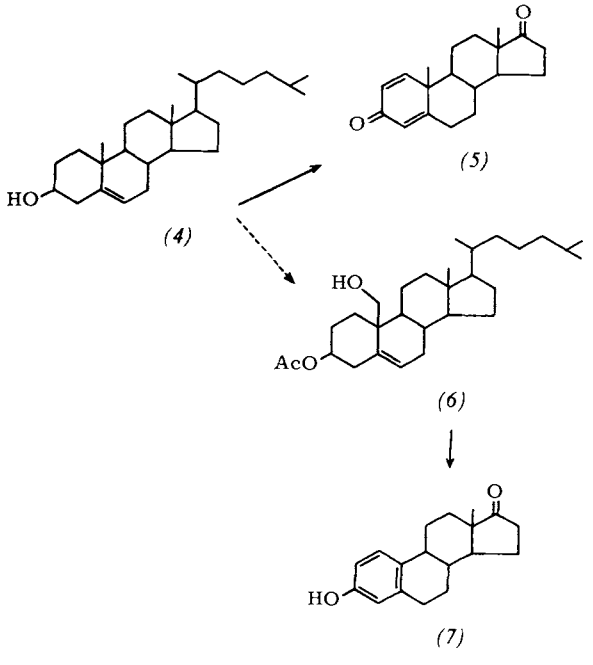
[5] See *L. Fieser* and *M. Fieser*: Steroids. Reinhold, New York 1959.

Nearly all the steroids in therapeutic use can now be obtained on the industrial scale from diosgenin *via* 3β-hydroxy-5,16-pregnadien-20-one *(2)* and 3β-hydroxy-5-androsten-17-one *(3)* [6].

Stigmasterol from soybean sterols is of limited importance as a raw material for the synthesis of corticosteroids.

As a result of the development of new microbiological processes, cholesterol *(4)* or β-sitosterol could regain interest as raw materials in the future, particularly for the synthesis of 19-nor steroids. Whereas the oxidative chemical degradation of the C-17 side chains, as used in the past, gave only small yields, the microbiological degradation to 17-ketones gives yields of more than 70% in some cases.

Using cultures of *Mycobacterium phlei* with added nickel sulfate, a group of Dutch workers has been able to degrade cholesterol *(4)*, with simultaneous oxidation, double-bond isomerization, and dehydrogenation at C-1 and C-2, to the 1,4-diene-3,17-dione *(5)* [7].

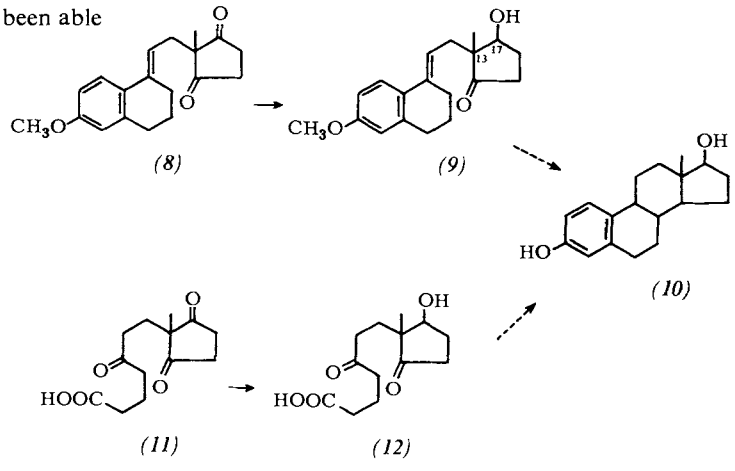


(4) *(5)* *(6)* *(7)*

Sih et al. [8] converted 19-hydroxycholesterol 3-acetate *(6)* directly into estrone *(7)* by means of a microorganism isolated from soil samples (CSA-10). *(6)* is obtainable from cholesterol in only three steps [9].

Progress in stereochemistry, and particularly the recognition of the stereoelectronic principle in additions to carbonyl and olefinic double bonds and of the importance of the energy of intermediates, as well as the estimation of the accessibility of reaction centers, have recently led to the development of total estrone syntheses for industrial use by the research groups of *Velluz* [10,11], *H. Smith* [12–14], and *Anachenko* and *Torgov* [15–17].

The successful use of enzymatic asymmetric reduction has made total steroid syntheses capable of competing economically with partial syntheses from plant or animal material.



(8) *(9)* *(10)* *(11)* *(12)*

By enzymatic reduction of one keto group in the prochiral diketone *(8)*, *Gibian et al.* [18,19] obtained the compound *(9)*, in which the later centers of asymmetry C-13 and C-17 already have the same configuration as

[6] *N. Applezweig*: Steroid Drugs. McGraw-Hill, New York 1962.

[7] *J. de Flines* and *W. F. van der Waard*, Brit. Pat. 1113887 (1968), Koninklijke Nederlandsche Gist en Spiritusfabrik, Delft.

[8] *Ch. J. Sih, S. S. Lee, Y. Y. Tsong, K. C. Wang*, and *F. N. Chang*, J. Amer. chem. Soc. *87*, 2765 (1965).

[9] *J. Kalvoda, K. Heusler, H. Ueberwasser, G. Anner*, and *A. Wettstein*, Helv. chim. Acta *46*, 1361 (1963).

[10] *L. Velluz, G. Nominé*, and *J. Mathieu*, Angew. Chem. *72*, 725 (1960).

[11] *L. Velluz, J. Vallis*, and *G. Nominé*, Angew. Chem. *77*, 185 (1965); Angew. Chem. internat. Edit. *4*, 181 (1965).

[12] *G. H. Douglas, J. M. H. Graves, D. Hartley, G. A. Hughes, B. J. McLoughlin, J. Siddall*, and *H. Smith*, J. chem. Soc. (London) *1963*, 5072.

[13] *H. Smith, G. A. Hughes*, and *B. J. McLoughlin*, Experientia *19*, 177 (1963).

[14] *H. Smith, G. A. Hughes, G. H. Douglas, D. Harthley, B. J. McLoughlin, J. B. Siddall, G. R. Wendt, G. C. Buzby, jr., D. R. Herbst, K. W. Ledig, J. R. McMeramin, T. W. Pattison, J. Suida, J. Tokolics, R. A. Edgren, A. B. A. Jansen, B. Gadsby, D. H. R. Watson*, and *P. C. Phillips*, Experientia *19*, 394 (1961).

[15] *S. N. Anachenko* and *J. V. Torgov*, Doklady Akad. Nauk SSSR *127*, 553 (1959).

[16] *S. N. Anachenko* and *J. V. Torgov*, Tetrahedron Letters *1963*, 1553.

[17] *A. V. Zaknarychev, S. N. Anachenko*, and *J. V. Torgov*, Tetrahedron Letters *1964*, 171.

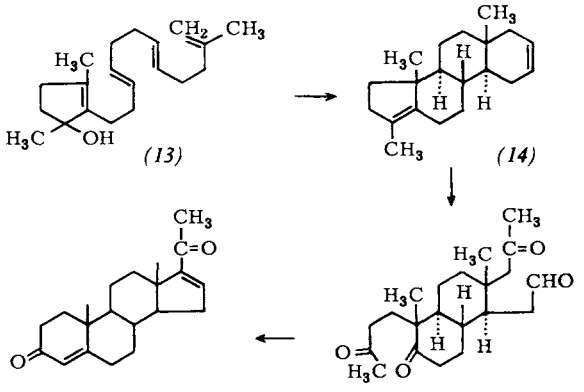
[18] *H. Gibian, K. Kieslich, H. J. Koch, H. Kosmol, C. Rufer, E. Schröder*, and *R. Vössing*, Tetrahedron Letters *1966*, 2321.

[19] *H. Kosmol, K. Kieslich, R. Vössing, H. J. Koch, K. Petzold*, and *H. Gibian*, Liebigs Ann. Chem. *701*, 198 (1967).

the natural steroids. With *Saccharomyces uvarum* (CBS 1508), this reduction gave a yield of 75%.

Another prochiral intermediate, the triketone *(11)*, also undergoes stereoselective enzymatic reduction to *(12)* with *Rhizopus arrhizus* Fischer [20].

An entirely new approach is found in a total synthesis of racemic 16,17-didehydroprogesterone *(16)* that was recently reported by *Johnson et al.* [21]. The key reaction is a non-enzymatic biogenesis-like olefin cyclization with stereospecific formation of five centers of asymmetry.



(13) *(14)* *(15)* *(16)*

The tetraenol *(13)* is stereospecifically cyclized to the tetracyclic diene *(14)* by the action of trifluoroacetic acid at −78 °C, and oxidation with osmium tetroxide followed by double alkaline ring closure in the intermediate triketo aldehyde *(15)* yields *(16)*.

In view of the constantly growing demand for steroids and the limited quantities of natural raw materials, total syntheses can be expected to increase in importance in the future. Total syntheses also have the advantage of a wide scope for variation in the preparation of new steroids.

3. Contraceptive Steroids

The groundbreaking work of *Pincus* [22] has led in the last decade to the use of steroids for fertility control.

The sociopolitical and biological consequences of hormonal contraception are among the most discussed topics of our time. According to *Mohr* [23], the greatest dangers to man's existence at present are ideologies, atomic or microbiological warfare, and population explosion. It should be possible to entrust the first two problems to the sagacity of the politicians. Birth control could offer an escape from the dangers that will come with the huge increase in the earth's population even in the next few decades.

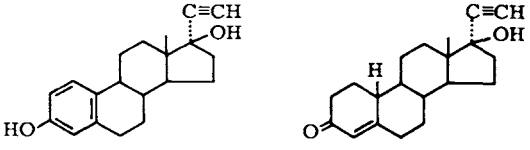
The possibility of hormonal birth control has found remarkably rapid acceptance by women. In the Federal Republic of Germany, about one woman in every seven of child-bearing age now uses steroid contraceptives.

The steroids used are thought to act by reducing the secretion of a series of proteohormones and so preventing maturation and release of the ovum [24]. The administration of gestagenic and estrogenic hormones inhibits ovulation as a result of their braking action on the hypothalamus and pituitary gland.

The steroids are mainly administered as a mixture of the two components over a period extending from the 5th to the 24th day of the cycle. Sequential therapy, which is based on the natural rhythmic formation conditions of the hormones, represents another method of administration. Only estrogens are given in this case from the 5th to the 19th day of the cycle, and a combination of gestagens and estrogens is then given from the 19th to the 24th day. The subsequent pause in consumption is followed in both cases by withdrawal bleeding resembling menstruation.

Since the natural ovulation inhibitors, *i.e.* the estrogens (estrone, estradiol, estriol) and the endogenous gestagen progesterone are inactive when administered orally, it was necessary to develop orally active compounds.

The only estrogenic components in use at present are 17α-ethynylestradiol *(17)* [25] or its 3-methyl ether.



(17) *(18)*

In the great majority of preparations, the gestagen is a 17α-ethynyl-17-hydroxy-19-nor steroid. The interesting chemical history of the first compound of this type, 17α-ethynyl-17-hydroxy-19-nor-4-androsten-3-one *(18)* [26] has recently been described by *Djerassi* [27].

Development began as early as 1938 with the ethynylation of the 17-keto group by *Inhoffen et al.* [25] and the first synthesis of a 19-nor progesterone by *Ehrenstein* in 1944 [28].

Variants of the compound *(2)* that have proved themselves in clinical trials were obtained by displacement of the C-4–C-5 double bond into the 5(10) position to give *(19)* [29], acetylation of the 17-hydroxyl group to form *(20)* [30], and introduction of additional double bonds into positions 9 and 11 to give *(21)* [31], and of a methyl group into position *(18)* to give *(22)* [14].

[20] *P. Bellet, G. Nominé*, and *J. Mathieu*, C. R. hebd. Séances Acad. Sci. *263*, 88 (1966).

[21] *W. J. Johnson, M. F. Semmelhack, M. U. S. Sultanbawa*, and *L. A. Dolak*, J. Amer. chem. Soc. *90*, 2994 (1968).

[22] *G. Pincus*: The Control of Fertility. Academic Press, New York 1965.

[23] *H. Mohr*: Wissenschaft und menschliche Existenz. Verlag Rombach, Freiburg 1967.

[24] *J. Haller*: Ovulationshemmung durch Hormone. Thieme-Verlag, Stuttgart 1968.

[25] *H. H. Inhoffen, W. Logemann, W. Hohlweg*, and *A. Serini*, Ber. dtsch. chem. Ges. *71*, 1024 (1938).

[26] *C. Djerassi, L. Miramontes, G. Rosenkranz*, and *F. Sondheimer*, J. Amer. chem. Soc. *76*, 4092 (1954).

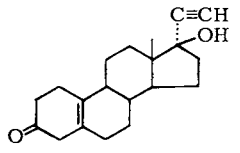
[27] *C. Djerassi*, Science (Washington) *151*, 1055 (1966).

[28] *M. Ehrenstein*, J. org. Chemistry *9*, 435 (1944).

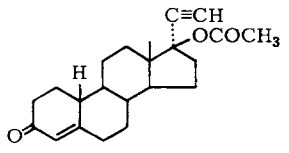
[29] *F. B. Colton*, US-Pat. 2725389 (1955), Searle; Chem. Abstr. *50*, 9454e (1956).

[30] *O. Engelfried, E. Kaspar, A. Popper*, and *M. Schenck*, German Pat. 1017166 (1957), Schering AG; Chem. Zbl. *1959*, 2232.

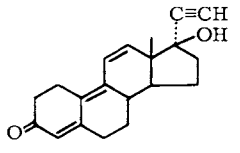
[31] *L. Velluz, J. Mathieu*, and *G. Nominé*, Tetrahedron Suppl. *8*, 405 (1966).



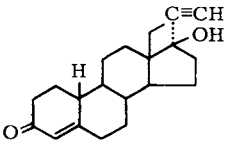
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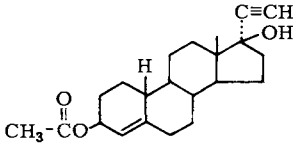
(20)



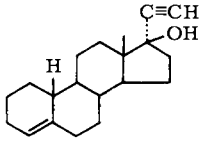
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(22)



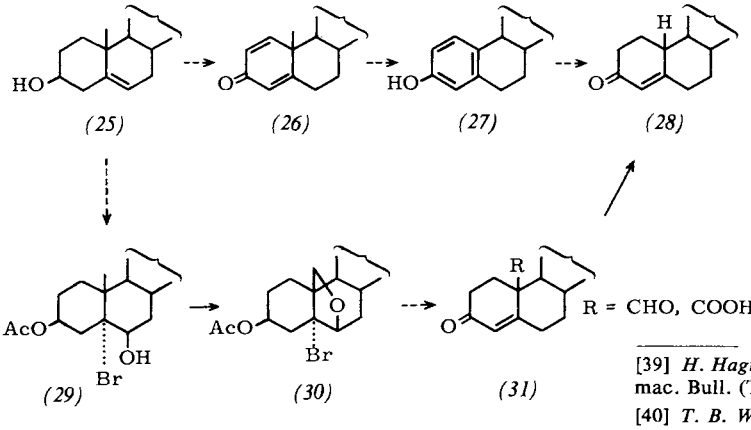
(23)



(24)

Further changes in the A ring gave the 3β-acetoxy-4-ene *(23)* [32] and the 3-deoxy-4-ene *(24)* [33]. The steroids *(21)* and *(22)* are prepared by total synthesis.

In the synthesis of 19-nor steroids from compounds of animal or plant origin, a technically satisfactory solution to the central problem, *i.e.* the elimination of the methyl group from C-10, has now also been found.



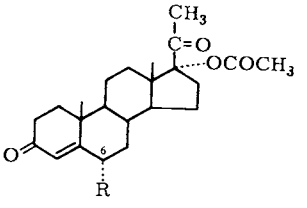
(25) (26) (27) (28) (29) (30) (31)

R = CHO, COOH

In addition to the thermal free-radical aromatization [34,35] of 1,4-dien-3-ones *(26)*, a low-temperature ionic aromatization with lithium in biphenyl solution has also been known since 1963 [36]. 19-Nor-4-en-3-ones *(28)* and 5(10)-en-3-ones are then formed from *(27)* *via* 3-methoxy-2,5-(10)-dienes by Birch reduction [37,38].

A second route that can be used for the practical synthesis of 19-nor steroids *(28)* is the elimination of the methyl group from C-10 [39,40] after oxidation to the formyl or carboxyl group [*(31)*→*(28)*].

The key reaction in this multi-step sequence from *(25)* *via* *(29)*, *(30)*, and *(31)* to *(28)* is a 1,3-diaxial "functionalization" of the unactivated angular methyl group *via* intermediate 6β oxygen radicals [*(29)*→*(30)*] [41] which are produced by nitrite photolysis [42], hypoiodite reaction [43], or direct oxidation with lead tetraacetate [44].



(32a), R = H
(32b), R = CH_3 [45]
(32c), R = CH_3 + Δ^6 [46, 47]
(32d), R = Cl + Δ^6 [48, 49]

The second group of progestagenic steroids that are currently used with estrogens for fertility control are the 17α-acetoxyprogesterones *(32a)*–*(32d)*, which are structurally much closer to progesterone than the 19-nor-17α-ethynyl compounds *(18)* to *(24)*.

The development of these compounds followed from *Junkmann*'s observation [50] that esterification of the

[32] *P. D. Klimstra*, US-Pat. 3176013 (1965) corresponding to Belg. Pat. 650922; Chem. Abstr. *62*, 14776h (1965).

[33] *M. S. de Winter*, *C. M. Siegmann*, and *S. A. Szpilfogel*, Chem. and Ind. *1959*, 905.

[34] *H. H. Inhoffen*, Angew. Chem. *53*, 471 (1940).

[35] *H. H. Inhoffen* and *G. Zühlsdorf*, Ber. dtsch. chem. Ges. *74* 1911 (1941).

[36] *H. L. Dryden*, *G. M. Webber*, and *J. J. Wieczorek*, J. Amer. chem. Soc. *86*, 742 (1964).

[37] *A. J. Birch*, Quart. Rev. (chem. Soc., London) *4*, 69 (1950).

[38] *A. L. Wilds* and *N. A. Nelson*, J. Amer. chem. Soc. *75*, 5366 (1953).

[39] *H. Hagiwana*, *S. Noguchi*, and *M. Nishikawa*, Chem. pharmac. Bull. (Tokyo) *8*, 84 (1960).

[40] *T. B. Windholz* and *M. Windholz*, Angew. Chem. *76*, 249 (1964); Angew. Chem. internat. Edit. *3*, 353 (1964).

[41] *K. Heusler* and *J. Kalvoda*, Angew. Chem. *76*, 518 (1964); Angew. Chem. internat. Edit. *3*, 525 (1964).

[42] *D. H. R. Barton*, *J. M. Beaton*, *L. E. Geller*, and *M. M. Pechet*, J. Amer. chem. Soc. *82*, 2640 (1960).

[43] *J. Kalvoda*, *K. Heusler*, *H. Ueberwasser*, *G. Anner*, and *A. Wettstein*, Helv. chim. Acta *46*, 1361 (1963).

[44] *A. Bowers*, *R. Villotti*, *J. A. Edwards*, *E. Denot*, and *O. Halpern*, J. Amer. chem. Soc. *84*, 3204 (1962).

[45] *J. C. Babcock*, *E. S. Gutsell*, *M. E. Herr*, *J. A. Hogg*, *J. C. Stucki*, *L. E. Barnes*, and *W. E. Dulin*, J. Amer. chem. Soc. *80*, 2904 (1958).

[46] *H. J. Ringold*, *J. P. Rülas*, *E. Batres*, and *C. Djerassi*, J. Amer. chem. Soc. *81*, 3712 (1959).

[47] *B. Ellis*, *D. N. Kirk*, *V. Petrow*, *B. Waterhouse*, and *D. M. Williamson*, J. chem. Soc. (London) *1960*, 2828.

[48] *H. J. Ringold*, *E. Batres*, *A. Bowers*, *J. Edwards*, and *J. Zderic*, J. Amer. chem. Soc. *81*, 3485 (1959).

[49] *K. Brückner*, *B. Hampel*, and *U. Johnson*, Chem. Ber. *94*, 1225 (1961).

[50] *K. Junkmann*, Naunyn-Schmiedebergs Arch. exp. Pathol. Pharmakol. *223*, 244 (1954).

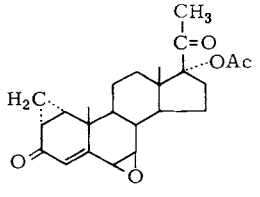
progestationally inactive 17α-hydroxyprogesterone to *(32a)* gives a gestagen that exhibits strong activity when administered subcutaneously or orally.

The gestagen/estrogen combinations do not always prevent conception by inhibiting ovulation. According to investigations by *Goldzieher et al.* [51], ovulation was not suppressed in about 7% of the cycles in women.

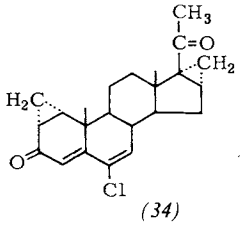
With the compound *(32d)*, almost total fertility prevention could be achieved without the addition of estrogens by daily oral administration of 0.5 mg, while ovulation was maintained [52–55].

This new principle of action of the gestagens probably results from a change in the cervical mucus and prevention of penetration by the sperm. It may be expected that future work on contraceptives will be concerned less with the synthesis and investigation of new ovulation-inhibiting steroids with stronger or longer-lasting effects than with the investigation of new modes of action. Increasingly difficult methods will be used, *e.g.* to try to obtain information about sperm transport, sperm capacitation, egg transport, and implantation.

Indications that the biological spectrum, particularly of progesterone derivatives, can be varied by chemical modification are shown in Table 1. The variation of the partial effects in both directions is very clearly recognizable in the 6,7β-epoxide *(33)* [56] and in the 1α, 2α; 16α, 17α-dimethylene steroid *(34)* [57].



(33)



(34)

Table 1. Relative oral complete inhibition of ovulation (tube inspection in rats) and relative oral progestational action (Clauberg test on rabbits) of some progesterone derivatives.

Cpd.	Relative inhibition of ovulation	Relative progestational action
(18)	1	1
(32d)	1	35
(33)	1	130
(34)	10	0.04

[51] *J. W. Goldzieher, L. E. Moses*, and *U. L. T. Ellis*, J. Amer. med. Assoc. *180*, 359 (1962).

[52] *H. W. Rudel* and *J. Martinez-Manatou*, Proc. II Int. Congr. Hormonal Steroids, Milan, Int. Congr. Ser. No. 132; Excerpta Med.-Foundation *1967*, 884.

[53] *J. Martinez-Manautou, J. Giner-Velasquez*, and *H. Rudel*, Fertil. Steril. *18*, 57 (1967).

[54] *J. Martinez-Manautou, J. Giner-Velasquez, V. Cortes-Gallegos, R. Aznar, B. Rojas, A. Guitterez-Najar*, and *H. W. Rudel*, British med. J. *5554*, 730 (1967).

[55] *J. Zamartu, G. Rodriguez-Moore, M. Popkin, O. Salas*, and *R. Guerrero*, British med. J. *5600*, 263 (1968).

[56] *H. Laurent, G. Schulz*, and *R. Wiechert*, Chem. Ber., in press.

[57] *R. Wiechert* and *F. Neumann*, Brit. Pat. 1095858 (1968), Schering AG.

[58] *V. Regnier*, C. R. Séances Soc. Biol. Filiales *127*, 519 (1938).

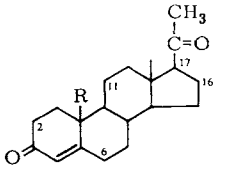
[59] *F. Neumann*, Sympos. for Methods on Drug Evaluation, Milan 1965, p. 548, North Holland Publ., Amsterdam.

It has been known since 1938 that the actions of androgenic hormones are influenced by estrogens [58]. However, this effect occurs indirectly *via* gonadotropin inhibition.

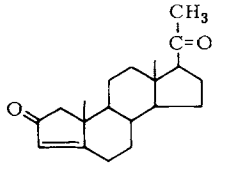
The term "antiandrogen" should be applied to compounds that directly influence the receptors of all organs or systems of organs that are in any way functionally or morphologically androgen-dependent [59]. They thus have no effect on the biosynthesis of testosterone.

This action has been found in various types of steroids in recent years in the systematic search for antiandrogenic substances. The antiandrogenic steroids that have been investigated belong mainly to the androstane and pregnane series.

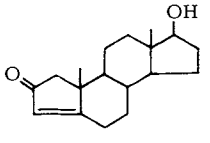
Compounds from the pregnane series that exhibit antiandrogenic effects include progesterone *(35a)* [60–62], its derivatives with methyl, hydroxyl, or halogeno substituents in positions 2, 6, 11, 16, 17, and 21, *e.g.* *(35b)–(35h)* [60–65], 19-norprogesterone *(35i)* [63], and A-norprogesterone *(36)* [63,66].



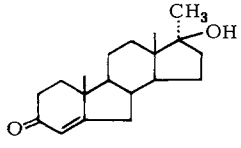
(35)



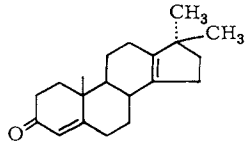
(36)



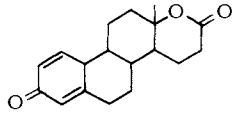
(37)



(38)



(39)



(40)

(35a), R = CH_3
(35b), R = CH_3 + 2α-CH_3, 11 = O
(35c), R = CH_3 + 11β-OH, 21-F
(35d), R = CH_3 + 11α-OH
(35e), R = CH_3 + 17-OH
(35f), R = CH_3 + 16α-CH_3, 21-OH
(35g), R = CH_3 + Δ^6-6-Cl, 17-OAc
(35h), R = CH_3 + Δ^6-6-CH_3, 17-OAc
(35i), R = H

[60] *R. J. Dorfmann*, Methods Hormone Res. *2*, 315 (1962).

[61] *R. J. Dorfmann*, Acta endocrinol. *41*, 268 (1962).

[62] *R. J. Dorfmann*, Proc. Soc. exp. Biol. Med. *111*, 441 (1962).

[63] *R. J. Dorfmann*, Steroids *2*, 185 (1963).

[64] *W. W. Byrnes, R. O. Stafford*, and *K. J. Olson*, Proc. exp. Biol. Med. *82*, 243 (1953).

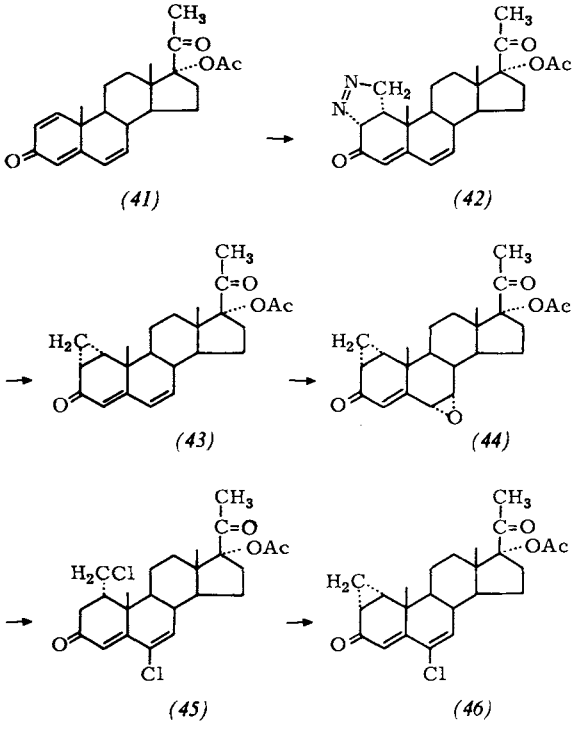
[65] *E. L. Jones* and *L. Woodbury*, J. invest. Dermatol. *43*, 165 (1964).

[66] *L. J. Lerner*, Recent Progr. Hormone Res. *20*, 435 (1964).

Active androstane derivatives include compounds such as A-nortestosterone *(37)* [66–68], the B-nor *(38)* [69,70] and 18-nor compounds *(39)* [63,71], and D-ring lactones *(40)* [63,72].

Hamada, *Neumann*, and *Junkmann* [73] discovered a new, extremely powerful antiandrogen in 1963 by accidental observation of intrauterine feminization phenomena in animal experiments. Pregnant rats treated with this substance apparently bore only female offspring. The development of the rudimentary male genitalia had been suppressed.

This compound, 6-chloro-1α,2α-methylene-17-acetoxy-4,6-pregnadiene-3,20-dione *(46)* (cyproterone acetate) had been synthesized for the purpose of the development of luteohormones [74,75].



(41) *(42)* *(43)* *(44)* *(45)* *(46)*

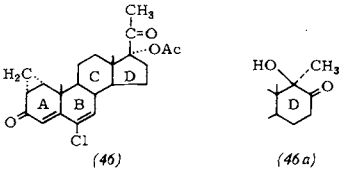
The synthesis of the antiandrogen begins with the trienedione *(41)* [76]. 1,3-Dipolar addition of diazomethane leads stereoselectively, by α-side attack on the C-1—C-2 double bond, to the 1-pyrazoline *(42)*. Thermal or Lewis acid catalyzed cleavage of *(42)* gives the 1α,2α-methylene compound *(43)* [77], which is also formed by direct methylenation [78] of the trienone system *(41)* with dimethyloxosulfonium methylide [79]. Because of a side reaction of the α-acetoxy ketone side chain, however, hydrolysis of *(41)* is essential as an intermediate operation [80]. Stereoselective epoxidation with peroxy acids leads from *(43)* to the 6α,7α-epoxide *(44)*. On treatment of *(44)* with hydrogen chloride in glacial acetic acid, *(45)* is obtained by diaxial epoxide cleavage and elimination of hydrogen with simultaneous opening of the 1α,2α three-membered ring. Treatment of *(45)* for a short time with a base finally leads to *(46)*.

To illustrate purely empirical relations between structure and antiandrogenic action, Table 2 shows the most active of the many subsequently investigated compounds with structures similar to cyproterone acetate. The complete inhibition of the effects of exogenous testosterone propionate on the seminal vesicles and prostates of rats requires 30 times as much cyproterone acetate, while 10 times as much is required to inhibit the effect on cocks' combs.

Replacement of the 6-chloro substituent with fluorine or alteration of the stereochemistry of the three-membered ring to a 1β,2β methylene group leads in *(46)* to total loss of the antiandrogenic action.

The first observations by *Hamada*, *Neumann*, and *Junkmann* [73] and their logical interpretation as an antiandrogenic effect led to a series of biological and clinical studies with new antagonists.

Table 2. Relative antiandrogenic action [81] of derivatives of cyproterone acetate *(46)* against the effect of testosterone propionate on subcutaneous application in rats.



(46) *(46a)*

	Relative antiandrogenic action	Ref.
changes in *(46)*	1	[75]
−4-H + 4-Cl	1	[82]
−1α,2α-CH_2 + 1-H + 2-H	0.3	[83, 84]
−1α,2α-CH_2 + 1α-CH_3	0.3	[85]
−3-O + 3-OH + 3-H	0.9	[86]
−6-Cl + 6-H	0.6	[77]
−17-OAc + 17-OH	0.5	[74]
D ring homorearrangement as in *(46a)*	0.7	[87]

[67] *L. J. Lerner*, Steroids *6*, 215 (1965).

[68] *L. J. Lerner*, Steroids *6*, 223 (1965).

[69] *H. L. Saunders*, *K. Holden*, and *J. Kerwin*, Steroids *3*, 687 (1964).

[70] *H. L. Saunders* and *J. F. Kerwin*, Proc. II. Int. Congr. Hormonal Steroids, Milan *1967*, 599.

[71] *A. Segaloff* and *R. B. Gabbard*, Steroids *4*, 433 (1964).

[72] *L. J. Lerner*, *A. Bianchi*, and *A. Borman*, Cancer *13*, 1201 (1960).

[73] *H. Hamada*, *F. Neumann*, and *K. Junkmann*, Acta endocrinol. *44*, 380 (1963).

[74] *R. Wiechert*, German Pat. 1158966 (1961), Schering AG; Chem. Abstr. *59*, 722h (1963).

[75] *R. Wiechert* and *F. Neumann*, Arzneimittelforsch. *15*, 244 (1965).

[76] *W. Hiersemann*, *E. Kaspar*, and *U. Kerb*, US-Pat. 2962510 (1960); Chem. Abstr. *56*, 14373f (1962).

[77] *R. Wiechert* and *E. Kaspar*, Chem. Ber. *93*, 1710 (1960).

[78] *H.-G. Lehmann*, German Pat. 1183500 (1962); Chem. Abstr. *62*, 6540 (1965).

[79] *E. J. Corey* and *M. Chaykovsky*, J. Amer. chem. Soc. *84*, 867 (1962).

[80] *H.-G. Lehmann*, Angew. Chem. *77*, 808 (1965); Angew. Chem. internat. Edit. *4*, 783 (1965).

[81] *R. Wiechert*, *H. Steinbeck*, *W. Elger*, and *F. Neumann*, Arzneimittelforsch. *17*, 1103 (1967).

[82] *R. Wiechert*, Experientia *24*, 767 (1968).

[83] *H.-J. Ringold*, *E. Batres*, *A. Bowers*, *J. Edwards*, and *J. Zderic*, J. Amer. chem. Soc. *81*, 3485 (1959).

[84] *K. Brückner*, *B. Hampel*, and *U. Johnson*, Chem. Ber. *94*, 1295 (1961).

[85] *R. Wiechert*, 1963, unpublished.

[86] *R. Wiechert* and *F. Neumann*, Belg. Pat. 690011 (1967), Schering AG.

[87] *J. Hader*, *F. Neumann*, and *R. Wiechert*, Belg. Pat. 690965 (1967), Schering AG.

It was possible for the first time to eliminate the effects of testosterone by means of cyproterone acetate, without disturbing other factors that are important to sexual differentiation [88].

Studies on male fetuses have provided important information on the decisive early role of testosterone in the development of the genital tract [88–92] and of the sexual center in the brain [93–98].

Information about the differentiation of the mammary glands was also obtained by treatment of pregnant animals with antiandrogens. Male rats and mice do not normally develop nipples. Feminized males, on the other hand, had nipples that were indistinguishable from those of female animals [99–101].

Central processes induced by testosterone, *e.g.* testicular functions in male animals [102–104] and ovulation in females [105, 106], can be inhibited in adult animals.

The activity and size of the sebaceous glands of humans [107, 108] and of animals [109, 110] depend on androgens. The antihormones were found to eliminate the effect of testosterone on the sebaceous glands [111]. The atrophy of the sebaceous glands as a result of treatment with cyproterone acetate is clear in Figures 1a and 1b.

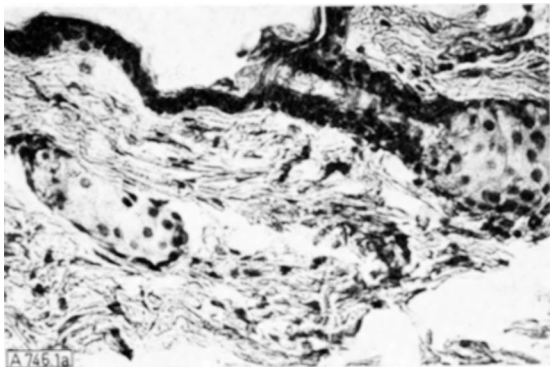


Fig. 1a. Skin section intact male mouse, untreated (magnification 300×).

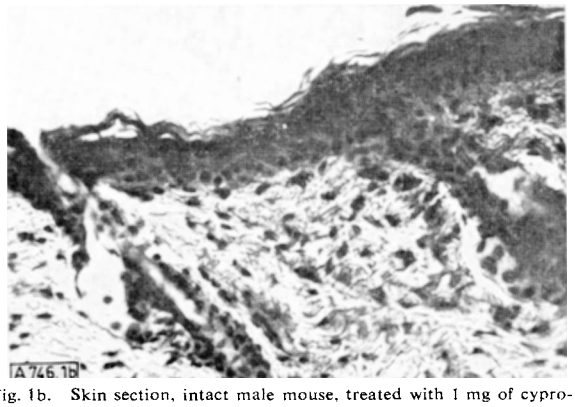


Fig. 1b. Skin section, intact male mouse, treated with 1 mg of cyproterone acetate (i.m.) every second day for 4 weeks (magnification 300×).

Since testosterone is presumably an important contributory cause of acne, this skin disorder should be alleviated by antiandrogens [112–114].

Another interesting clinical possibility is the use of antiandrogens to control the libido of males with disturbed instincts, such as sexual offenders [115–117].

Investigations on the inhibition of the partly androgen-dependent growth of carcinomas of the prostate by antiandrogens could also be important [118, 119].

5. Cardioactive Steroids

Steroid glycosides from several types of digitalis have been in use for almost 200 years for the treatment of cardiac insufficiency. Plant extracts have been increasingly replaced in recent years by homogeneous pure glycosides.

[88] *W. Elger*, Arch. Anatom. microscop. Morphol. experiment. *55*, 658 (1966).

[89] *F. Neumann*, *W. Elger*, and *M. Kramer*, Endocrinology *78*, 628 (1966).

[90] *F. Neumann*, Proc. Int. Sympos., Milan 1965.

[91] *F. Neumann*, *R. v. Berswordt-Wallrabe*, *W. Elger*, *H. Steinbeck*, and *J. D. Hahn*, Excerpta Med. int. Congr., Ser., in press.

[92] *F. Neumann*, *W. Elger*, and *H. Steinbeck*, J. Reproduct. Fertil., in press.

[93] *F. Neumann* and *W. Elger*, Ghent. Excerpta Med. int. Congr., Ser. No. 101, 168 (1965).

[94] *F. Neumann* and *W. Elger*, 5. Acta Endocrinologica Congress, Hamburg 1965; Acta endocrinol., Suppl. *100*, 174 (1965).

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[99] *F. Neumann* and *W. Elger*, J. Endocrinology *36*, 347 (1966).

[100] *F. Neumann*, *W. Elger*, and *R. v. Berswordt-Wallrabe*, J. Endocrinology *36*, 353 (1966).

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[104] *F. Neumann*, *H. Steinbeck*, *W. Elger*, and *R. v. Berswordt-Wallrabe*, Acta endocrinol. *57*, 639 (1968).

[105] *F. Neumann* and *R. v. Berswordt-Wallrabe*, Excerpta Med. int. Congr., Ser. No. 133, 129 (1967).

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[107] *J. S. Strauss* and *P. E. Pochi*, Recent Progr. Hormone Res. *19*, 385 (1963).

[108] *P. E. Pochi*, *J. S. Strauss*, and *H. Miscon*, J. invest. Dermatol. *39*, 475 (1962).

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[111] *F. Neumann* and *W. Elger*, J. invest. Dermatol. *46*, 501 (1966).

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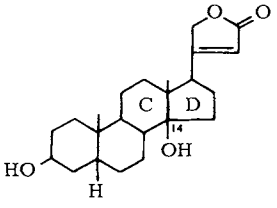
[117] *F. Ott* and *H. Hoffet*, Schweiz. med. Wschr. *98*, 1812 (1968).

[118] *J. Geller*, *G. Vazakas*, *B. Fruchtmann*, *H. Newman*, *K. Kakao*, and *A. Loh*, Surgery, Gynecol. Obstr. *127*, 749 (1968).

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The historical development of this field, the contributions of various laboratories, and the biological mode of action of this class of substances have been described by *Tschesche*[120], *Fieser*[5], and *Haede* and *Lindner*[121]. The chemistry of the sugar residues is summarized in articles by *Zorbach*[122] and *Reichstein*[123].

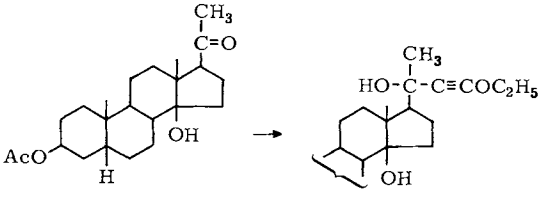
The most difficult problem in the synthesis of the steroid part of the digitalis ingredients, *e.g.* of digitoxigenin *(47)* from readily obtainable steroids is the preparation of the 14-hydroxy-CD-*cis*-17β-butenolide structure.



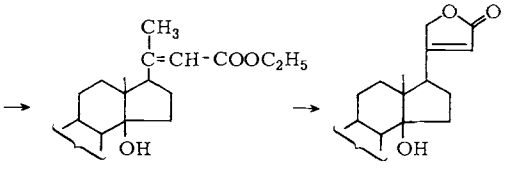
(47)

The 14β-hydroxyl group is easily removed. Another difficulty is the fact that the 17β-side chain in CD *cis*-fused steroids is thermodynamically less stable than the 17α side chain. Furthermore, undesirable side reactions frequently occur between the 17β side chain and the 14β hydroxyl group as a result of the steric arrangement.

Following the fundamental work carried out in the 1940's by the research groups of *Plattner*, *Reichstein*, *Ruzicka*, and *Elderfield*, an elegant synthesis of digitoxigenin from the 20-oxo pregnane derivative *(48)* was achieved in 1962 by *Danieli*, *Mazur*, and *Sondheimer*[124].



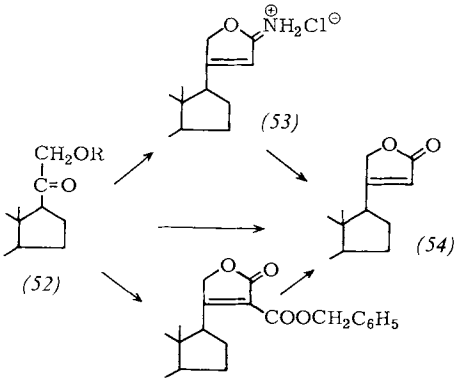
(48) *(49)*



(50) *(51)*

Mild acid treatment of the ethoxyacetylene alcohol *(49)* gave *(50)* which reacted with selenium dioxide in boiling benzene to give the butenolide *(51)*.

14β-Hydroxy steroids have become more readily obtainable through the possibility of microbiological hydroxylation in the 14α, 15α, or 15β position[125].



(52) *(53)* *(54)* *(55)*

(a), R = $OCOCH_3$
(b), R = H
(c), R = $OCOCH_2-COOCH_2C_6H_5$
(d), R = $OCOCH_2-\overset{\oplus}{P}(C_6H_5)_3Br^{\ominus}$
(e), R = $OCOCH_2-PO(OC_2H_5)_2$

The partial formulas *(52)–(55)* are to be understood as representing the synthesis of other butenolides from the corticosterone side chains.

(54) was obtained from *(52a)* by Horner olefination with diethyl cyanomethyl phosphate *via* the imino lactone[126].

Fritzsch, *Stache*, and *Ruschig*[127] obtained the butenolide ring directly from *(52b)* with diethyl methoxycarbonylmethyl phosphate.

The same authors synthesized *(54)* *via* *(55)* from *(52c)* by intramolecular cyclization[128, 129].

The necessary activation of the condensing methylene group can also be achieved with phosphonate ester or phosphonium salt groups. Thus the butenolide ring was obtained in this way from *(52d)* or *(52e)* in yields of up to 50%[130].

Another cardenolide synthesis is based on the ability of 17β-furyl steroids to be converted into cardenolides[131].

The second group of cardioactive steroids are the bufadienolides, which occur in toad secretions and plants. The characteristic structural features of these compounds are an α-pyrone ring in the 17β position and either a hydroxyl group in the 14β position or a 14β,15β-epoxide.

The first natural bufadienolides to be synthesized (*Sondheimer et al.*[132]) were bufalin *(56)* and resibufalin *(57)*.

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[127] *W. Fritzsch*, *U. Stache*, and *H. Ruschig*, Liebigs Ann. Chem. *699*, 195 (1966).

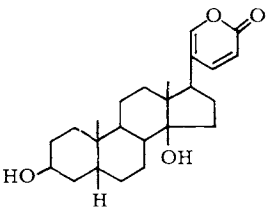
[128] *W. Fritzsch* and *H. Ruschig*, Liebigs Ann. Chem. *655*, 39 (1962).

[129] *W. Fritzsch*, *U. Stache*, *W. Haede*, *K. Radscheit*, and *H. Ruschig*, Liebigs Ann. Chem. *721*, 168 (1969).

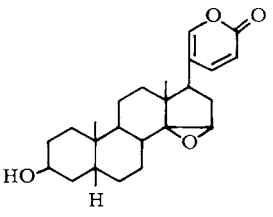
[130] *H.-G. Lehmann* and *R. Wiechert*, Angew. Chem. *80*, 317 (1968); Angew. Chem. internat. Edit. *7*, 300 (1968).

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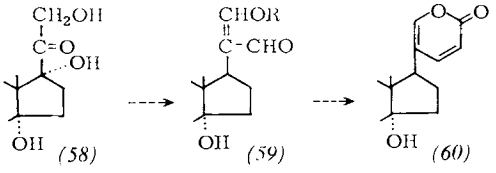


(56)



(57)

Starting from a readily obtainable 14α,17α,21-trihydroxy 20-one *(58)*, these authors synthesized the α-pyrone structure *(60)* by an interesting multistage synthesis with final Reformatzky reaction of an enolized β-dialdehyde *(59)* with methyl bromoacetate.



(58) (59) (60)

While great progress has been made in the synthesis of cardioactive steroids, treatment with those compounds has advanced very little.

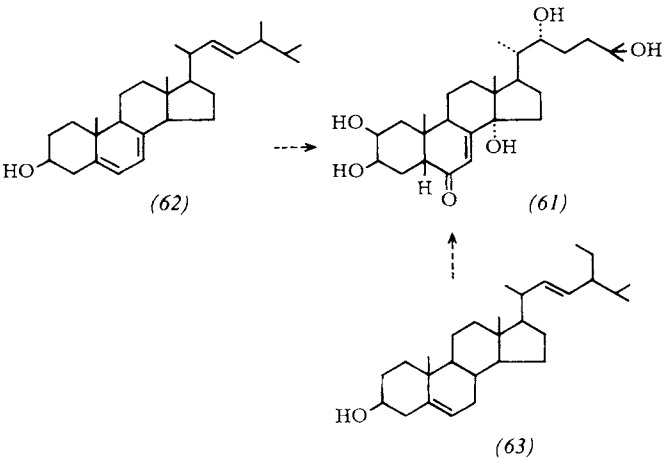
The therapeutic range is extremely narrow, and the use of the drugs is consequently difficult. However, the use of these steroids for nearly two hundred years shows their value as drugs that are as yet irreplaceable. It remains to be seen whether structural modifications, as in the case of steroid hormones, lead to fundamental or advantageous changes in the biological effects of the natural steroids.

In this connection, mention should be made of the cytotoxic effects observed with cardenolides[133–137].

6. Steroid Metamorphosis Hormones

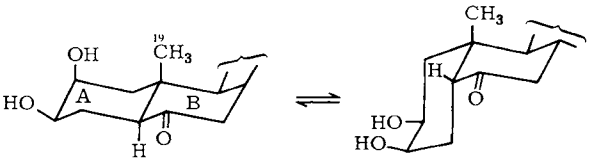
In 1954, *Butenandt* and *Karlson*[138] succeeded in isolating the hormone responsible for molting in the development of insects, which they called ecdysone, from the pupae of silkworm moths. The steroid structure of ecdysone was recognized nine years later[139], and after a further two years its complete structure was found by X-ray analysis[140] as 22*R*-2β,3β,14α,22,25-pentahydroxy-5β-cholest-7-en-6-one *(61)*.

Two independent multi-stage syntheses of the molting hormone starting with ergosterol *(62)*[141–144] and stigmasterol *(63)*[145,146] were published in 1966.



(62) (61) (63)

The syntheses were based on the ability of 2β,3β-dihydroxy-6-oxo-AB-*trans* steroids *(64)* to be converted into AB-*cis* 6-ketones *(65)*, which had first been postulated from models and then demonstrated.



(64) (65)

The preferred stable AB ring fusion of 6-oxo steroids is the *trans* linkage. The 1,3-diaxial interaction between the 2β-hydroxyl group and the 19-methyl group in *(64)* favors the displacement of the equilibrium toward the *cis* compound *(65)*.

A second insect molting hormone, which also initiates molting in crustaceans, is 20-hydroxyecdysone (crustecdysone). It can be isolated from insects[147–150] and lobsters[151], and has now also been synthesized[152,153]. A 20,26-dihydroxyecdysone has been

[133] *J. E. Pike, J. E. Grady, J. S. Evans*, and *C. G. Smith*, J. med. Chem. *7*, 348 (1964).

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[136] *R. B. Kelly, E. G. Daniels*, and *L. B. Spaulding*, J. med. Chem. *8*, 547 (1965).

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[141] *U. Kerb, P. Hocks, R. Wiechert, A. Furlenmeier, A. Fürst, A. Langemann*, and *G. Waldvogel*, Tetrahedron Letters *1966*, 1387.

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[147] *P. Karlson*, Vitamins and Hormones *14*, 227 (1956).

[148] *P. Hocks* and *R. Wiechert*, Tetrahedron Letters *1966*, 2989.

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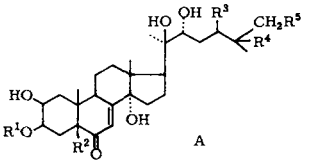
[152] *G. Hüppi* and *J. B. Siddall*, J. Amer. chem. Soc. *89*, 6790 (1967).

[153] *U. Kerb, R. Wiechert, A. Furlenmeier*, and *A. Fürst*, Tetrahedron Letters *1968*, 4277.

isolated from the tobacco hornworm (*Protoparce sexta*)[154].

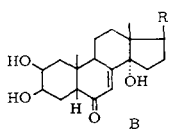
A wave of publications, which has not yet stopped, resulted from the surprising first isolation of ecdysone-like compounds, the ponasterones, from the conifer *Podocarpus nakii* by *Nakanishi et al.*[155]. Ecdysone[156,157] and 20-hydroxyecdysone[156–161] have also been found in the plant kingdom. To provide some idea of the range, Table 3 shows the structures and names of steroids related in structure and action to the natural molting hormones and isolated from the leaves, wood, or roots of Podocarpaceae, Taxaceae, Polypodiceae, Amaranthaceae, and Verbenaceae.

Table 3. Plant steroids having an ecdysone-like action [a].

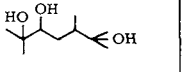
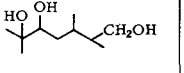
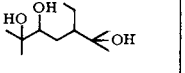
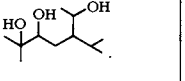
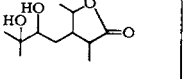
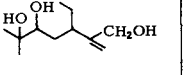
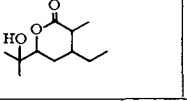


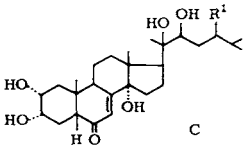
A

R^1	R^2	R^3	R^4	R^5	
H	OH	H	OH	H	polypodine [162, 163]
H	H	H	H	H	ponasterone A [155, 164–166]
H	H	H	H	OH	inokosterone [167]
H	H	OH	H	H	pterosterone [168]
$C_6H_{10}O_5$	H	H	H	H	ponasteroside A [166]



B

R = 	makisterone A [169, 170]
R = 	makisterone B [169, 170]
R = 	makisterone C [169–171]
R = 	makisterone D [169, 170]
R = 	cyasterone [172, 173]
R = 	ajugasterone B [174]
R = 	capitasterone [175]



C

R^1 = H, ponasterone B [176]

R^1 = OH, ponasterone C [176]

[a] The configuration of the side chain is unknown in sections B and C.

The side chain attached to C-17 of ecdysone can be varied within certain limits without loss of molting hormone activity.

Table 4 lists a number of results which were obtained under identical conditions in the Calliphora test and which illustrate relationships between structure and activity.

The significance of the 14α-hydroxy group and the high activity of the compound having an unsubstituted cholesterol side chain are worthy of note, while changes in the stereochemistry or a shortening or loss of the side chain practically leads to inactivation.

A complete change in the action of this class of compounds occurs on inversion of the AB ring linkage to give the *trans* series. Certain ecdysone-antagonistic effects, such as inhibition of post-ecdysonal molting and sclerotization of the larva cuticulae were observed, *inter alia*, with a number of 2,3-dihydroxy-6-oxo-5α steroids of the pregnane *(66a)*, *(66b)* and cholestane series[177,178] *(66c)–(66e)*.

[154] *M. J. Thompson, J. N. Kaplanis, W. E. Robbins*, and *R. T. Yamampto*, Chem. Commun. *1967*, 650.

[155] *K. Nakanishi, M. Koreeda, S. Sasaki, M. L. Chang*, and *H. Y. Hsu*, Chem. Commun. *1966*, 915.

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[165] *G. Hüppi* and *B. Siddall*, Tetrahedron Letters *1968*, 1113.

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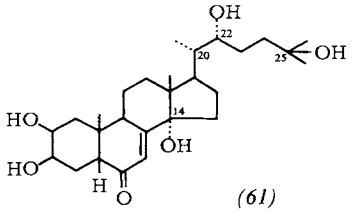
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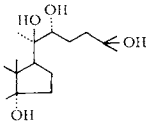
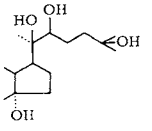
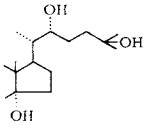
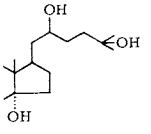
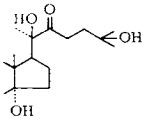
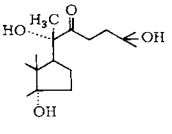
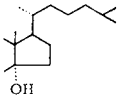
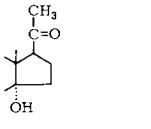
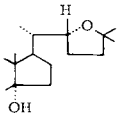
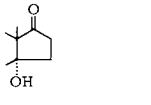
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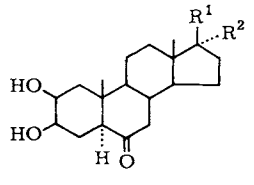
Table 4. Relations between structure and action in derivatives of ecdysone *(61)*. In the Calliphora test, 0.05 µg of *(61)* were required for pupation of one larva.



(61)

Change in *(61)*	Relative activity (%)	Change in *(61)*	Relative activity (%)
	125–170		inactive
	25		inactive
	15		inactive
	70		inactive
	20		inactive

Correspondingly substituted steroids of the androstane series *(66f)*, *(66g)* [179] exhibited a toxic action towards the final larva stage of *Pyrrhocoric Cysterus* L. In addition, compound *(66f)* is reported to have a sterilizing effect on the common house fly.



(66a), $R^1 = COCH_3$, $R^2 = H$
(66b), $R^1 = CH(\beta\text{-}OH)\text{–}CH_3$, $R^2 = H$
(66c), $R^1 = CH(CH_3)\text{–}(CH_2)_3\text{–}CH(CH_3)_2$, $R^2 = H$
(66d), $R^1 = CH(CH_3)$-*trans*-$CH{=}CH\text{–}CH(\beta\text{-}F)\text{–}CH(CH_3)_2$, $R^2 = H$
(66e), $R^1 = C(CH_3)(\alpha\text{-}OH)\text{–}(CH_2)_3\text{–}CH(CH_3)_2$, $R^2 = H$
(66f), $R^1 + R^2 = O$
(66g), $R^1 = OH$, $R^2 = H$

[179] *L. Labler, K. Slama*, and *F. Sorm*, Collect. czechoslov. chem. Commun. *33*, 2226 (1968).

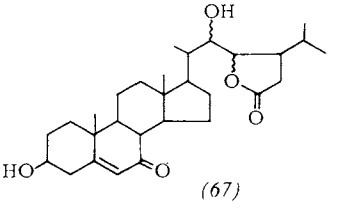
The investigations on the role of ecdysone in protein synthesis proceed beyond the bounds of entomology, and are of general importance. It has been shown experimentally that ecdysone increases and initiates DNA and RNA synthesis [180–183]. *Karlson* [184] derived a general hypothesis on the mode of action of hormones on the basis of the direct activation of certain gene sites as observed together with *Clever* [185].

Molting hormones were also found to cause a dose-dependent increase in the incorporation of ^{14}C-leucine into the protein of mammalian livers [186]. Some ecdysone-like steroids have protein-anabolic effects on mice [187, 188].

The possibility of obtaining molting hormones readily by synthesis or from plants provides a broad base for biological studies on this interesting class of compounds *e.g.* in plant protection, in pharmacology, or for fundamental growth processes in warm-blooded animals.

7. Novel Steroids

From cultures of the aquatic fungus *Achlya bisexualis*, *McMorris* and *Barksdale* (1967) [189] isolated a crystalline substance that causes the growth of cell filaments or hair-like outgrowths at points where the propagative cells develop in the male plant. It thus induces the sexual reproduction in this species. This plant sex hormone, which the authors called antheridiol, has the structure of the steroid lactone *(67)* [190].



(67)

Antheridiol has now been synthesized from stigmasterol [191]. This presents possibilities for a broad investigation of this interesting steroid.

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[189] *T. C. McMorris* and *A. W. Barksdale*, Nature (London) *215*, 320 (1967).

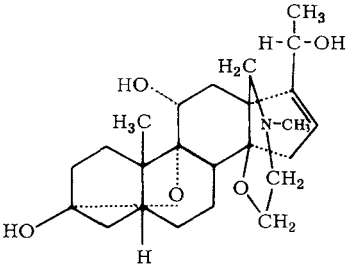
[190] *G. P. Arsenault, K. Biemann, A. W. Barksdale*, and *T. C. McMorris*, J. Amer. chem. Soc. *90*, 5635 (1968).

[191] *J. A. Edwards, J. S. Mills, J. Sundeen*, and *J. H. Fried*, J. Amer. chem. Soc. *91*, 1248 (1969).

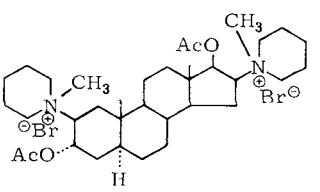
The Cholo Indians of western Colombia use the venom of the poison frog (*Phyllobates aurotaenia*) for hunting. *Witkop et al.* were able to isolate several poisons, the batrachotoxins, from the secretion obtained from the animals on heating [192]. These compounds are the strongest known cardiotoxins. Paralysis and convulsions are followed by death within a few minutes.

An artifact of the batrachotoxins is batrachotoxinin A *(68)*, which is equivalent to strychnine in its toxicity. X-ray structure analysis [193] of *(68)* gave the unusual steroid alkaloid structure indicated.

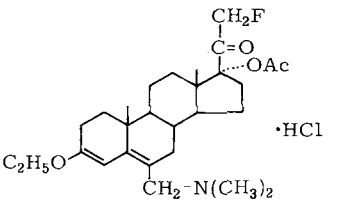
Interesting new synthetic developments in the steroid field include the bis-quaternary piperidinium compound *(69)* and the 21-fluoro-6-dimethylaminomethyl-17α-acetoxyprogesterone derivative *(70)*.



(68)



(69)



(70)

When the compound *(69)* is administered to humans in small doses, it causes a neuromuscular block, which can be removed by neostigmine [194]. The authors classify the action as being of the curare type.

A remarkable analgesic action, which is superior to that of codeine and cannot be eliminated by morphine antagonists, is shown by the steroid *(70)* in animal experiments [195].

I am grateful to Dr. H. Steinbeck and Dr. A. Jäger (Schering AG) for supplying the biological results in Tables 1, 2, and 4.

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Macromolecular Chemistry and Medicine

By Garth W. Hastings [*]

Macromolecular substances are used in medicine both as materials and as reagents. In the former category polymers serve as replacements for soft tissue, as cardiovascular and orthopedic implants, and as adhesives. When employed as reagents, macromolecules interact with living tissue and play an active part in bodily repair processes.

1. Introduction

One of the earliest uses of a macromolecular material in surgery was that of celluloid in 1890, but only the past decade has seen really significant developments in this field. One of the factors in this increasing application is that the needs of the surgeon have changed, as the whole concept of surgical care has been transformed from a passive repair role to a much more aggressive attack upon disease embracing reconstruction or replacement of diseased or damaged organs. There are problems associated with the collection and storage of human organs, in addition to the questions of possible rejection of the transplant by the host tissues, and in consequence there has been great use of non-biological materials. The use of metals for devices intended for permanent implantation within the human body dates back to the sixteenth century. Nowadays, and in the future too, metals continue to play an important role in surgery. Metals undoubtedly offer a satisfactory solution where strength and resistance to the bodily environment are required, but limitations have led to the search for alternative materials. Metallic corrosion is one factor in the very hostile bodily environment, but there is no agreement as to its importance. A more serious limitation is that

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the metal implant cannot match the properties of the tissues in which it is placed.

Mechanical and frictional properties of a normal hip joint are very different from those of a prosthetic joint where two metal surfaces are in contact, and since the tissues which are the source of the synovial fluid lubricant in the normal joint have been removed, the joint may be very poorly lubricated. It is very doubtful if synovial fluid can ever be expected to lubricate the hard impermeable metal surface when this is compared with the resilient, sponge-like nature of cartilage which can hold lubricant in the interstices[1]. The weight of metal prostheses represents a further disadvantage.

2. Choice of Macromolecular Materials

The favorable mechanical, thermal, electrical, and optical properties of synthetic organic polymers stimulated interest in their widespread use as a new class of materials. Developments in textiles, plastics, rubbers, adhesives, and other new systems meant inevitably that the performance of these materials in medical applications would be tested.

In nature, organic polymers provide not only the framework of living organisms, but also serve to carry the life functions themselves. Fibrous proteins provide the main structural elements in animals, and water soluble proteins, polysaccharides, and nucleic acids, carry on the processes of life. The use of organic macromolecules to replace tissues damaged by injury or disease is a development of the understanding of the role played by such structures in nature.

There are two ways in which synthetic macromolecules can be considered for medical applications. The first of these, typifying the current surgical applications, is as materials, plastics, fibers, elastomers, or adhesives. The emphasis is then principally on mechanical properties and biostability. Modern macromolecular materials science endeavors to relate these properties to the basic polymeric structure, and this has led to a high degree of predictability of the behavior of new

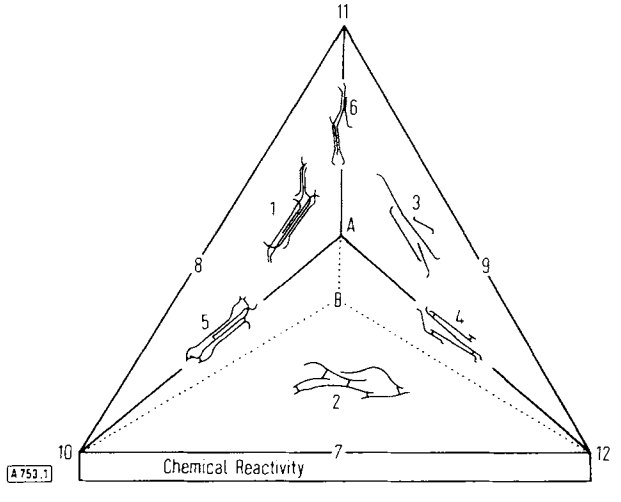


Fig. 1. Structure-property pyramid for polymers used in surgery (see also Table 1).

[1] *J. Charnley*, New Scientist *6*, 60 (1959).

Table 1. List of polymers having potential surgical applications. The combination of various macromolecular characteristics enables considerable modifications to be made to properties. (The numbers and letters in the first column refer to Fig. 1.)

No.	Nature	Typical materials	Surgical use, if any
1	Flexible and crystallizable	polyolefins	very high density material in joint replacements
		polyethylene	
		polyvinylchloride	catheters
		polyamides - nylons	sutures
2	Crosslinked amorphous networks	vulcanized natural rubber	tubing
		silicone rubber	tubing, heart valves
		polyurethane rubbers	artificial limbs
		formalized polyvinyl alcohol	soft tissue replacement (foam)
		epoxy resins	adhesives
3	Stiffened chains — substituent groups	a) polystyrene	joint prostheses — discontinued
		polymethyl methacrylate	
		polymethyl α-cyanoacrylate	adhesive
	Rigid backbone	b) polyimides	
		ladder polymers	
		polycarbonates	in heart valve assembly
		epoxy resins	adhesives
4	Crystalline rigid chains	polyester fiber	arterial replacement (woven)
		cellulose ester fibers	
5	Crystalline crosslinked chains	synthetic rubbers — *e.g.* neoprene	
		collagen	catgut sutures, in reconstituted form as various prostheses
		proteins	
6	Rigid chains, crosslinked	rigid epoxies	
A	Rigid chains, crystalline and crosslinked	modified cellulose fibers	
7	Crosslinked, chemically reactive	hydrophilic gels	breast augmentation
			tubing
			prostheses
8	Crystalline, chemically reactive		
9	Stiff chains, chemically reactive	nonthrombogenic polycarbonates	heart valve components
		modified adhesives	dental adhesives
10	Crosslinked, crystallizable, chemically reactive		
11	Crystallizable, rigid chains, chemically reactive	characteristic of naturally occurring macromolecules, *e.g.* enzymes, viruses, immunologically active compounds	
12	Crosslinked, rigid chains, chemically reactive		
B	Rigid chains, crosslinked, crystallized, and reactive	the ultimate combination of all principles	

polymers, and the possibility of designing materials for specific applications, eliminating empirical synthetic efforts, and simplifying subsequent formulations since plasticizing and other functions can be built into the macromolecule. Adaptability *via* structural modification gives a means by which the materials may be modified to meet the requirements of surgical technique and of *in vivo* conditions (see Fig. 1 and Table 1).

The alternative to this approach is to consider the macromolecules, not as materials, but as chemical reagents. They will be the catalysts or stabilizers involved in processes of bodily repair, and will take part in the functions of the organism. This way has, until recently, received little attention in relation to surgical uses, but has been followed in research into the structure of proteins, enzyme action, and the nature of the specific groups involved in this or in immunological reactions, *i.e.* topics which can be studied by the use of synthetic macromolecular analogs.

This "reagent" approach has received little attention in surgical research, because the main objective here has been to obtain an inert material. By this the surgeon does not mean the absence of any tissue-polymer reaction, but rather that any reaction produced is not harmful to healing and restoration of function. Since certain polymers have not met this requirement (polyurethanes and cyanoacrylates, see Sections 3.2.2, 3.4, 4.3, and 4.2.2.1), there has been an increasing concern to use completely inert materials.

It is suggested that the Food and Drug Administration (FDA) in the United States will require proof of the inertness of a material for prosthetic application. This could seriously limit the applications of plastics if, thereby, research is directed towards finding non-reactive polymers. Any implant material will cause inflammation in the tissues since this is the defensive reaction of the living body to any irritant, physical (*e.g.* burns), chemical (*e.g.* toxins), or bacterial. The trauma of the surgeon's knife evokes an inflammatory response, and so do surgical sutures; in these cases the action is only transitory in nature.

Implants intended to remain permanently in the body should produce no irreparable tissue damage nor initiate any long-term pathological state, *e.g.* carcinogenesis. It may be advantageous to promote an implant-tissue reaction, for example, to improve an adhesive bond, and for this reason it may be better to define a *benign reactivity* or a *benignly reactive material.*

For the present, there is no certainty that any plastics material will perform its intended role over the whole lifetime of the recipient.

3. Surgical and Biochemical Problems

There is no unique surgical problem and hence no single solution but this situation is well fitted to the versatility of plastics. At the same time, this very versatility has resulted in a failure to realize that terms such as PVC used in the plastics industry by no means specify a definite material. Add to this the complications of additives used in compounding or contaminants picked up during processing, together with unreacted monomers and catalysts from the polymerization, and it will be seen that one of the most acute problems for satisfactory surgical use is a clear specification of the material. The standardization of materials for medical use is, and will rightly remain, of great importance[2]. Adequate standards specification will require critical examination of the resistance of the material to the biochemical environment, which involves a systematic study of the chemistry of the degradation processes.

3.1. Skin or Temporary Tissue Contact

Contact with the skin or temporary contact with the tissues imposes the least stringent requirements, although as the time of contact increases beyond a few hours restrictions on the usability of materials will increase. This is illustrated by the common incidence of dermatitis as an occupational disease in the plastics industry[3,4].

The cases where a plastic device in contact with skin has caused a reaction may be due to the abrasive nature of the surface, and attention to the particle size and shape of filler particles may eliminate this factor. A chemical cause is to be found in toxic catalyst residues or other additives in the material. Unreacted amines can be leached out of cured epoxy resins, and these are well known to be a causative factor in dermatitis.

Tissue contact increases the problems since the implant is in contact with enzymes and other degradative systems, and the presence of tissue fluids increases the likelihood of leaching out of toxic substances.

For short term use, say for under six to seven hours, unless there is gross surface contamination from *e.g.* exuded plasticizer, or a readily leachable component, the criteria are similar to those for skin contact.

With longer term use, *i.e.* up to three weeks, the problems arise from toxic ingredients leached out or from the abrasive action of the surface. The first case is illustrated by a series of administration devices, from different sources, but all fabricated from polyvinyl chloride. Twenty-five out of forty-eight showed toxic reactions in animal tests, and the most probable irritants are the organometallic stabilizers[5].

Even the process of sterilization can introduce irritative materials. Ethylene oxide gas is readily retained by plastics, and leads to subsequent hemolysis[6], accountable for by its ready reaction with the NH_2 or OH groups in proteins.

[2] In the United States the F-4 committee of ASTM is considering tests to be used for evaluation of surgical plastics. In Australia, committee MD3 of the Standards Association of Australia is engaged on the same problems. Great Britain also has a Ministry of Health committee.

[3] *R. Lefaux*: Chemie und Toxikologie der Kunststoffe. Krausskopf-Verlag, Mainz 1966.

[4] *D. Kenwin Harris*, Chem. and Ind. *1968*, 236.

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Another gaseous sterilant, β-propiolactone is suspect as a carcinogen [7]. Acrylic contact lenses readily absorb up to 7 per cent of a quaternary ammonium halide sterilant solution, and corneal burns can result [8].

Toxic compounds are avoidable by precise formulation and by processing under clean conditions with strict product control. The absence of standards is a major barrier at present.

The second, or surface irritative effect, is poorly documented in terms of a precise correlation between surface morphology and tissue reaction. Gross roughness, protruding filler particles, and hard areas are the most probable sources of trouble.

Incidences of irritation arising from catheters are known, but not studied in relation to the nature of the plastic. A serious case, which may be a surface effect, is the destruction of a child's larynx by the use of an endotracheal tube for a three week period [9].

3.2. Permanent Implantation

Here are considered, *inter alia*, orthopedic and cardiovascular [10] uses, where the period of implantation in difficultly accessible, deep seated tissue is limited only by the lifetime of the recipient and the behavior of the material. Not only is the number of suitable materials much less, but the tissue/implant reactions are not well understood. The biophysical lifetime required without mechanical failure or tissue reaction may exceed 250000 hours. The task lies not only in designing an adequate prosthetic device, but in doing so within the performance limits of the available materials.

The applications of chemical principles and known structure/property relationships to the production of materials having expected performance are seen industrially, in the design of new textile fibers and in the development of high temperature resistant materials. The use of plastics as materials has dominated the surgical area, yet in general there has been little systematic design of these materials.

Polydimethyl siloxane (silicone) elastomers have been studied extensively to determine their suitability as non-reactive implant materials [11]. Studies with blood-compatible polymers have led to a more systematic approach (see later), and attempts to reduce the toxicity of α-cyanoacrylate adhesives have led to the use of higher esters. However, there are still large unexplained areas in the chemistry and poorly substantiated conclusions.

3.2.1. Soft Tissue Replacement

In addition to non-toxicity and long-term biostability, the principal requirement is comformability to contours and tissue softness. These latter requirements are best met by the use of foams, preferably of closed pore structure, to prevent excessive ingrowth of tissue which may lead to hardening. An alternative method has been to use a viscous polydimethyl siloxane gel enclosed in an elastomeric bag [12].

3.2.2. Cardiovascular System

This presents a more complex problem since it also involves the reaction of blood with the prosthetic surface. Not only must the mechanical properties of a blood vessel be reproduced, in terms of elasticity to accommodate the regular pulsation of blood flow, flexibility without kinking, porosity sufficient to permit ingrowth of tissues but able to prevent leakage of blood, but the surface properties must not promote damage to blood platelets or their adherence to the wall.

In heart valve replacements, the correct haemodynamics is related to valve design in the mechanical sense, but also to the blood/plastic interaction. The ability of the material to withstand the continual flexing of valve movement imposes a primary limitation on the choice of material, but even a well designed valve may fail within a short time due to clotting. The surface properties are related to hardness and/or roughness, chemical groups present in the surface layers, and a consequent charge distribution on the surface. Crystalline/amorphous ratios in the plastic will also affect surface structure.

Any plastic implant will change the natural environment and cause some effect on blood flow and properties. When normal blood vessels become calcified, the hard areas result in changes in blood constituents. Adherence of platelets is followed by fibrin deposition and a clot forms. If the area is small, it is possible for the clot to be incorporated into a new vessel-lining by normal repair processes. If it is large, the clot may increase in size, the vessel may be obstructed, or portions of clot may be detached to form emboli.

When a plastic device is used, the changes occurring are similar, but the possibility of natural repair is reduced. Porosity permits cell penetration and the synthetic vessel becomes lined with a surface similar to that of the host vessel [13]. In large replacements, a new vessel lining may only be formed at the junction with the natural vessel and the probability of embolus formation increases.

3.2.3. Orthopedic Implants

These implants are subject to the mechanical stresses of weight bearing and movement. There are two main uses: fracture repair and joint replacement. The former is primarily an adhesives application. Design of joint prostheses involves the chemist or materials scientist in the production of dimensionally stable plastics, with no creep, stress cracking, or other fatigue symptoms, which will operate as a bearing surface in contact with the articular cartilage of the normal joint (a fibrous collagen-polysaccharide system), or with another plastic or with metal (see also Section 1).

[7] *A. I. Walpole*, Ann. New York Acad. Sci. *68*, 750 (1958).

[8] *B. Smith, D. Woodsmith, H. L. Gould*, and *J. M. Converse*, Plastic reconstr. Surgery *34*, 387 (1964).

[9] *K. Little*, Bio-Medical Engng. (9) *3*, 404 (1968).

[10] *B. Bloch* and *G. W. Hastings*: Plastics in Surgery. Thomas, Springfield, USA, 1968.

[11] Dow Corning Center for Aid to Medical Research Midland, Michigan, USA, publishes a regular survey of silicone uses in surgery entitled "The Bulletin".

[12] *J. R. Lewis*, Plastic reconstr. Surgery *35*, 51 (1965).

[13] *J. H. Harrison*, Amer. J. Surgery *95*, 3 (1958).

In walking one kilometer with the acceleration and deceleration of movement, over 600 reversals are involved. Normal joints have an inbuilt shock absorbing mechanism, and since the forces on a joint may be 5 to 7 times the body weight, this may represent a continued impact of 300–500 kilograms. The internal structure of a bone is adapted to the mechanical requirements, and the modulus of elasticity may vary segmentally, and in cross section, along a bone. Enormous reserves exist in the body for adaptation to demands. The enormous distension of womb and abdominal wall structures during pregnancy illustrates this. No form of implant can achieve all of the many properties of living tissue, nor have the capacity for self-healing or replenishment.

A bone adhesive is required to function in conditious which are, in general, the very opposite of those with which an adhesive designer usually chooses to work. The environment is wet, blood will be present, and fat from the marrow in the medulla contaminates the surfaces to be bonded. It is obviously not possible to use high pressures and temperatures to effect curing. Solvent based adhesives are not usable: water-based will not harden in the tissues, and organic solvent-based are usually toxic. The limitation of body-temperature curing, low exotherm, low toxicity adhesives, restricts the choice of materials.

3.3. Effect of Implant on Tissues

3.3.1. Additives

The aim in surgical work should always be to use the plastic in the most pure state possible. As already stated, industrially acceptable materials will contain various nonmacromolecular materials. Residual monomer or initiators, mold release agents, and lubricants are common, but there are also antioxidants, plasticizers and other added chemicals. Whereas a flexible polyvinyl chloride, containing 40–60 per cent of additives may be acceptable in tubing for non-medical use, it is not cleared for implantation. Even acceptance as food packaging is no safeguard. Toxicity quotient [14] and other standards [15] are a guide, but more precise information is needed.

Highly toxic additives have been found in tubing actually in use in catheters [16]. These sorts of devices are being left *in situ* for increasingly long times, *e.g.* with developments in intermittent dialysis for renal failure, where the arterial and venous limbs through which blood flows to the dialysis unit are a more or less permanent implant. The most satisfactory material to date has been silicone rubber tubing.

However, these direct effects are complemented by indirect effects from devices not specifically designed for implantation. Syringes, transfusion units, containers for collection and storage of drugs and nutriments, are made from plastics. The rubber plungers of syringes have been shown to release contaminants to solvents placed in the syringe [17]. In heart-lung machines, some types of tubing were shown to affect the blood passing through them [16], and the adhesives used in a membrane oxygenator were found to be toxic upon extraction [18].

The important element in these indirect effects is the time factor. In general the concentration of substances extracted is low, but any effect may be cumulative, and for an already ill patient can be serious. The most usual effect of extraction of toxic materials is local cell death or local inflammation. Unless the causative effect is only minor, local inflammation is not self-contained. Toxins or bacteria present may rapidly bring on constitutional reactions, *e.g.* fever.

In studies on skin dermatoses, two classes of chemical are differentiated: the primary irritant and the sensitizing substance. The two are not a clear-cut classification, since a primary irritant may act also as a sensitizer. The former always produce a direct effect on the tissues, either physical or chemical, combining with or removing vital components. Examples of the more aggressive primary irritants include oxidants (peroxides), solvents or emulsifiers for fats (organic solvents and basic detergents), keratin solvents (soaps), substances damaging to proteins causing cross-linking or "tanning" (heavy metal salts), which may be present in some plastics formulations.

The mode of action of the sensitizing substances is not so clear, and the behavior has been likened to antigen-antibody reactions. Since histamine will produce a reaction, some authors have proposed that sensitizing substances must be histamine-like although distinct from histamine [19].

The major studies of these substances have been related to contact dermatoses arising in the plastics industry and other industries. It is important, in formulating materials for surgical use, that known irritants or sensitizers should be avoided. In epoxy resin technology, use is made of the decreased dermatitis potential achieved by using polyamines or amine adducts for curing agents.

3.3.2. The Polymeric Material

The reaction of the polymer to the tissues can be discussed from chemical and physical effects. Overlapping both divisions is the problem of carcinogenesis, and this will be reviewed separately.

Most of the reactions are related to small amounts of nonpolymeric materials or degradation products leaching out. The question of degraded polymer fragments will be dealt with in the section on the effect of the tissues on plastics. Polymers containing obviously irritant chemical groupings are not used in surgery. One exception is the alkyl α-cyanoacrylates used as tissue adhesives. These have an unfortunate history of toxic reactions, but this appears to be related more to the mode of biodegradation and the nature of the degradation products, believed to be formaldehyde and a cyanoacetic ester, than to the polymer itself considered as a reagent [10, 20, 21] (see Sections 3.4 and 4.3).

[14] Second report of the Toxicity Subcommittee of the Main Technical Committee, British Plastics Federation, London 1962.

[15] A series of reports in the Federal German Health Gazette between Vol. 1, (No. 15), p. 235 (1958), and Vol. 6, (No. 15), p. 239 (1963), illustrate this.

[16] *J. Autian*, Ann. New York Acad. Sci. *146*, 255 (1968).

[17] *M. A. Inchiosa jr.*, J. pharmac. Sci. *54*, 1379 (1965).

[18] *T. Hirose, R. Goldstein*, and *C. P. Bailey*, J. thoracic cardiovasc. Surg. *41*, 404 (1963).

[19] *A. Tzanck* and *E. Sidi:* Les dermatoses allergiques. La pathalogie cutanée réactionelle. Masson, Paris 1959.

[20] Plastics in Surgery. Proceedings of Symposium in Vienna, Sep. 1967. Verlag der Wiener Medizinischen Akademie, Vienna 1968.

[21] *F. Leonard, R. K. Kulkarni, G. Brandes, J. Nelson*, and *J. J. Cameron*, J. appl. Polymer Sci. *10*, 259 (1966).

The activating effect of the electrophilic C≡N and the COOR groups on the same carbon atom contribute to the ready polymerization of the monomer, and it is suggested that initiation of polymerization by NH_2 groups of tissue proteins gives direct primary bonds between the proteins and the terminal unit of the polymer chain. Primary chemical bonding, to increase adhesive strength, between polymer and tissues is also utilized in dentistry [22].

The polar nature of the surface of most surgical plastics has important implications. During processing, contaminants are retained on the surface, *e.g.* oils, release agents, or grease from fingerprints. Even when the surface is clean, chemical or gaseous sterilants are adsorbed and retained by the plastic. Upon implantation, tissue compounds may be specifically adsorbed with consequent change in surface properties, and of the immediate environment of the implant. This latter factor has important consequences for plastics in contact with blood where the problems of coagulation and hemolysis are obstacles to the use of many plastics. The surface rapidly adsorbs blood proteins, and the blood is thus rapidly in contact, not with the plastic, but with a protein layer. It is not possible to correlate zeta potentials to thrombogenicity since the initially negative zeta potential is rapidly changed due to protein adsorption [23]. Neither can wettability be correlated with thrombogenic properties, probably for similar reasons [24].

The physical effects of polymers on tissues are even less well understood than the chemical effects. Since it is the surface which is in direct, intimate contact with the tissues, an understanding of the role played by surface physical phenomena is essential. A wide range of properties may be exhibited by a small area of surface. Smoothness would be thought to be a necessary factor, but thrombogenic properties, for example, are considered not to depend on this. In this case, the main factor is non-turbulent flow through the prosthesis [25]. Hard, abrasive filler particles protruding from the surface, oxidized areas which have hardened, irregularities resulting from cutting or machining which have a hardness different from the bulk material, are sources of potential tissue damage. Blood vessels are damaged, and local bleeding, clot formation, and invasion by fibrous tissue results in encapsulation of the implant by thick scar tissue. In extreme cases, migration through the tissues can occur.

Crystallinity affects the nature and mechanical behavior of polymers. The properties of polyethylene are dependent not only on molecular weight, but also on the crystalline/amorphous ratio [26]. Cellulose hydrolysis is retarded in the crystalline regions as a result of the closer, more ordered, packing of the chains [27]. The density variations between crystalline and noncrystalline regions, leading to differences in surface hardness, may be an important factor at the level of cellular response.

The major protein of connective tissue, collagen, can be reconstituted from solutions in differing structures representing different crystal forms [28], only one of which is specific for calcium phosphate nucleation from saturated solutions. This epitactic relationship is observed during *in vivo* studies of calcification of tissues [29, 30]. This may be related to the tissue reactions of certain plastics.

3.3.3. Carcinogenic Properties

The implantation of Bakelite (phenol-formaldehyde resin) discs in rats for long periods of time gave rise to sarcomas at the implant site [31]. *Oppenheimer et al.* first observed tumor formation in rats whose kidneys were wrapped with cellophane film [32].

This team believe that the form of the physical implant is more important than the material itself. Studies have been performed on films of a great range of materials, including cellophane, fluorocarbons, glass, nylon, polystyrene, polyesters, silicone elastomers, as well as stainless steel, silver, and other metals. Perforation of the material greatly reduced tumor formation, and when powders, sponges, or fibers were used, there was almost no tumor incidence. They argue for physical forces between the plastic and tissues, and show that once a fiber pocket has formed round the implant, tumor growth proceeds even on removal of the plastic [16, 33]. In an earlier paper [34], *Oppenheimer et al.* had discussed the unsatisfactory hypothesis of "metabolic interference by mere physical obstacles", and favored a chemical or physicochemical interaction between the polymer, or its degradation products, and cell components. Either active centers in the polymer, or free radicals, both possible products of degradation, were suggested as the actual carcinogenic entities.

A chemical activation is favored by *Hueper* [35], who induced cancers with both water-soluble and water-insoluble polymers.

The carcinogenic free radicals are not likely to be those remaining from the addition polymerization, since these would be deactivated during processing. In any case, radicals in the bulk of the material could not diffuse to the surface to interact with the tissues. However, oxidative degradation in normal polymers takes place by a free radical mechanism, and since

[22] *M. Buonocore*, *W. Wileman*, and *F. Brudevold*, J. dental Res. *35*, 846 (1956).

[23] *V. Mirkovitch*, *R. E. Beck*, *P. G. Andrus*, and *R. I. Leininger*, J. Surg. Res. (9) *4*, 395 (1964).

[24] *H. Lampert*: Die physikalische Seite des Blutgerinnungsproblems. Thieme, Leipzig 1931, cited in *R. I. Leininger*, *R. D. Kalb*, and *G. A. Grode*, Ann. New York Acad. Sci. *146*, 11 (1968).

[25] *F. J. Fry*, *R. C. Eggleton*, *E. Kelly*, and *W. J. Fry*, Trans. Amer. Soc. artificial internal Organs *11*, 307 (1965).

[26] *R. B. Richards*, J. appl. Chem. *1*, 371 (1951).

[27] *E. M. Fettes*: Chemical Reactions of Polymers. Interscience, New York 1964, pp. 59ff, 322.

[28] *R. D. Harkness*, Biol. Rev. Cambridge philos. Soc. *36*, 399 (1961).

[29] *W. F. Neuman* and *M. W. Neuman*: The Chemical Dynamics of Bone Mineral. University of Chicago, Chicago 1958.

[30] *J. Willems*, Discuss. Faraday Soc. *25*, 111 (1958).

[31] *F. C. Turnes*, J. nat. Cancer Inst. *2*, 81 (1941).

[32] *B. S. Oppenheimer*, *E. T. Oppenheimer*, and *A. P. Stout*, Proc. Soc. exp. Biol. Med. *67*, 33 (1948).

[33] *H. Nothdurft*, Strahlentherapie, Suppl. *34*, 14 (1956); Abh. dtsch. Akad. Wiss. Berlin, Kl. Med. *3*, 98 (1960).

[34] *B. S. Oppenheimer*, *E. T. Oppenheimer*, *I. Danishefsky*, *A. P. Stout*, and *F. R. Eirich*, Cancer Res. *15*, 333 (1955).

[35] *W. C. Hueper*, Arch. Pathology *67*, 589 (1959).

certain biological oxidations appear to involve odd electron intermediates [36], these could lead to polymer degradation. It was observed, for example, that polyethylene implanted in rats was degraded *in vivo*, and when a ^{14}C-labeled material was used, radioactivity was observed in the urine within 26 weeks [34]. The carcinogenic activity then arises from the nature of the degradation product, perhaps by inhibition of cellular free radical processes.

To put these observations of tumor formation into perspective it should be emphasized that up to the present time, no tumor formation in man has been traced to an implanted polymer. In 8000 human cases, involving 16000 foam implants for mammoplasty, no malignancy was observed [37]. More recently, it has been suggested that polyethylene intrauterine contraceptive devices might be a causative factor in cervical cancer of females, but this is not established [38].

The evidence for tumor formation comes from animal work, and there will always be uncertainty in applying results from small animals (rats) to humans. *Oppenheimer* believes that what happens in two years in a rat may take 20—30 years in humans, if in fact it occurs at all. It is always necessary to evaluate carefully the risks involved. The use of plastics for cardiac valve replacements is a case where the risk of death from refusal to use an implant is greater than the long-term hazard of cancer. A plastic hip joint in an aged person of 70 years poses different considerations than the case of a young person in their twenties.

The nature of the causative factor is still unknown, and it is not yet possible to separate physical or "solid surface" carcinogenesis from chemical activation. The human record is good, but indiscriminate use of medical plastics should be avoided.

3.4. Effect of Tissues on Implant

There is a scarcity of information in this area, perhaps because a long time interval is needed to determine if changes have occurred in an implanted material. Body fluids resemble dilute sea water [39] in composition: Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, HCO_3^-, PO_4^{3-}, and SO_4^{2-} are present along with oxygen and carbon dioxide, although in certain necrosed tissues there may be an anaerobic state. Then there are the proteins, polysaccharides, and macromolecular complexes, plus trace element components, together with enzymes involved in varying metabolic functions. At cellular level local pH variations occur.

Only the most inert polymers will be chemically or physically unaffected in long term implantation. Polyurethanes are extensively degraded and for this reason are no longer used in fracture repair [40]. Nylon was found to lose approximately 80% of its tensile strength over three years of implantation. Polytetrafluoroethylene solid sheet was invaded by tissues in mice and made water-permeable [41]. Embrittlement was also found by other workers [42], and the rapid abrasion of Teflon when used as the acetabular cup in a hip joint prosthesis, with consequent severe tissue inflammation by the abraded particles, led to abandonment of the technique [43] (see below).

Changes in tensile strengths of different fabrics after implantation in canine aortas are listed in Table 2 [44].

Table 2. Loss of tensile strength of different fabrics after implantation in canine aortas [44].

Fabric	Implanted (days)	Tensile strength loss (%)
Nylon	1073	80.7
Dacron	780	11.4
Orlon	735	23.8
	670	1.0
Teflon	677	5.3
	675	7.0

The degradation of ^{14}C-labeled polyethylene was mentioned above (Section 3.3.3), and polystyrene and polymethylmethacrylate behave similarly. When foamed polyvinyl formal (polyvinyl alcohol crosslinked with formaldehyde) was implanted, it became hard as the pores were invaded by tissues, and eventually contained calcium deposits [45]. This is confirmed in clinical practice in augmentation mammaplasty. The physical character of the polymeric material is important. Crystallinity affects swelling in water, and in turn the rate of hydrolysis [27,46].

Silicone rubber balls used in heart valves were always considered to be inert, but a few cases of altered characteristics in balls used in the aortic valve have been reported [47]. The material appeared to have adsorbed a fat-like substance, but laboratory tests could not duplicate the findings. A fatal case occurred where the ball extruded through the metal cage of the valve and lodged in the aorta. This ball had decreased in size, and was opaque and irregularly worn [48].

In tissue adhesives, and other applications, controlled biodegradability is an advantage. Collagen-Dacron composite vascular grafts are an example where the graft is initially impermeable, but the progressive removal of the degradable collagen permits ingrowth of tissue without loss of impermeability.

Alkyl α-cyanoacrylate adhesives are slowly degraded in the body and removed from the site of application. This is an ideal property for an adhesive in vascular and other applications, but the toxic nature of the degradation products severely limits the usefulness. ^{14}C-tracer studies on animal implantation showed that the methyl polymer was degraded more rapidly than the higher esters, and that no degradation products were stored in the tissues. It is believed that the

[36] *S. J. Leach*, Advances in Enzymology related Areas molecular Biology *15*, 1 (1954).

[37] *H. I. Harris*, J. int. Colloquium Surgeons *35*, 630 (1963).

[38] *J. C. Ayre*, Ind. Med. J. *34*, 393 (1965).

[39] Documenta Geigy, Scientific Tables. Geigy, Basel 1956.

[40] *I. Redler*, J. Bone Joint Surgery *44a*, 1621 (1962).

[41] *J. Calnan*, Nature (London) *191*, 1017 (1961).

[42] *R. I. Leininger*, Plastics in Surgical Implants. ASTM, Philadelphia 1965, No. 386, p. 71.

[43] *J. Charnley*, J. Bone Joint Surgery *45b*, 622 (1963).

[44] *J. H. Harrison*, Surgery Gynecol. Obstetr. *108*, 433 (1959).

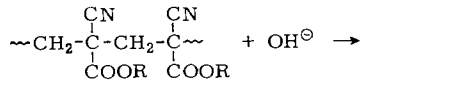
[45] *A. W. Schwartz* and *J. B. Erich*, Plastic and reconstr. Surgery *25*, 1 (1960).

[46] *S. M. Atlas* and *H. F. Mark* in [42], p. 63.

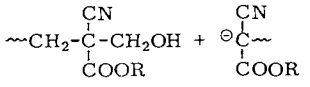
[47] *A. Starr et al.*, cited in ref. [16].

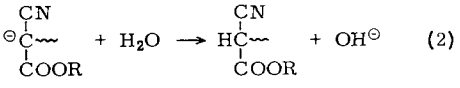
[48] *S. G. G. Ablaza, G. Blanco, U. Maranhao*, and *H. Goldberg*, J. thoracic cardiovasc. Surg. *50*, 401 (1965).

toxicity results from the formation of formaldehyde and a cyanoacetate. It has been suggested[21] that main chain hydrolysis occurs, catalyzed by OH^-:

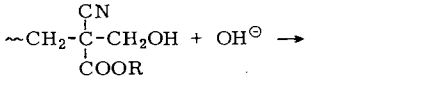


(1)

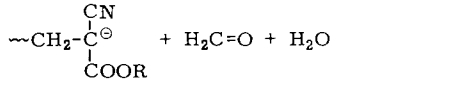




(2)



(3)



Further degradation according to equation (2) is expected to yield cyanic esters as further products. It is argued that lower concentrations of these toxic products are given by the less rapidly degradable higher esters, and that this accounts for their lower toxicity. The less toxic isobutyl ester is currently being evaluated for clinical use[20].

Knowledge of biodegradation mechanisms of plastics can lead to ways of improving performance by possible structure modification. Polyesters, polyurethanes, and nylons may be hydrolyzed under the influence of H^+ or OH^- ions, or hydrolytic enzymes may be involved. Hydrocarbon polymers may be oxidized by tissue components. It is always the nature and fate of the degraded chain fragments which is important, in addition to the impairment of the properties of the plastic material.

For example, polymethylmethacrylate used as a ball head in a femoral head prosthesis (*Judet*) became crazed and cracked, and quite unsuitable for use[10]. With a polytetrafluoroethylene acetabular cup, abrasive wear was so great that the metal femoral head protruded through to the posterior side, and diffusion of fragments into the tissues caused irritation and toxic reaction[43]. In some applications, 10 years may be needed before the prosthetic device causes problems to the patient due to malfunction. The majority of defects are found within three to five years. It is reasonable that for adequate evaluation this period of time must be given to a trial under proposed conditions of use.

At the Royal National Orthopaedic Hospital, Stanmore, England, *Scales* is using a simulator which will impart all the possible motions and forces of a hip joint to a prosthesis[50], using physiological lubricants. For a suitable chemical environment, immersion in boiling 2% peracetic acid has been suggested[49].

[49] *D. J. Lyman*, Rev. macromolecular Chem. *1*, 355 (1966).

[50] *J. T. Scales*, Proc. Instn. mechan. Engr. *181*, part 3, (1966/1967).

In certain cases, the adverse reaction caused by an implant is not restricted to the localized tissues. There may be a fever or other generalized reaction. The polymer itself may also evoke an antigen-antibody response. Local trauma and necrosis of tissues act as centers of infection, with the infection itself being systemic in nature. Thus it is necessary to consider an implant as not causing adverse body reactions for satisfactory application.

Biomechanical design, *e.g.* of a hip joint, must consider the replacement in relation to the overall pattern of forces at rest and during motion. Plastics do not of course regenerate and will not respond to changing demands of growth or of aging. The body in turn must continually readjust to a replacement with a different function from that of the normal organ. This can impose a continuous trauma or stress, with resulting secondary manifestations in other organs or tissues. This is important to remember as more elaborate implants are being designed, and in such cases these biophysical factors may be of greater importance than the choice of a right material[9].

4. Current Uses of Plastics Implants in Surgery

4.1. Cardiovascular Surgery

The first recorded attempt at human arterial repair was in 1759[51], but significant work only began at the beginning of this century. Glass, gold, silver, rubber, aluminum, and tubes lined with paraffin wax were used, but only temporary patency was obtained[52].

Between 1944 and 1946 methylmethacrylate polymers tested in dogs showed that under certain conditions prostheses made from these materials resisted thrombosis. This was the now classic work of *Hufnagel* using a rigid, solid wall tube for permanent implantation[53]. Certain simple factors were utilized in prevention of thromboses. A hemorepellant surface was suggested by the longer clotting time of blood in paraffin wax lined tubes.

Water absorption appeared to promote clot formation, and hence plastics with a lack of water absorption were sought for. Mechanical smoothness of the surface of the material in the biological interface was another requirement. The factors of toxicity and tissue tolerance already discussed were also accounted for. However, these criteria alone are not sufficient to prevent thrombus formation.

4.1.1. Vascular Prostheses

In 1952 *Voorhees et al.*[54] introduced the concept of a porous arterial prosthesis, and a number of synthetic fibers were found to have satisfactory performance.

[51] *Hallowel*, cited in ref. [10], p. 73.

[52] *A. Carrel*, Surgery Gynecol. Obstetr. *15*, 245 (1912).

[53] *C. A. Hufnagel*, Arch. Surgery *54*, 382 (1947).

[54] *A. B. Voorhees et al.*, Ann. Surgery *135*, 332 (1952).

Nylon (polyamide), Dacron (polyester), and polytetrafluoroethylene have been the materials most used, with Dacron being widely accepted. Flexibility must be coupled with a resistance to kinking, or to collapse. The tube should also be seamless, be nonfraying when cut, and give ease of suturing and handling. The extent of porosity is a subject of argument, but some is needed so that the initially deposited fibrin layer may be replaced by fibrous tissue, which eventually produces an inner surface similar to that of the host vessel. Kinking in the initial stages is largely overcome by the use of a crimped tube. Textile technology demonstrates that a material may eventually show no elastic recovery after a series of stress cycles. Thus nylon loses tensile strength too rapidly to be of value.

One problem still centers around the question of porosity, and whether it is to be porosity to tissues, or only to ions. Noncorrosive metals, *e.g.* platinum, where there should be no surface contaminant complication, thrombose relatively quickly, and there is of course no ion-permeability[55]. Too great a tissue-porosity may be a disadvantage. Development of solid wall prostheses must await developments in surface structures.

Porous prostheses will continue to be used and one important trend is towards the use of extremely fine yarn bundles – *Gossamer Concept*. A knitted material with a needle density of 40 needles/inch (usual prosthesis 22 to 30) which does not need to employ stretch, bulk, or texturized yarns, has given a prosthesis which is much more akin to natural tissues. Although the material is highly porous, preclotting reduces this to 10% of the initial value. Experimental and clinical results look promising.

A desire for low initial porosity, together with a subsequent higher biological porosity, has led to the development of compound prostheses in which an absorbable coating of, *e.g.*, collagen is incorporated with the permanent material The challenge is to develop a material for implantation into a child which will not inhibit natural growth, and will remain complication-free for the lifetime of the individual.

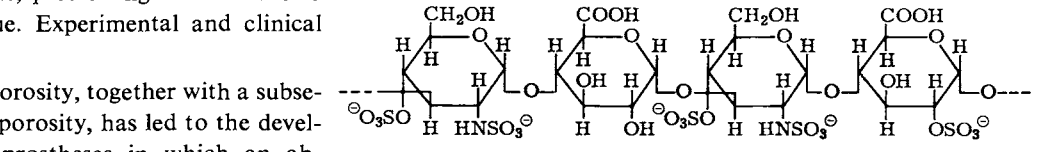
4.1.2. Heart Valves

Polytetrafluoroethylene, polycarbonate, silicone rubber, polyester fabric, polymethylmethacrylate, and stainless steel have been the main materials of choice. Provided that the valve performs its hemodynamic function satisfactorily, it need not necessarily resemble the natural valve which it is intended to replace. The design must avoid embolic and hemolytic dangers. Opening and closing must be gentle but rapid, with minimum turbulence and pressure gradient across the prosthesis, and the seal should be competent without trauma to the blood cells.

One of the first clinical uses was by *Hufnagel* in 1952 [56] and was a simple, silicone-rubber ball valve, several of which are still functioning in patients up to 13 years later. The more well-known ball valve is the Starr-Edwards prosthesis which employs a silicone rubber ball in a stainless steel cage, and has an artificial stroma of the cloth around the base. *Hufnagel* has also developed a tricuspid leaflet valve of silicone rubber coated Dacron, and in another more recent leaflet valve due to *Gott* [57] the leaflets are of Teflon fabric, reinforced at the hinge with percale fabric, and silicone rubber coated. The rigid housing is a polycarbonate. Teflon and polypropylene are used in the Alvarez mitral valve prosthesis. The Smeloff-Cutter prosthesis is a double-caged valve using titanium for the cage. Sutureless valves use retractable curved pins to grasp the tissues, and silicone rubber cuffs.

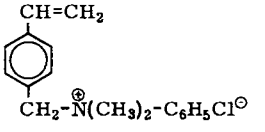
There were still problems with these valves in terms of an adequate lifetime of the ball or the leaflets, and in terms of tendency to thrombus formation. Newer materials and composite designs have helped to increase the lifetime. The Gott valve uses a reinforced Teflon fabric, and *Hufnagel* has employed a polypropylene cloth as the core material for the leaflets.

The first significant step towards thrombus prevention was in the Gott valve [57] with the use of heparinized surfaces. The polycarbonate was first graphite coated, and then a benzalkonium compound was adsorbed on to this. Heparin *(1)* could then be bonded to this surface, and the plastic was non-thrombogenic *in vitro* and *in vivo*. Clinical trials are promising.

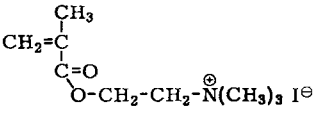


(1)

Heparin is known to form insoluble complexes with quaternary ammonium compounds and this has been the basis for synthesizing polymers to which heparin could be bonded directly. Chloromethylation of polystyrene with an $AlCl_3/ClCH_2OCH_3$ mixture in nitrobenzene, followed by treatment with a methanol solution of dimethylaniline gave a quaternary ammonium salt *(2)*, which would bond sodium heparinate.



(2)



(3)

Trimethyl[2-(2-methyl-1-oxo-2-propenyloxy)ethyl]-ammonium iodide *(3)* is a polymerizable quaternary ammonium salt. Butadiene-co-vinylpyridine polymers have been quaternized and treated with heparin.

[55] *P. N. Sawyer*, cited in *S. A. Wesolowski et al.*, Ann. New York Acad. Sci. *146*, 325 (1968).

[56] *C. A. Hufnagel et al.*, Ann. New York Acad. Sci. *146*, 262 (1968).

[57] *V. L. Gott et al.*, J. thoracic cardiovasc. Surg. *48*, 713 (1964).

(Various plastics and elastomers have been prepared and are being evaluated [58].) The final development is in the fully artificial implant.

4.2. Orthopedics

4.2.1. Prosthetics

There have been important developments in the uses of plastics materials in orthopedics, particularly in the use of adhesives. Some of the earliest uses were of celluloid plates to repair cranial defects during World War I but were not particularly successful. Acrylic plates were used towards the end of World War II but some reports indicated a loosening, and doubt has been cast on the value of this approach. An acrylic (polymethylmethacrylate) was the material from which the Judet femoral head prosthesis (see Fig. 2)

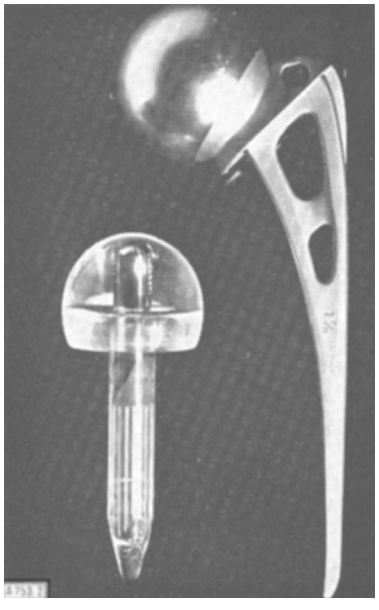


Fig. 2. Left: Judet femoral head prosthesis in polymethylmethacrylate. Right: Austin-Moore femoral head prosthesis in stainless steel. Early attempts to use plastics in hip surgery were unsuccessful due to excessive wear of surface [58a].

was constructed [10], but these gave unsatisfactory results, wearing badly, and also crazing on the surface. This crazing may have resulted from strains imparted during fitting the stem, or during insertion into the bone, or it may be a true tissue reaction. The property of creep (cold flow) shown by acrylics would indicate against their use in a continuously stressed location. This, and the mechanical failure resulting from crazing, is a factor against use of these materials in weight bearing prostheses.

Nylon has been tried for intramedullary nails, and nylon membrane in arthroplasty of the knee in chronic arthritis [59], but is unsuitable for hip or shoulder prostheses since abrasion is too rapid [43]. The particles of nylon released lead to a tissue reaction which can cause bone destruction [50]. Dacron polyester fabric has been used to replace ligaments in the knee. Polytetrafluoroethylene implants have also been used in the knee in arthroplasty [60], but this material is unsuitable for hip prostheses because of excessive wear and fragmentation [43].

High density polyethylene (Ruhr-Chemie-Hoechst RCH 1000) is used by *Charnley* as the acetabular cup, in combination with a stainless steel femoral head, for total replacement of the hip joint. A cold-curing acrylic resin is used to bond both components to underlying living bone. A meticulous technique and close attention to perfection of surface finish gives a highly successful prosthesis. There is some wear of the polyethylene cup, but no adverse tissue reaction is observed over a four- to five-year follow up.

4.2.2. Adhesives

4.2.2.1. Polyurethanes

Adhesive uses have seen three main developments. The application of polyurethane foam *in situ* to support fractures was one of the very controversial uses of this material [40,61].

The mixed, uncured ingredients were applied to a trough cut into the bone surfaces, around the fracture site, and a hard, rigid foam was produced at the fracture site. The progressive replacement and absorption of the foam was of interest, and after 12 months only 1/4 to 1/6 remained. Early workers reported no toxic effects. Subsequent workers reported a high incidence of non-union and infection, with a difficulty in obtaining reproducible curing and adhesion to the bone.

The real problems are:

1. Poor mechanical and cohesive strength.

2. Unknown nature of breakdown or route of excretion.

3. Volume spread of foam at operation site makes removal difficult.

4. Numerous complications in clinical use necessitated difficult removal operations, and studies showed that the material did not possess any of the properties claimed for it.

5. Animal results later indicated that polyurethane gave rise to appreciable foreign-body reaction, tended to retard bone union, and became encapsulated in fibrous tissue.

One report showed that out of 51 operations (42 patients) only 9 resulted in stable fixation and healing; in 37 cases the plastic broke in the medullary canal or loosened. 21 were complicated by infection and the development subsequently of draining sinuses [40].

[58] *Leininger et al.*, see ref. [24].

[58a] Figures reproduced by courtesy of the Department of Medical Illustration, University of New South Wales and Teaching Hospitals.

[59] *J. G. Kuhn*, J. Bone Joint Surgery *46a*, 446 (1964).

[60] *F. W. Taylor*, J. Bone Joint Surgery *45b*, 617 (1963).

[61] *M. P. Mandarino* and *J. E. Salvatore*, Arch. Surgery *80*, 623 (1960).

[62] *B. Bloch*, J. Bone Joint Surgery *40b*, 804 (1958).

4.2.2.2. Epoxy Resins

Golovin [63] originally used the material in a technique similar to that used for polyurethane, but then used it as a glue between fracture ends, supplemented by bonded sliding grafts or bone transplants. He stressed the importance of dried surfaces. In 32 patients successful healing was obtained. *Bloch* [62] originally applied the resin as a cuff of resin-impregnated glass fiber around the bone ends, using also polyethylene plugs inserted into the medulla. Experiments in sheep showed rapid restoration of function, with weight bearing in 2 days. In 2 human cases, there was rapid restoration of function but necrosis occurred in one. However, one patient is still trouble free nearly 10 years later.

More recently we have used a filled resin to cement femoral head prostheses in place [64]. In 3 recent human cases over the past 2 years, satisfactory fixation has been obtained and one successfully sustained a heavy fall which actually bent the metal prosthesis without loosening the glue line (Fig. 3). The mixed resin is one



Fig. 3. Left: a room temperature hardening epoxy resin was used to anchor the stem of this specially designed hip prosthesis into the remaining bone. Right: the same prosthesis two years later after a severe fall. The adhesive joint was secure and the stem was successfully straightened [58a, 64].

developed for adhesion to wet surfaces and for curing in a wet environment. Polyamide is used to cure the resin instead of the toxic amines. The whole medulla is filled *via* a nylon tube from an injecting gun nozzle. Sterilization of all resin ingredients and equipment has been by gamma irradiation. Hardening occurs about 1/4 hour after insertion of the prosthesis, and temperature rise is negligible.

Reitz [65], using a different resin system, found that hardening was delayed in the stratum next to the bone. His technique, in rabbits, using a glass-fiber reinforced cuff was not successful in 1/3 of the cases, due to lack of adhesion between bone and cuff.

4.2.2.3. Acrylics

The usual cold cure system is a mixture of two components, a fine powder of polymethylmethacrylate, containing a suitable initiator, and a liquid monomer, containing an amine as activator. On mixing, the polymer is swollen by the monomer, polymerization in the monomer phase is initiated, and after a few minutes, and considerable evolution of heat, a fairly homogeneous solid is obtained. Methyl methacrylate was used in neurosurgery for cranioplasty [66] and many workers report absence of complications. The use for aneurysm investment also appears successful. In 1951 it was first used for fixation of an acrylic hip prosthesis and for a metal prosthesis in 1953. *Charnley* has used the technique very extensively, using a large amount of plastic to fill the complete space between prostheses and bone [67]. He has reported on 455 cases with no evidence of loosening or bone reaction, and has given considerable attention to the biomechanics of the system. He claims that this method eliminates fretting between bone and implant and gives an even weight distribution. Other workers adapted the technique to fixing pertrochanteric fractures of the femor in combination with a pin and plate, but reported complications [68]. It should be noted that free monomer appears to be toxic to the tissues but in *Charnley*'s technique the material is used as a dough. *Reitz*, using the material for fixing femoral prostheses in dogs, obtained only 3 out of 14 successful results with maintained fixation and stability. He puts it down to malfitting and malalignment of the prosthesis, and incomplete filling with the plastic.

It appears that there is a place for the acrylics, and modifications to the systems used may give desirable improvements of increased adhesion and matching of the tissue properties.

4.3. Tissue Adhesives

There is some overlap here between this and the preceeding section, though the problems in orthopedics are made more acute by the mechanical demands of weight bearing and movement.

Work on suitable adhesives has taken place over the past ten years. Some was stimulated by the results on reinforcing intercranial aneurysms, where adhesion to the tissues was found to be satisfactory.

The attractions of adhesives are:

1. The rapidity with which repair may be accomplished.

2. Possibility of complete closure with lack of seepage.

3. Bond formation without undue deformation of tissue.

[63] *G. V. Golovin*, Vestnik Kir. *83*, 45 (1959).

[64] *B. Bloch, G. W. Hastings*, and *G. R. Wollwork*, Med. J. Australia, in press.

[65] *K. A. Reitz*, Acta chirurg. scand. Suppl. *1968*, 388.

[66] See references cited in [65].

[67] *J. Charnley*, J. Bone Joint Surgery *46b*, 518 (1964); *47b*, 56 (1965).

[68] *G. Scheuba*, cited in ref. [65].

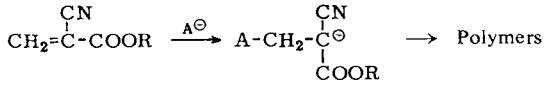
4. Enhanced repair of weakened tissue resulting from age or disease.

In addition to the requirements of non-toxicity and absorbance, the adhesive must have a high degree of initial tack, to hold while hardening is completed, and must bond rapidly to tissue.

The NH_2, OH, and COOH groups present in the collagen of connective tissue are available for primary bond formation with an adhesive. However, water present in the tissues will often react more readily with some of the possible adhesives. Hardening which takes place by polymerization of monomers or of low molecular weight polymers is the most profitable area for study. Solvent removal will be less satisfactory, since the organic solvents will be undesirable, and water soluble adhesives do not usually have sufficient water resistance. For this latter reason, emulsions are not expected to be so satisfactory. Another group which is promising is that where polymerization is initiated by interaction with the bodily environment. Speed of cure is another limiting factor, and would rule out *e.g.* epoxy resins for soft tissue applications, in spite of their low toxicity and the fact that curing is only slightly exothermic.

Methyl α-cyanoacrylate was the first material to come into prominence and has been used in a wide range of applications. These include anastomoses of small blood vessels, nonsuture closing of skin, applying patches to arteries, reinforcement of suture lines, nephrotomy, *etc.* Its use in bone surgery has also been reported.

Polymerization is believed to be base-catalyzed and initiated even by water, alcohols, other weak bases, or possibly the NH_2 groups of tissue proteins[21]. Only a few seconds are required for reaction.



The alkyl α-cyanoacrylates are increasingly difficult to polymerize as the length of the α-alkyl group (C_2 to C_{10}) increases. The higher esters appear to be less toxic and since they spread more rapidly and completely on the tissues to form continuous films their polymerization is initiated more readily by water. A reverse effect is observed when spreading and polymerization are studied on distilled water.

4.4. Polymer Membranes

In many areas of the body macromolecular membranes are of great biological importance, especially in connection with selective permeability. Synthetic polymer membranes have been used for purification purposes in artificial kidneys, lungs, and liver.

The uses and problems of plastics for connecting patients to the hemodialyzer (artificial kidney) have already been mentioned (Section 3.3.1). In the dialysis apparatus, cellophane has been employed for the membrane, and acts essentially as a microporous barrier. Selectivity is small for related molecules of similar size, unless this is approximately the size of the pore, when the interactions between polymer, surface, and solute will affect the rate of transfer. The rate of transfer through cellulose membranes is slow, but pore size can be increased by biaxial stretching of the film[43]. Cellulose acetate films which are deacetylated give a more porous film.

If a membrane could be designed, in which interaction between solute molecules and membrane were high, this could give to the membrane a partitioning function. Work has been carried out to produce membranes which are water swellable and partitioning, yet are mechanically strong. Block copolymers have been evaluated. These are polymers based upon two (perhaps more) component monomers, in which the monomer units are incorporated into the polymer as macrosegments of sufficient length, such that the properties of each component are imparted to the material. Hence for a partitioning membrane, one component would give mechanical strength, the other would impart the swelling and extracting properties. The molecular structure must be such that a good membrane, free from pinholes, can be produced in a reproducible manner, and this in general implies a linear molecule, for casting from solution, or melt pressing. Compatibility with blood is an important factor also.

Block copolymers of polyoxyethylene glycol with ethylene terephthalate were tested, and appear to offer a partitioning mechanism. In another version[69], the more hydrophobic polyethylene-terephthalate sections were replaced with polyurethane segments to test the effect of structural changes, and indicated that in this type of membrane there is also an effect due to the hydrophobic segments. Some animal work has been reported[49].

As an artificial lung, the membrane separates blood from gas, and acts to control the exchange of O_2 and CO_2. Polytetrafluoroethylene and silicones appear to have the right properties of permeability and selectivity. Blood damage, and blood clotting are problems, and the turbulence caused by the high flow rate necessary for the required degree of oxygenation also increases the damage. Nonthrombogenic surfaces represent the next step forward in design of more satisfactory oxygenators. Direct exposure of the blood to the gas is prevented with these membranes.

5. Polymers as Reagents

5.1. Bioplastic Materials

The name Bioplast has been used for polymers of natural origin which are adapted for surgical use. They may have been partly modified by chemical means, *e.g.* cross-linked to reduce biodegradability, and/or produced in a different form, *e.g.* molded.

A typical use of bioplasts is the preparation of molded prostheses from a pure form of fibrin[70]. One application was as a cup implant over the femoral head in arthroplasty of the hip. Within six months, the fibrin had been absorbed, and healthy cartilage had regenerated. Fibrin films[71] and foam[72] and regenerated collagen[73] have all been used in surgery.

[69] *D. G. Lyman et al.*, Trans. Amer. Soc. artificial internal Organs *11*, 91 (1965).

[70] *M. Gerendas*, Therapia Hungarica 7, 8 (1959).

[71] *F. D. Ingraham* and *O. T. Bailey*, J. Neurosurgery *1*, 23 (1944).

[72] *F. D. Ingraham* and *O. T. Bailey*, J. Amer. med. Assoc. *126*, 680 (1944).

[73] *D. G. Kline*, Arch. Surgery *91*, 924 (1965).

In the field of plasma expanders, gelatin of molecular weight approx. 37000 has been used in aqueous solution [10]. Reaction with succinic anhydride has led to the stable product called "Modified Fluid Gelatin". Gelatin sponge has a wide use in surgery, generally as a hemostatic agent or a resorbable dressing [74].

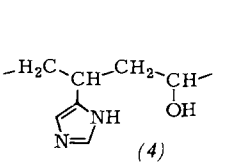
The attraction of bioplastic materials is that they are not completely foreign to the body, and would be expected to be more compatible than purely synthetic materials. The criterion of success would be a capacity to integrate with the living tissue and allow its regeneration, without antigenic and inflammatory response, while still retaining the desired mechanical properties.

5.2. An Analytical Tool in Medical Science

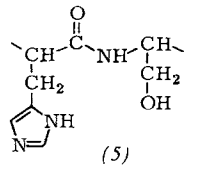
Studies of muscle action are studies of the contractile properties of proteins under the action of chemical or neurological stimulants. Much of the earlier work on protein structure was carried out on fibers, wool, and keratin using X-ray diffraction methods [75], and it was possible to show than an extended β-form and a folded α-form could both exist. However, there was little quantitative data on the relationship between the two forms, and the environmental or free energy changes associated with transitions. Synthetic polypeptides of known chemical composition gave an important tool and permitted proposals to be made for an exact structural model of the polypeptide helix [76]. X-ray determinations of periodic spacings in the molecule were compared with results from natural proteins, and eventually the elucidation of the natural structure was possible. The advantage of the synthetic model is that materials having definite structures can be prepared, and substituted at will.—The synthesis of polymers having a nonthrombogenic group as an integral part of the molecule gives interesting possibilities to investigate the mechanism of blood clotting (see Section 4.1.2).

Polymers have also been used in studying enzyme activity and especially the mode of action of thiol groups [77]. In another direction the proteolytic activity of enzymes, *e.g.* papain, is known to be retained even if part of the molecule is degraded, and thus appears to be related to the interactions of certain functional groups, rather than of the whole molecule. Copolymers containing imidazole and benzimidazole groups were prepared and their esterolytic action was observed [78]. Background studies on chymotrypsin indicated that the imidazole group of the histidine unit was the reactive center, and that activity was enhanced by a neighboring OH group from a serine unit, which could complex with the imidazole group. The synthetic polymers were made containing a pendant imidazole group from 4- (or 5) -vinyl imidazole, and other functional groups, OH or COOH as required. It was hoped to achieve the correct steric relationship between the groups by the chain coiling in solution, and hence enhance the activity over that for a single imidazole compound, or a polymer with imidazole groups alone.

A hydrolyzed copolymer *(4)* of 4-vinylimidazole and vinyl acetate is similar to a peptide *(5)* with neighboring histidine and serine

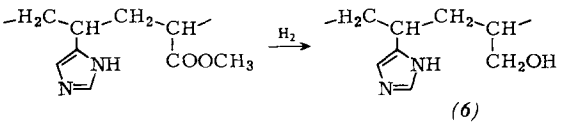


(4)



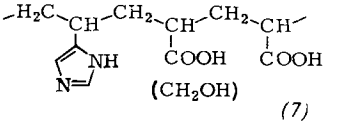
(5)

except that the secondary OH is less reactive. Hence use of methyl acrylate followed by reduction would give a primary alcohol *(6)*.



(6)

Polymers *(7)* containing an additional acidic group could be provided by terpolymerization, or by partial reduction of an acrylic acid copolymer which had adjacent carboxyl groups.



(7)

Hydrolysis of *o*-nitrophenylacetate and 3-nitro-4-acetoxybenzoic acid was found to be catalyzed more effectively by poly-5-(6)-vinylbenzimidazole than by poly-4(5)-vinylimidazole; both compounds proved 50 times as effective as benzimidazole and imidazole, respectively, at pH 10.

Thus even in a homopolymer, the spatial arrangement of the groups is significant. The copolymer of 4(5)-vinylimidazole with acrylic acid affords an opportunity of studying the effect of a negatively charged chain. With uncharged esters the copolymer is not very effective, but for positively charged esters the copolymer was up to four times more active above pH 9. Conversely, positively charged polymers (copolymer with methylimidazolium groups) were very effective for anionic ester substrates [79]. The binding of a charged substrate by the polyanion of opposite charge, giving increased catalytic activity of neighboring groups, was confirmed by experiments in which a highly charged polyanion preferentially binds a cationic substrate, thereby protecting it from hydrolysis. The hydrolyzing $-OH^{\ominus}$ groups were repelled by the highly anionic polymer chain.

These carefully designed polymers will undoubtedly be followed by others which can assume some of the functions of natural proteins and can be used in surgery.

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[80] *H. Morawetz* and *J. A. Shafer*, Biopolymers *1*, 71 (1963).

Some Aspects of the Active Transport of Amino Acids[**]

By Klaus Ring[*]

Active transport is the transport of substances against their activity gradients. In the cell, metabolic processes provide the energy for active transport through the membrane, during which amino acids are coupled with a carrier system located in the membrane. Some of the proteins involved in the translocation of amino acids have now been isolated from E. coli.

1. Introduction

The purpose of the present article is to describe some aspects of the transport of amino acids through biological membranes (see[1]). Amino acids are very important compounds since they participate in a great variety of metabolic processes; their permeation through membranes depends on their predominantly hydrophilic character, so that coupling with carrier systems must be assumed for their transport. Another feature is the structural variety of their side chains, which necessitates many specific carrier systems since transport processes are often as specific as enzymatic reactions.

Owing to the large amounts of amino acids required by growing cells for protein synthesis and intermediate metabolism, there is a close relation between transport and metabolism, which is reflected in the often considerable capacity of the transport systems and in the many ways in which they can be regulated.

The main emphasis in the investigation of active transport has shifted in recent years from a physiological aspect to a more biochemical one. The chemistry of active transport can already be better understood through the combination of enzymological, physicochemical, and genetic techniques. *Skou*[2] discovered the first enzyme that could be regarded as a component of an active transport system; *Kaback* and *Stadtman*[3] were able to prepare from *E. coli* pure membranes capable of actively transporting amino acids and sugars. Finally, proteins that may be regarded as components of transport systems have been isolated from microorganisms in several laboratories.

"Transport research" has now reached the stage at which it is no longer possible to present an exhaustive survey, even of only a limited field such as the active transport of amino acids, within the framework of a brief review article. The subject matter will therefore be restricted, of necessity rather arbitrarily, to the more recent aspects of biochemical interest. In addition to enzymological and preparative topics, we shall be concerned with questions of regulation, which may be important to the economy of the cell in view of the large quantities of energy required for amino acid transport. (For comprehensive reviews, see[4–19].)

2. Processes Involved in Permeation

The description of the permeation processes will be limited here to what is necessary for an understanding of the following sections. (For detailed descriptions, see[1,6,7,10,12,13,19].)

There are three ways, of widely differing physiological significance, in which metabolites can pass through biological membranes.

2.1. Free Diffusion

Free diffusion is approximately realized only for a few low molecular weight metabolites such as amino acids (but see[19], p. 106 for non-electrolytes). Owing to their hydrophilic character as electrolytes, these

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[**] The author's own work reported in this article was supported by the Deutsche Forschungsgemeinschaft.

[1] For transport phenomena in synthetic membranes see *P. Läuger*, Angew. Chem. *81*, 56 (1969); Angew. Chem. internat. Edit. *8*, 42 (1969).

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[18] *A. Rothstein*, Annu. Rev. Physiol. *30*, 15 (1968).

[19] *W. D. Stein*: The Movement of Molecules across Cell Membranes. Academic Press, New York 1967.

substances require water-filled pores in the membrane; the size of such pores, however, is limited. *Kromphardt* was able to show conclusively that the transport of taurine in Ehrlich ascites tumor cells (EMAT cells) involves a diffusion component of this nature [20].

A special case of free diffusion in which the particles move consecutively in a linear chain and cannot change their places in this chain, is assumed for the flow through very narrow pores [21–23]. This "single-file" diffusion can be distinguished kinetically from the normal free diffusion. One of its characteristics is the saturation of the flux with increasing particle concentration. The importance of "single-file" diffusion in the permeation of amino acids through biological membranes is unknown.

2.2. Facilitated Diffusion

Facilitated diffusion is also a "passive" flux, the driving force of which can be entirely derived from the concentration gradient (or electrochemical potential gradient) of the particles between the two sides of the membrane. Facilitated diffusion, unlike free diffusion, is characterized by high specificity. The particle flux can be saturated with increasing particle concentration in front of the membrane. A sub-phenomenon of facilitated diffusion is "counterflow" [6]. Many substances can mutually accelerate one another's flux if they are situated on opposite sides of the membrane.

The difference between facilitated diffusion and that form of passive permeation known as free diffusion can be very satisfactorily explained by assuming the participation of a carrier. In this view, a specific carrier molecule, which may itself be unable to permeate the membrane, forms a complex with its transport substrate on or in the membrane. The complex dissolves in the membrane, through which it is then able to pass by diffusion, rotation, oscillation, contraction and expansion, or the like, and dissociate on the other side.

An important characteristic of facilitated diffusion is that it proceeds with no perceptible chemical change in the partners involved; the only chemical reactions are the association and dissociation of the carrier and the substrate. This kind of diffusion may be discontinuous or continuous; in the former case, association and dissociation take place only on the outsides of the membrane, while in the latter, as exemplified by the transport of O_2 by hemoglobin, these processes also occur during passage through the membrane [24].

Facilitated diffusion appears to be of considerable importance in the absorption of some amino acids in microorganisms. *Brock* and *Moo-Penn* [25] found that in *Streptococcus faecium*, extracellular serine, glycine, and threonine, which are essential amino acids for these cells, are transported into the interior of the cells against their concentration gradients by a specific system without the direct expenditure of energy. This is due to an obligate coupling of these inward fluxes with the efflux of alanine, which is synthesized in large quantities in the cells. The concentration gradient for alanine from the inside outward is thus used to pump extracellular amino acids into the cell against their concentration gradients.

Kaback and *Stadtman* [26] have shown that though the accumulation of glycine through isolated membrane preparations from *E. coli* is energy-dependent as an overall process, the actual transport (translocation) through the osmotic barrier occurs by facilitated diffusion, *i.e.* independently of energy.

2.3. Active Transport

Active or uphill transport exhibits the same kinetic characteristics as facilitated diffusion, *i.e.* saturation of the flux at high substrate concentrations, usually high specificity, susceptibility to competitive inhibition, exchange diffusion, and the "preloading effect" [27–30]. A carrier mechanism is therefore generally assumed to operate here also. The essential difference between this and facilitated diffusion is that in active transport the particle flow is directly coupled with the free energy of a chemical reaction taking place in the transport region. The energy liberated is converted into pumping work, and so allows the accumulation of the particles against their osmotic or electrochemical gradient.

Active transport generally leads to the establishment of a steady state in which the distribution of the substrate between the intracellular and extracellular space is constant. The accumulation depends on the capacity of the transporting system, the magnitude of the efflux (free diffusion and/or exchange diffusion), and the rate of breakdown of the substrate inside the cell. Cases of enrichment by a factor of more than a thousand are not uncommon. *Johnstone* and *Scholefield* [31] have reported that under certain conditions, about 50% of the cellular ATP can be utilized for the accumulation of glycine in EMAT cells. *Quastel* [11] has pointed out the great selection advantage that cells with efficient active transport systems can have in their development as compared with cells having lower transport capacities. For example, tumor cells, which are among the most active of animal cells as far as transport is concerned, can withdraw important nutrients from neighboring cells.

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As was first shown by *Heinz* [27–29] for the transport of glycine in EMAT cells, the total flow of this amino acid involves an appreciable exchange diffusion component. In the steady state more than 90% of the intracellular glycine is exchanged for extracellular glycine within a period of five minutes [28]. The exchange fluxes are about five times as fast as the net transport [32]; this means that about 80% of the total flux is due to the exchange diffusion. The reason for this is thought to be that the charged carrier is more mobile (soluble) in the membrane than the uncharged carrier [16, 29, 30]. As a component of an active carrier system, exchange diffusion, like facilitated diffusion, is independent of energy; both can be attributed to the same type of reaction.

To illustrate the individual reactions to be expected in the transport of amino acids, we shall first consider the carrier model proposed by *Heinz* and *Walsh* [29] (Fig. 1).

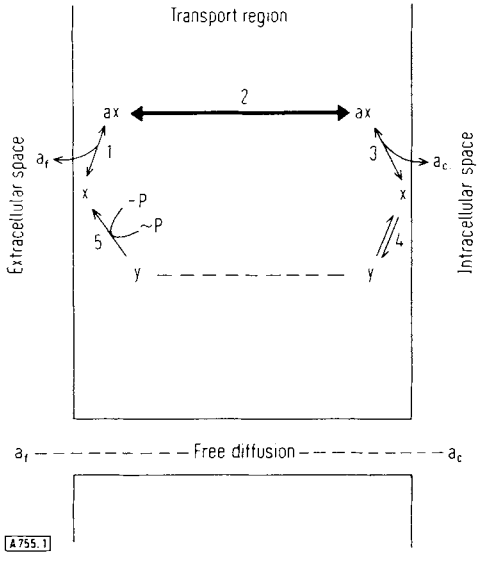


Fig. 1. Model of the amino acid transport in Ehrlich ascites tumor cells, after *Heinz* and *Walsh* [29]. a_f and a_c: extracellular and intracellular transport substrate; x active carrier, y inactive carrier ax carrier-substrate complex; ~ P and —P substrate and product of an exergonic reaction coupled with the transport. For explanations, see text.

The amino acid a combines temporarily with its own specific carrier x to form ax (formally comparable to an enzyme-substrate complex), which passes through the membrane. On the inside of the membrane ax dissociates into a_c + x. It is assumed that the binding and the dissociation of a are fast in relation to the translocation of ax. Exchange diffusion involves the reactions 1–3, which must be reversible. The accumulation inside the cell results from the fact that after the dissociation of ax, x is inactivated by conversion into y, as a result of which the affinity for a is completely or at least partly lost. After diffusion to the outside of the membrane, y is reactivated by conversion back into x by the energy-dependent reaction 5. According to kinetic findings, the diffusion of y or reaction 5 is rate-determining.

This model satisfies all the requirements apparent from investigations on the transport of amino acids in EMAT cells, and appears to be applicable to some microbial systems [33], though not unrestrictedly so. Thus some of the amino acid transport systems studied by us in *Streptomyces hydrogenans* lack the exchange diffusion component [34].

The model originally proposed by *Kepes* [35] for β-galactoside transport in *E. coli* and later extended by *Koch* [36, 37] (permease model) is also based on a carrier. Unlike the carrier model described above and the almost identical "permease model" of *Cohen* and *Monod* [5], *Kepes*' model involves two catalytic components, *i.e.* a specific permease (P) and a less specific transporter (T) (Fig. 2). P is firmly fixed to the outside of the membrane and catalyzes the binding of the substrate (G) to the transporter. The complex GT passes through the membrane and dissociates on the inside into T and G. The actual translocation is again reversible. The active transport requires the participation of ATP in the synthesis of the active transporter T ~ R.

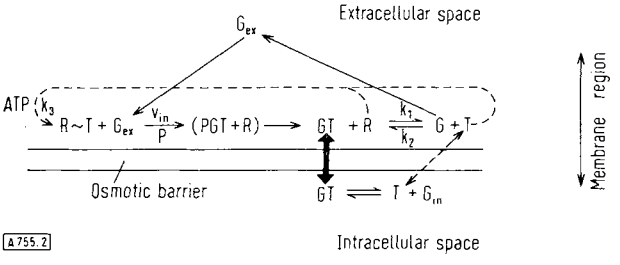


Fig. 2. Model of the β-galactoside transport in *E. coli* (permease model) after *Kepes* [35]. P = permease, T = transporter, G = substrate, R ~ T = activated transporter. For explanations, see text.

Observations on *E. coli* [36] and genetic studies on the transport of sugars in *Staphylococcus aureus* [38] have provided indications of a two-component system of this type with a multifunctional carrier. However, this also seems to be limited in its applicability. Thus the exchange diffusion of amino acids in many microorganisms is strictly specific; this means that either a specific transporter must be involved as well as the permease, or a second permease must be present on the inside of the membrane [*].

3. Enzymes as Components of Transport Systems

It is not clear at present how the active transport of amino acids is connected with the energy metabolism ("chemo-osmotic coupling"), though direct links have

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[*] For a discussion see [39].

[39] *W. Wilbrandt*, see [9], p. 112.

been found in recent years between several enzyme systems that catalyze the energy-transferring reactions and the active transport of solutes. One of these systems, the membrane ATPase discovered by *Skou* [2,40], is a component of the transport system for K^+ and Na^+ in animal cells. Its reaction sequence includes a phosphate transfer from ATP to a membrane protein and subsequent dephosphorylation of the latter. The first step requires Na^+, and the second K^+. The enzyme can be inhibited by strophanthin (for review, see [12, 16–18, 40]). ATPases have also been detected in bacterial membranes; however, they differ considerably from enzyme preparations of animal origin in their cation dependence and their sensitivity to strophanthin [41–52]. It is not yet certain how far ATPases are directly (*i.e.* independently of a symporter mechanism, see Section 4) involved in amino acid transport.

Kundig et al. [53] isolated from *E. coli* a phosphotransferase system that is involved in the active transport of sugars, and which consists of two enzymes (I and II) and low molecular weight, heat-stable protein, HPr. The membrane-bound enzyme II is decisive for the substrate specificity of the reaction. Phosphoenol pyruvate acts as the energy donor:

$$\text{Phosphoenol pyruvate} + \text{HPr} \underset{\text{I}}{\overset{Mg^{2+}}{\rightleftharpoons}} \text{pyruvate} + \text{phospho-HPr}$$

$$\text{Phospho-HPr} + \text{sugar} \xrightarrow[\text{II}]{Mg^{2+}} \text{sugar 6-phosphate} + \text{HPr}$$

$$\text{Phosphoenol pyruvate} + \text{sugar} \xrightarrow[\text{I}+\text{II}]{Mg^{2+}+\text{HPr}} \text{sugar 6-phosphate} + \text{pyruvate}$$

Considerable evidence has recently been adduced to show that this energy transfer system is an integral part of a series of sugar transporting systems in various microorganisms [54–60]. In contrast with earlier views, the substrate is modified by covalent bonds during transport in these cases.

Van Steveninck [61,62] has described a system in yeast that also phosphorylates the transport substrate, and which is a constituent of an energy-dependent sugar "permease". The energy donor in this system is polyphosphate.

The models described appear to be restricted to the transport of cations or sugars. There is no evidence of the participation of comparable reactions in the active transport of amino acids; in particular there is no evidence that amino acids even temporarily enter into covalent bonds during translocation.

4. Ion Dependence of Amino Acid Transport

Interesting relationships between amino acid transport and monovalent cations have been found in particular in animal cells. The absorption of amino acids in various types of cells can be influenced by the ionic medium in the extracellular space. The transport of amino acids in animal cells (EMAT cells, erythrocytes, mucosa cells, pancreas cells, *etc.*), like the transport of sugars in many tissues, depends on the extracellular Na^+ concentration [9,63–68]. The maximum accumulation of glycine in EMAT cells requires a Na^+ concentration of about 130 mmole/l.

Many kinetic and electrophysiological studies have been carried out in attempts to explain the influence of Na^+ on the transport of amino acids and sugars (for literature review and discussions, see [11,12,15,16,18,19]). According to the hypothesis most often advanced nowadays [67,68], the amino acid (or sugar) influx is assumed to be coupled with the Na^+ influx. The two transport substrates use a common carrier, and pass through the membrane in a ternary complex ("symporter" in *Mitchell*'s nomenclature [12]). Inside the cell, the Na^+ and the amino acid (or sugar) dissociate from the carrier molecule. The Na^+ that has penetrated is carried out of the cell by the Na^+ pump ("membrane ATPase"), so that if the pump capacity is sufficient, the intracellular Na^+ concentration is low in relation to the extracellular concentration. Thus a gradient for Na^+ is maintained across the cell membrane from outside to inside, and this is the driving force for the simultaneous influx of Na^+ and amino acid. The accumulation of the amino acid is consequently a function of the Na^+ gradient.

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Owing to the high physiological outside concentration of Na^+, the Michaelis constant K_m for the amino acid is reduced; inside the cell, at a low Na^+ concentration, the high K^+ concentration built up by the inward-directed K^+ pump increases K_m, so that the carrier loses part of its affinity for the amino acid. Thus a further driving force for the inward flow of the amino acid is provided by the asymmetric distribution of K^+.

According to this hypothesis, the Na^+-dependent transport of amino acids in the cells in question is not true active "primary transport", but must be regarded as facilitated diffusion. Owing to its dependence on the active transport of K^+ and Na^+, it can be inhibited by all inhibitors of the cation pump, such as strophanthin.

A similar Na^+-dependence was found by *Kleber* and *Aurich*[69] for the active transport of carnitine in *Pseudomonas aeruginosa;* K^+ and Mg^{2+} also have activating effects. It was surprising to find that g-strophanthin inhibits carnitine transport. On the basis of these findings, the authors assume that the transport of carnitine involves a strophanthin-sensitive membrane ATPase that can be stimulated by K^+ or Na^+. A symporter mechanism may also occur here.

Some halophilic microorganisms also require sodium ions for their amino acid transport[70–73]; unlike in the cases described above, however, they act only in combination with chloride. High salt concentrations are also required to maintain the extremely labile structure of these organisms and to activate some enzymatic reactions. It is therefore not very likely that the dependence of the amino acid uptake on NaCl can be explained in this case too by a symporter hypothesis.

However, monovalent cations can also influence the active transport of amino acids in another way. *Gross*[74] found that the active glutamate transport in *Streptomyces hydrogenans* is significantly activated by K^+ and Rb^+. The interpretation of the findings was made difficult by the fact that enzymatic reactions are also activated by these ions. Since, however, the intracellular K^+ concentration increases with the intracellular glutamate concentration, it may be assumed that K^+ enters the cell with the anionic glutamate. These findings confirm earlier studies by *Gale*[4], *Davies et al.*[75], and *Eddy* and *Indge*[76], according to which the absorption of glutamate in many microorganisms is associated with a gain in intracellular K^+.

On the other hand, the absorption of neutral amino acids by *Streptomyces hydrogenans* is independent of monovalent cations, provided that their concentration does not exceed about 5×10^{-2} mole/l[77,78]. Higher concentrations inhibit the amino acid transport. The inhibition is reversible, nonspecific, and competitive, and is not due to an osmotic effect. Monovalent cations in high concentrations probably prevent the bonding of the neutral amino acids to the transport system by occupying the anionic bonding sites on the carrier molecule in competition with the NH_3^+ groups of the amino acids[78].

Christensen and *Handlogton*[79] found that the transport of basic amino acids in EMAT cells is inhibited by neutral amino acids in combination with sodium ions. The results are interpreted as indicating that neutral amino acids can occupy the bonding site for basic amino acids on the carrier molecule and inhibit their transport if an accompanying cation such as Na^+ occupies the binding site for the distal cationic group of the basic amino acid.

5. Regulation of Amino Acid Transport

The regulation of the active transport of amino acids is of special physiological importance. It is evidently the same as or very similar to the control of enzymatic processes. It is necessary to distinguish between two independent control cycles, one of which appears to act *via* the change in the *concentration*, and the other *via* the change in the *activation state*, of the transport system. The first control cycle acts on the genetic level. A transport substrate can specifically induce the *de novo* synthesis of the transport system, or repress it in case of an excessive supply in the nutrient medium. Adjustments of this nature require a certain time lag. The second control cycle acts instantaneously, and can be interpreted as a sort of feedback, in which the transported substrate or one of its metabolic products inside the cell inhibits or stimulates the active transport of further molecules. Examples of all four possibilities have been found, though almost exclusively in microorganisms so far.

5.1. Induction and Repression

Many genetically controlled microbial transport systems have been described in recent years. These include, above all, systems for the absorption of the many metabolically utilizable carbohydrates and other substances involved in catabolism. The ability of bacterial cells to induce absorption systems for such a wide variety of physiological energy donors is undoubtedly associated with a selection advantage. Thus only the transport system needed by the cell at the moment in question is synthesized. The capacity of a single system is sufficient to satisfy all the carbohydrate requirements of the cell[80].

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On the other hand, only a few inducible transport systems for amino acids are known at present. This was not surprising, since the inducibility of the amino acid transport would not necessarily mean a selection advantage [80]. It must be remembered that the cells are generally capable of satisfying their requirements of the twenty or so amino acids, according to the medium, either by absorption from the nutrient medium or by synthesis for themselves. Biosynthesis, which requires more energy, is known to be provided in some synthesis sequences with a feedback control, the regulation circuit of which works most effectively if the amino acids present in the outer solution are very rapidly absorbed into the interior of the cell, where they can exercise their control function as required. However, this is possible only if the transport systems involved are permanently present in their maximum concentration, irrespective of the external concentration of their substrate.

Some cell species, on the other hand, appear to have inducible capacity reserves available, and these can be advantageous if the culture medium contains high concentrations of only one or just a few amino acids. The cell is then enabled to satisfy its nitrogen requirements wholly or partly from the exogenous amino acid nitrogen.

The first inducible uptake system for amino acids was discovered by *Boezi* and *DeMoss* [81] in the investigation of the absorption of tryptophan by a tryptophan-auxotrophic mutant, *E. coli* T_3A. Another inducible tryptophan transport system observed in *Ps. acidovorans* has been described by *Rosenfeld* and *Feigelson* [82]. Both transport systems are energy-dependent; their specificity is limited to tryptophan and structurally related derivatives. Maximum induction of the *E. coli* system requires 500 μg of tryptophan/ml of culture medium, and increases the transport by a factor of ten; even "uninduced" cells have a measurable transport capacity.

In *Ps. acidovorans*, the tryptophan transport is induced by 5 mmole/l of L-tryptophan in an inorganic medium containing asparagine; maximum induction requires incubation for about six hours. Two tryptophan-degrading enzymes are induced simultaneously with the transport, though not strictly coordinated with it. The key position in the induction appears to be occupied, not by the transport substance, tryptophan itself, but by its degradation product kynurenine; this product can also induce the tryptophan transport, as well as its own transport system. Induction by tryptophan presumably does not occur directly, but only after endogenous conversion into kynurenine. There should thus be a close relationship between metabolic activity and transport induction.

A relationship of this nature is also found in the induction of citrulline transport in *Streptococcus faecalis* [83]. This microorganism converts arginine into citrulline, and the latter into ornithine. Cells grown in inorganic medium have a relatively poor permeability for citrulline; on addition of arginine to the culture medium, the permeability to citrulline is increased by a factor of four. This increase in transport is selective; the concentration of the citrullinase is not affected. Maximum induction requires a relatively long incubation, and is complete after 12–16 hours. The inducer is presumably again not the added amino acid, arginine, but the degradation product citrulline accumulated in the cell.

An inducible active transport system for L-glutamate in mycobacteria has been described by *Lyon et al.* [84]. The inducer is the transport substrate, L-glutamate. Maximum induction requires the relatively high inducer concentration of 2×10^{-2} mole/l. A basic transport activity is again present in "uninduced" cells, and induction increases this transport by a factor of about three.

It was also found for the inducible oxidative degradation of L-hydroxyproline to α-ketoglutarate in *Ps. putida* [85] that hydroxyproline together with the degrading enzymes again induces its transport system. It is not yet known to what extent the induction of the enzymes and of the "permease" is coordinated.

The microorganism used by us, *Streptomyces hydrogenans*, has an inducible transport system for neutral amino acids, as was first reported by *Hübener* [86]. Further investigations [87,88] were performed on the kinetic characterization of the induced system. The induction was carried out in an inorganic medium with succinate and glucose as energy sources and NH_4Cl as a nitrogen donor. Despite the absence of amino acids, the cells develop a sometimes considerable transport capacity for neutral amino acids in this medium. The addition of some neutral amino acids to the culture medium increases the maximum transport by a factor of ten. Glycine and alanine are good inducers, as is also α-aminoisobutyric acid (AIB), an amino acid that is similar in structure to glycine and alanine, but which is not metabolizable. This observation is important to the interpretation of the experiments, since it shows that the transport substrate itself, and not one of its metabolic products, is the inducer.

Maximum induction requires an inducer concentration of about 10^{-1} mole/l. This value seems very high at first sight, but becomes understandable when compared with the intracellular alanine and glycine concentration. Next to glutamate, alanine is the principal constituent of the amino acid pool in this organism; its concentration in the cell fluid is about 10 mmole/l, and that of glycine is about half of this. It is obvious

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that induction can occur only at inducer concentrations above this value.

The physiological function of a regulation of this nature was discussed in Section 5. Let us consider here whether the basic transport capacity in uninduced cells might not even be the product of an incomplete induction that is permanently stimulated by the intracellular amino acids. This assumption is supported by the observation that the basic transport activity appears to depend on the quality of the growth and varies widely and that the Michaelis constants of the transport systems for α-aminobutyric acid in induced and uninduced cells are indistinguishable (see below).

The induction is inhibited by chloramphenicol, actinomycin C, proflavine, and mitomycin, thus showing that intact DNA as well as RNA and protein synthesis are necessary. Addition of non-inducing amino acids such as asparagine has a strong promoting effect [88], but the function of these amino acids is not yet clear.

According to kinetic studies, induction increases the maximum rate of the influx without affecting the affinity between the transport system and the substrate. Besides the influx, the enrichment in the steady state and the efflux are also increased. The kinetic parameters of an experiment of this type are summarized in Table 1. Since both undirectional fluxes, *i.e.* influx and efflux, can be seen to increase, it might be assumed at first that the increase in influx is due to an increase in the mobility of the carrier in the membrane. However, the dependence on protein synthesis would be difficult to understand if this were so.

Table 1. Kinetic parameters of the transport of α-aminoisobutyric acid of induced and "uninduced" cells of *Streptomyces hydrogenans* (from [88]). The "uninduced" cells were cultured for 13 h in inorganic medium, and the induced cells in inorganic medium containing 2×10^{-1} mole/l of DL-alanine.

Parameter	"uninduced"	induced
Influx constant (k_{in}) (ml × g^{-1} × min^{-1})	10.20	37.82
Efflux constant (k_{ex}) (ml × g^{-1} × min^{-1})	0.136	0.244
Influx (v_{in}) (μmole × g^{-1} × min^{-1})	25.2	81.0
Distribution ratio (1 min) (R_a 1 min) [a]	28.0	90.0
Distribution ratio (steady state) ($R_{a\infty}$)	300.0	620.0
"Michaelis constant" (mole/l)	2.73×10^{-5}	2.73×10^{-5}

[a] The distribution ratio (R_a) is the ratio of the intracellular amino acid concentration (a_c) to the extracellular (a_f): $R_a = a_c/a_f$. The rate of absorption du/dt of AIB can be described by the following equation: $du/dt = \Phi^{in}_{max}\, a_f/(a_f + K_m) - k_{ex} \times a_c$, where Φ^{in}_{max} is the maximum influx. In the steady state, $R_a = k_{in}/k_{ex}$.

The observations can be more readily explained if it is assumed that the induced cells have a greater number of active carrier molecules available in the membrane. The increase in both flow constants, k_{in} and k_{ex}, means that the induced protein must be accessible to the substrate from both sides of the membrane.

Attempts to interpret the results on the basis of the permease model in Fig. 2 leads to difficulties when one regards the "permease" as the only inducible component of the entire system, since it is arranged asymmetrically in the membrane and with respect to the transporter. On the other hand, the findings are compatible with the carrier model in Fig. 1, provided that the carrier is assumed to be inducible. Difficulty arises, however, in the interpretation of the kinetic data, since k_{in} increases more than k_{ex}. No plausible mechanistic explanation has yet been advanced.

An opposing regulation of the transport of neutral amino acids was observed by *Inui* and *Akedo* [89] in *E. coli* K10, and was interpreted as repression. An excess of a single amino acid, *e.g.* leucine, in the nutrient solution leads to a decrease in the absorption of the same and structurally related amino acids. No inhibition develops in resting cells on incubation in nitrogen-free solution or in the presence of chloramphenicol; mitomycin C, on the other hand, has no effect. The inhibition is specific for amino acid transport; α-methylglycoside transport and the Na^+ and K^+ distribution remain constant. Kinetic studies have shown that the influx in particular is affected. The distribution of the amino acid between the intracellular and the extracellular spaces in the steady state is reduced to 1/10 of the normal value, the efflux has increased by a factor of only three. It is therefore unlikely that an efflux-specific transport system has been induced during preincubation.

5.2. Feedback Control

A control of the active transport of amino acids that is independent of the genetic regulation, and which acts on the level of the transport system like a feedback control, was first described a few years ago. As we found in the case of *Streptomyces hydrogenans*, all the amino acid transporting systems are subject to control by two opposing regulating systems, one of which inhibits the active absorption of amino acids, while the other promotes it [33,90–93]. Both effects can be demonstrated for the absorption of ^{14}C-labeled α-aminoisobutyric acid (AIB) by cells that have received different pretreatments. If the cells are preloaded with unlabeled AIB for one hour, the absorption decreases, whereas it increases after preloading for one hour with L-glutamate. These preincubations influence both the initial rate of absorption and the distribution of the test amino acid in the steady state.

5.2.1. Transport Inhibition

The inhibition of the AIB influx is a function of the intracellular concentration of the inhibitor AIB. The inhibition increases with increasing internal AIB con-

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[90] *E. Heinz*, *K. Ring*, and *W. Gross*, Federat. Proc. *26*, 393 (1967).

[91] *K. Ring*, *W. Gross*, and *E. Heinz*, Ber. Bunsenges. physik. Chem. *71*, 893 (1967).

[92] *K. Ring*, *W. Gross*, and *E. Heinz*, Arch. Biochem. Biophysics *137*, 243 (1970).

[93] *W. Gross*, *K. Ring*, and *E. Heinz*, Arch. Biochem. Biophysics *137*, 253 (1970).

centration until a maximum value is reached; the maximum inhibition by loading with AIB varies between 40 and 70%, depending on the cell material. However, only the inward flux is decreased when the AIB concentration on the other side of the membrane ("transconcentration") is increased; the efflux of labeled AIB increases with increasing transconcentration. Whereas the last observation can be readily explained by the carrier model in the sense of the preloading [27–30] or counterflow effect [6], additional assumptions are necessary to explain the inhibition of the influx (see below).

The influx inhibition ("transinhibition") is characterized kinetically as non-competitive, since the apparent Michaelis constant remains unchanged while the maximum rate of influx decreases. Other kinetic findings show that preloading influences only the influx, whereas the efflux remains constant. It may therefore be concluded that the transinhibitor does not affect the mobility of the carrier-substrate complex in the membrane.

It has also been shown that the transinhibition begins immediately and with maximum effect when the inhibitor reaches the inside of the cell. The inhibition is reversible and, after the inhibitor has been washed out, can be repeated by renewed preloading. The preloaded amino acid thus reduces the activity of its transport system from the inside of the cell.

The inhibition of transport by loading with AIB is not very specific; all the amino acid transport systems examined (for glutamate and aspartate, methionine, phenylalanine, leucine, proline, lysine, arginine, tryptophan, histidine) are partly inhibited. However, the inhibition appears to be confined to the transport of amino acids; neither the transport of potassium nor that of sorbose is affected by loading with AIB.

AIB was used as the inhibitor in all the experiments described so far, since this amino acid is not metabolized by *Streptomyces hydrogenans*, even on prolonged incubation. Other amino acids that are normal components of the cell amino acid pool also act as transport inhibitors. All the neutral amino acids studied so far, as well as arginine and lysine, can inhibit the active transport of amino acids from inside the cell (Table 2); other amino acids, such as aspartate or glutamate, evidently have no effect.

Table 2. Transinhibition of the [^{14}C]-AIB influx by intracellular amino acids. Measurement of the AIB absorption after preloading of the cells at −2 °C (20 min) with the amino acids indicated (20 mmole/l) followed by centrifugation and resuspension in a buffer containing no amino acid.

Preloaded with	Inhibition (%)
–	0
AIB	55.1
Cycloleucine [a]	87.3
Glycine	19.3
L-Alanine	56
L-Valine	50
L-Leucine	48.5
L-Isoleucine	46.7
L-Methionine	18
L-Lysine	17
L-Arginine	38
L-Aspartate	3

[a] 1-Aminocyclopentane-1-carboxylic acid.

The amino acids listed in Table 2 were introduced into the cells by cold shock treatment. The permeability of *Streptomyces hydrogenans* is greatly increased at temperatures around 0 °C [94,95], so that small molecules such as amino acids can pass rapidly through the membrane (see also [96–99]). Since the change in permeability is reversible, it can be used to introduce molecules rapidly into the inside of the cell or to remove substances from inside the cell. In this way, a metabolic attack on the amino acid during transport can be overcome. This process is thus comparable in its effect with the reversed hemolysis of erythrocytes [100, 101]. In connection with the transinhibition, it offered the only possibility of testing the inhibitor properties of rapidly metabolizable amino acids. Another advantage was that the "shocked-in" amino acids can always be brought to the same concentration, and a quantitative comparison of their inhibitor properties is therefore possible. However, this is so only if the amino acids are completely equilibrated between the intracellular and the extracellular spaces during the cold shock. This method has also been used to shock the normal culture medium for *Str. hydrogenans*, a nutrient broth containing casein hydrolyzate and yeast extract, into the cells and to test their action on the transport of AIB. An inhibition of up to 40% was observed.

A possible interpretation of the observations is that certain amino acids from the cell pool control the amino acid transport as effectors after the fashion of feedback regulation. It may be assumed that the inhibitor controls a limiting reaction in the overall transport process, which is inserted into the energy coupling between the transport and energy metabolism [92]. On the basis of the carrier model in Fig. 1, this would be step 5 of the cycle. It must be assumed that this reaction is common to all transport systems for amino acids.

Alanine, which is present inside the cell in an adequate concentration and which has very good inhibitor properties, could act as a physiological key substance in this control cycle.

A similar mode of amino acid transport appears to operate in *Bac. subtilis* [101a].

The observations described here are in agreement with results obtained by *Wiley* and *Matchett* [102], according

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[96] *J. Farrell* and *A. H. Rose* in *A. H. Rose*: Thermobiology. Academic Press, New York 1967, p. 147.

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to which the active transport of tryptophan in *N. crassa* is regulated by the intracellular tryptophan concentration. However, the transport inhibition is more specific than in *Strept. hydrogenans*, since it is limited to the amino acids transported by the tryptophan system. Independently of us, *Wiley* and *Matchett* have also reached the hypothesis that inhibition is the result of feedback control by the transport substrate that has accumulated in the cell.

Similar instances of feedback regulation have been described by *Benko et al.* [103,104]. In these cases, however, the inhibitor is not the transport substrate but one of its metabolic products. The active transport of methionine in *Penicillium* and *Aspergillus spec.* is inhibited by one of its sulfur-containing degradation products [103]. In the state of inhibition, the apparent Michaelis constant for methionine is increased by about two orders of magnitude; V_{max}, on the other hand, is only slightly changed. Evidence has also been produced [104] to show that a second, non-specific amino acid permease is also subject to feedback regulation; the effector appears to be NH_4^+.

Specific transport inhibition by degradation products of other metabolites is involved in the absorption of sulfate in *E. coli* [105], *Penicillium chrysogenum* [106,107], and *Salm. typhimurium* [108], the absorption of glucose in muscle cells [109] and *E. coli* [110,111] and of monosaccharides in baker's yeast [112], and the nucleotide transport in *Bac. subtilis* [113].

5.2.2. Stimulation of Transport

The AIB transport in *Streptomyces hydrogenans* cells is increased by preincubation for one hour with L-glutamate ("transstimulation" [93]). Unlike transinhibition, transstimulation cannot be detected immediately after the penetration of the effector into the cell, but only after about 15–20 minutes. This is seen in the time-absorption curve for glutamate in *Strept. hydrogenans* from the fact that the net absorption increases again at this instant, *i.e.* the curve becomes steeper and finally tends toward a new steady state [114]. Like transinhibition, transstimulation is non-specific with respect to the transport systems for amino acids, but is confined to these. Potential stimulators are metabolizable amino acids such as L-glutamate, L-lysine, L-proline, and L-aspartate.

Kinetic studies show that the transstimulation, like inhibition, does not affect the mobility of the carrier-substrate complex in the membrane. The affinity of the transport system for the substrate was also unaffected. A preloading or counterflow effect was also ruled out as a possible cause of the increased flux.

The lag phase indicates that the stimulation is preceded by a metabolic change in the amino acid. In view of the uniformity of action of such different amino acids as glutamate, leucine, or lysine, it was to be assumed that the stimulator is one of their common metabolites. All attempts to identify it have been unsuccessful. The simplest explanation at present is provided by the hypothesis that the stimulation is effected by the aminoacyl-t-RNA derivative, and is thus closely related to protein synthesis. This assumption is supported by observations that RNA appears to be essential to transstimulation. Prolonged preincubation of the cells with inhibitors of the RNA synthesis prevents transstimulation; this action is not observed with inhibitors of DNA or protein synthesis.

Both feedback systems appear to ensure rapid adjustment of the amino acid transport to the different requirements of the cells during growth.

Another means by which the cell could adjust its amino acid transport to meet the requirements for an optimum supply was recently described for *N. crassa* [115]. A relatively specific transport system prevails in young, rapidly growing cells; in older cultures, on the other hand, the absorption is effected by a second system having very little specificity. Its physiological function appears to be the supply of residues of exogenous amino acids to the cell metabolism.

6. Relationship Between Amino Acid Transport and Protein Synthesis

It has been found in recent years that amino acid transport systems both of animal and of microbiological origin exhibit a striking sensitivity to inhibitors of protein and RNA synthesis [82,102,104,116–121]. However, the inhibitors do not act immediately, but cause a gradual loss of transport activity. The most spectacular example of this is the transport of tryptophan in *Neurospora crassa*; 50% of the transport activity is lost

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[113] *R. D. Berlin* and *E. R. Stadtman*, J. biol. Chemistry *241*, 2679 (1966).

[114] *W. Gross, K. Ring*, and *E. Heinz*, unpublished.

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[119] *W. Gross* and *K. Ring*, FEBS-Letters *4*, 319 (1969).

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[121] *C. Yamada, A. J. Clark*, and *M. E. Swendseid*, Science (Washington) *158*, 129 (1967).

only 15 min after the addition of cycloheximide (4-[2-(3,5-dimethyl-2-oxocyclohexyl)-2-hydroxyethyl]-piperidine-2,6-dione), whereas the tryptophan-degrading enzyme kynureninase is unaffected [102]. The protein synthesis must evidently remain intact to maintain the transport function.

Two hypotheses have so far been proposed to explain the inhibition. *Elsas* and *Rosenberg* [116] and *Holden* and *Utech* [118] attributed the susceptibility of the transport system to inhibition to a particularly high turnover rate of a transport protein. An equilibrium exists between degradation and resynthesis in uninhibited cells. This equilibrium is disturbed by the addition of an inhibitor of the RNA or protein synthesis, so that the relatively fast degradation can no longer be compensated by resynthesis. *Grenson et al.* [117], on the other hand, believe that the transport inhibition is indirect, and is due to the increase in the intracellular amino acid pool as a result of the uncompensated protein degradation; the inhibition is thus interpreted mainly as feedback inhibition.

Since the amino acid transport in *Streptomyces hydrogenans* can also be inhibited by chloramphenicol, actinomycin, and related inhibitors, while it is also regulated by feedback control, we have investigated the applicability of the second hypothesis to this system [119]. Use was made of the fact that the cell amino acid pool can be removed very rapidly by cold shock treatment. When the cells are washed out by this method, the transport inhibition is reduced by only 10–20%, though the feedback inhibition due to preloading with AIB is completely reversible under these conditions [92]. It has also been found that the transport in chloramphenicol-inhibited cells can be inhibited by loading with AIB to almost the same degree as in chloramphenicol-free cells. Since the feedback inhibition in *Streptomyces hydrogenans* depends on the intracellular concentration of the transinhibitor and reaches a maximum at a concentration of only about 30 mmole/l, AIB together with the considerable quantities of amino acids liberated by the action of chloramphenicol cannot cause any additional inhibition. This observation is thus incompatible with the theory proposed by *Grenson et al.* [117]. Finally, kinetic measurements have shown that the influx and efflux of AIB both decrease by the same factor under the influence of chloramphenicol, an observation that is compatible only with the first hypothesis. We therefore assume that a protein involved in the carrier transport in *Streptomyces hydrogenans* has a much higher turnover than the other proteins.

The physiological significance of this special case is not yet clear. It is possible that there is again a relationship with the control of the transport.

7. Isolation of Transport Proteins

Many attempts have been made in recent years to label and isolate membrane components that are involved in the translocation of small particles such as amino acids, sugars, or ions, through the cell membrane. Owing to the important advances and the general importance to transport research the principal efforts will be described in some detail, though they are only partly concerned with the transport systems for amino acids. We shall not consider the special case of the phosphotransferase system (Section 3) [53].

It is still assumed that the transport substrate in the active transport of amino acids passes unchanged through the membrane and only the transporting agent is the substrate of an enzymatic reaction. The translocation of the substrate is thus not directly affected by the energy-dependent reaction. These assumptions are in agreement with the investigations on facilitated diffusion and exchange diffusion. However, they make clear the difficulties opposing the isolation of the translocator. All that can be said is that it must be a protein that can reversibly bind an amino acid. No measurable enzymatic activities are to be expected.

With few exceptions, the successful isolation attempts were carried out on microorganisms. The first transport protein, a component of the glucose transport system, was obtained by *Rogers* [122] from *E. coli* A by extraction with warm buffer at pH 7.3 under conditions in which the transport of glucose into these cells is known to be unstable. The transport protein has not yet been characterized in detail.

The preparative methods subsequently used were based on two requirements:

1. Specific labeling of the transport proteins with ^{14}C or ^{3}H; in this case the transport system must be inducible.

2. Solubilization of the proteins by osmotic shock in the cold; this is based on labile bonding of the proteins to the cell surface.

With the aid of the first method, *Fox* and *Kennedy* [123] isolated and purified an "M protein" (membrane protein) that is a component of the active transport system for β-galactosides in *E. coli*. This system is inducible, is coded by the y gene of the lactose operon, and together with the other two genes for β-galactosidase and β-galactoside transacetylase, is controlled by the regulator gene i. The authors used cells poisoned with azide, which can no longer accumulate the transport substrate; however, solute flux by facilitated diffusion is possible.

It was known from earlier observations that the transport of β-galactosides involves thiol groups, which can be protected against alkylation by bonding of a transport substrate, such as thiodigalactoside (TDG). With substrate protection of this nature, all the accessible SH groups that were not involved in the transport of galactoside were first blocked by reaction with *N*-ethylmaleimide (NEM) in induced and uninduced cells. In the second phase of the experiment, TDG was removed and the now liberated transport-specific SH groups were alkylated with radioactively labeled NEM, the induced cells receiving [^{14}C]-NEM and the uninduced controls [^{3}H]-NEM. After the reaction, equal parts of both lots were mixed and the cells were disrupted and fractionated.

Under these conditions all the accessible reactive proteins are doubly labeled, since induced and uninduced cells synthesize the same proteins, with the exception of those controlled by the lactose operon. These are practically absent from uninduced cells, but present in high concentrations in induced cells. On fractionation of the protein and investigation of its ^{3}H and ^{14}C fractions, an inducible protein should be recognizable by an increased $^{14}C/^{3}H$ ratio, provided that it is attacked by NEM [*].

[122] *D. Rogers*, J. Bacteriol. *88*, 279 (1964).

[123] *C. F. Fox* and *E. P. Kennedy*, Proc. nat. Acad. Sci. USA *54*, 891 (1965).

[*] β-Galactosidase and transacetylase are not labeled by NEM.

This technique allowed the discovery and isolation of a protein fraction that comes from the plasma membrane and has no enzymatic activity. This M protein is fixed in the cell membrane by nonionic bonds, and is readily dissolved out by Triton X-100, a nonionic detergent. Estimation of the content of M protein in the cells indicated that *E. coli* ML 308 contains about 9000 reactive functional units of the M protein, if one SH group of the M protein is assumed to be protected by one bound molecule of TDG [124]. Investigations on numerous mutants have confirmed [124] that the M protein is the product of the y gene from the Lac operon, and is thus coded by the same gene as the previously purely functionally and genetically characterized "β-galactoside permease".

However, the function of the M protein within the transport system is not yet known; according to *Kepes*' permease model, it may be the "permease" or the "transporter", *i.e.* the recognizing and selecting or the transporting agent. It is certainly not involved in the energy coupling between metabolism and transport, since the "active" component of the transport was blocked by azide.

The M protein has now been purified to an electrophoretically homogeneous state, and its molecular weight has been found to be 31000 [125].

Despite the great importance of these investigations to permeability research, it must not be overlooked that the protein molecules are irreversibly inactivated by labeling with NEM. *Kolber* and *Stein* [126] were able to overcome this disadvantage by the use of a different labeling technique for the isolation of the same protein from *E. coli*. These authors also used a double labeling technique. After cultivation of induced cells in the presence of [^{14}C]-phenylalanine and of uninduced cells in the presence of [^{3}H]-phenylalanine, the two cultures were mixed, the cells were disrupted, and a membrane fraction and a souble fraction were obtained from the digest. After chromatographic separation, ^{14}C and ^{3}H contents of the eluted proteins were determined. As expected, a total of three proteins having high ^{14}C/^{3}H ratios were isolated; two of these were identified as β-galactosidase and transacetylase. The third protein fraction had no measurable enzyme activity. Corresponding experiments with mutants without permease or galactosidase showed that the third fraction may be regarded as a product of the y gene, and so contains a transport protein. Though this protein should be identical with the M protein, it was found in the soluble supernatant instead of in the membrane fraction on centrifugation. This important and unexpected discrepancy has not yet been explained.

The same double labeling technique was used by *Haskovec* and *Kotyk* [127] to isolate the carrier of the galactose transport from baker's yeast. This transport system is also inducible; it differs fundamentally from the systems discussed already in this section in that it can catalyze only facilitated diffusion. It is thus one of the simplest carrier systems of all, and should be particularly suitable for investigations of this nature.

An entirely different isolation technique is based on the observation by *Neu* and *Heppel* [128] that osmotic shock in the cold causes certain gram-negative bacteria to give up enzymes and proteins to the shock liquid, without losing their viability. These proteins appear to come from the cell surface. It therefore seemed reasonable to extend these investigations to transport proteins. It was found that, in many microorganisms, some transport systems are particularly sensitive to shock, whereas others are practically unaffected.

Kundig et al. [129] found by this method that *E. coli* W 2244 lost 50—85% of its transport capacity for certain sugars as a result of shock, and simultaneously lost 50—80% of the "heat-stable protein" HPr, which is a part of the phosphoenol pyruvate-dependent phosphotransferase system. However, the original transport capacity could be restored if the shocked cells were incubated with isolated and purified HPr.

At the same time, in *Pardee*'s laboratory, it was found that about 80% of a protein involved in the active transport of sulfate in *Salmonella typhimurium* can be brought into solution by osmotic shock [130]. Spheroplasts give up this sulfate-binding protein readily without shock treatment; this is an indication of its weak bonding and its localization on the cell surface [131]. The molecular weight of the highly purified protein is 34000; it contains no lipids, carbohydrates, or phosphorus. Unlike the M protein, it contains no thiol groups [133]. One sulfate ion is bound per molecule of protein (but no calcium [132]). Its bonding is very strong; the dissociation constant of the sulfate complex is 0.1×10^{-6}. The fixation of the sulfate depends on the ionic strength of the solution; the bonding is reversible and independent of ATP. No conversion of the bound sulfate into a derivative can be detected. The protein accordingly exhibits no enzyme activity, and is not identical with the HPr. In view of the many features shared by the protein isolated and the *in vivo* transport system, it can be concluded that it is a component of this system. The common features include binding specificities for various anions, the occurrence after derepression, and susceptibility to genetic regulation; both systems are also sensitive to shock, and both are lost by the same mutation [131]. The protein has recently been obtained in the crystalline state [132, 134].

Oxender et al. [135, 136] used the shock method to obtain and characterize a leucine-binding membrane component from *E. coli* K 12 after finding that the active transport of leucine and valine, which occurs *via* the same system, is also sensitive to shock. The active transport of proline and alanine, on the other hand, was found to be resistant to shock. The leucine-binding factor was detected in the shock liquid, classified as a protein, chromatographically purified, and crystallized. This preparation was used for further characterization.

The protein was found to be homogeneous in the ultracentrifuge, on polyacrylamide disk electrophoresis, and in *Ouchterlony*'s immune diffusion test. Its molecular weight is 24000 according to measurements in the ultracentrifuge, 36000 according to gel filtration, and 34000 according to amino acid analysis. The binding properties for amino acids and derivatives as found by equilibrium dialysis correspond to those of the *in vivo* transport system. Optimum binding occurs between pH = 4 and pH = 9; the ionic strength has practically no effect between 0.004 and 0.8 equiv/l. There is no evidence of the presence of metal ions. As was to be expected from the amino acid analysis, *N*-ethylmale-

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[135] *J. R. Piperno* and *D. L. Oxender*, J. biol. Chemistry *241*, 5732 (1966).

[136] *W. R. Penrose, G. E. Nichoalds, J. R. Piperno*, and *D. L. Oxender*, J. biol. Chemistry *243*, 5921 (1968).

imide (NEM) is not bound by the protein and does not affect the binding of leucine. Like the transport proteins discussed so far, this protein showed no enzyme activity. It is interesting to note that the binding of the substrate to the isolated protein is strongly inhibited by a specific antiserum, whereas the transport in intact cells is not. The protein is evidently not localized *directly* on the membrane surface, and it is therefore protected from the antibody in intact cells.

After cultivation of the cells in a medium having a high amino acid content, the protein is not detected in the shock liquid; the transport of leucine is repressed under these conditions. A direct correlation exists between the transport capacity for leucine after cultivation under various conditions and the concentration of the leucine-binding protein in the shock fluid. All these observations provide strong evidence that the isolated protein is an essential component of the leucine transport system in *E. coli*.

Almost identical evidence was reported at about the same time by *Anraku* [137–139], who isolated a leucine-binding protein as well as the galactose-binding protein from *E. coli* K 12. Unlike *Penrose et al.* [136], *Anraku* found two leucine-binding fractions after chromatography on DEAE cellulose; the smaller of these fractions has not, however, been further characterized. The chemical and physical properties of the leucine-binding proteins from the laboratories of *Oxender* and *Anraku* largely agree. The two proteins have very similar affinities for their substrates leucine and isoleucine and a high binding specificity. As was also found by *Anraku* [138], the binding of leucine is not appreciably inhibited by iodoacetic acid, NEM, or other agents such as Zn^{2+} or EDTA, though these are known to be strong inhibitors of the active transport of leucine. The leucine-binding proteins isolated thus do not appear to belong to the energy-transferring part of the active transport of leucine. According to the models, therefore, their functions must again be merely recognition and/or translocation.

The most important additional information obtained by *Anraku* is the observation that, after osmotic shock, the leucine transport can be regenerated if the purified leucine-binding protein and a second protein from the shock liquid, which has not yet been characterized, are added to the cells [139]. The same is true of the galactose transport. The "recovery" depends on the energy metabolism; it signifies a true increase in the active transport capacity. The binding capacity of the shocked cells for purified protein exhibits saturation behavior. Another shock-sensitive transport system for the active uptake of arginine was studied by *Wilson* and *Holden* [140, 141] in *E. coli*. Arginine is actively transported by a specific system and is very rapidly metabolized by several pathways inside the cell. Osmotic shock treatment upsets both the active transport of arginine and the degradation induced by the arginine decarboxylase. The proteins in the shock liquid were fractionated chromatographically; four of these could bind arginine to a considerable extent. The fractions I and III have the highest specific affinity for arginine, which is bound about 20 times as strongly as lysine. The dissociation constants of the two complexes are the same, and lie between 0.5×10^{-6} and 1×10^{-6}. Neither fraction exhibits enzymatic activity toward arginine.

As in *Aranku*'s experiments, the transport capacity of the cells can be (at least largely) restored after reduction by shock. The reconstitution is concentration dependent; fraction I appears to affect the initial absorption rate more, whereas fraction II affects the distribution in the steady state. The other arginine-binding fractions have no influence on the reconstitution of the transport. Moreover, the reconstitution by fractions I and II is specific for arginine, since neither the transport of leucine nor that of lysine is regenerated.

Though all the observations in this case again indicate that the proteins isolated are part of a transport system, their role within the system as a whole is not yet known. As in the other systems that can be regenerated, it is particularly interesting that a certain membrane function is lost by relatively mild physical treatment of the cells, but is easily restored, evidently with no need for extensive reorganization or new synthesis of the membrane.

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Development of and Problems in the Chemistry of Mercury-Nitrogen Compounds

By Dietrich Breitinger and Klaus Brodersen[*]

There have been few recent additions to the group of mercury-nitrogen compounds. Current developments in this field are mainly concerned with the elucidation of the structures of these compounds. The structures of coordination-polymeric Hg–N compounds may be considered from the point of view of their relationship with silicates. The bond parameters of the Hg–N grouping are compared with the parameters of bonds between mercury and elements adjacent to nitrogen in the periodic system.

1. Introduction

The mercury-nitrogen compounds, which have been known and obtained in large numbers for a long time, have recently been systematized; their structure and bonding have been elucidated in many cases, and are now better understood than before. The recent developments started with the X-ray investigation of the structure of "fusible white precipitate" $(NH_3)_2HgCl_2$ by *MacGillavry* and *Bijvoet*[1]. Working on a broader basis, *Lipscomb*[2,3] and *Rüdorff* and *Brodersen*[4] undertook the X-ray structure analysis of related compounds.

The positions of nitrogen atoms can be found only very inaccurately in the presence of mercury, owing to the great difference in the X-ray scattering powers of the two types of atoms. Additional structural information was therefore obtained by other physical methods, such as broad line NMR[5], IR[6], and Raman spectrometry[7].

Vibration spectrometry has been used in combination with high-resolution NMR spectrometry in the study of liquid or soluble Hg–N compounds[8].

The situation regarding X-ray studies on coordination-polymeric mercury-nitrogen compounds is presented in reviews by *Lipscomb*[9] and *Grdenić*[10], while *Brodersen*[11] has correlated the results of X-ray structure analyses with IR-spectrometric findings.

On the basis of all the known facts, a great deal of Hg–N compounds can be assigned to one of two groups:

1. Those containing formally uncharged, electronegatively substituted nitrogen having a coordination number or valence of 3.

2. Those containing formally positive, electropositively substituted nitrogen having a coordination number of 4.

Within both groups it is possible to distinguish species of low molecular weight and high polymers. On the basis of this classification, the principal features of the chemistry of mercury compounds containing nitrogen having a negative oxidation number will be discussed with the aid of some typical examples.

2. Compounds Containing Nitrogen Having a Coordination Number or Valence of 3

The group of compounds in which nitrogen has a coordination number of 3 (Hg always having the characteristic coordination number of 2, cf.[10]) includes species of low molecular weight and high polymers in which the electron density on the nitrogen is reduced by two electronegative ligands, which are often identical. Considered from another point of view, the H–N analogs of the Hg–N compounds of this group are more acidic than ammonia (reduced basicity and nucleophilicity of the N atom). The nitrogen atom is accordingly in or close to the sp^2-hybridized state, as has been shown for a number of examples.

2.1. Mercury Trifluoromethylamides and Trimethylsilylamides

The simplest compound of this type is mercury bis[bis(trifluoromethyl)amide] *(1)*, which is formed by addition of mercury(II) fluoride to pentafluoro-*N*-methylenemethylamine in an autoclave at 100 °C[12], and which

$$2\ F_3C{-}N{=}CF_2 + HgF_2 \rightarrow [(F_3C)_2N]_2Hg \quad (1)$$

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is also obtained on fluorination of cyanogen or cyanogen chloride with HgF_2 [13]. The physical properties (m.p. 17.5 °C, b.p. 127 °C) indicate a molecular structure, but no detailed structural investigations have been carried out as yet. It is to be expected that the N–Hg–N grouping is linear and that the bond angle at the nitrogen is increased by the interaction of the trifluoromethyl groups.

The reactive, readily hydrolyzable diamide *(I)* can be used as a reagent for the transfer of the bis(trifluoromethyl)amino group, as is shown by its reaction with halogens to form *N*-halogenobis(trifluoromethyl)-amines $(F_3C)_2NX$ and mercury halides [12,14]. The *N*-halogenoamines can be used in turn for the synthesis of asymmetric mercury(II) bis(trifluoromethyl)amides

$$(F_3C)_2NX + HgR_2 \xrightarrow{20\,^\circ C} (F_3C)_2NHgR + RX$$
$$X = Cl, Br; \quad R = CH_3, SCF_3$$

which are chemically very similar to the symmetrical parent compounds [14]. Closely related compounds that should be mentioned here are mercury bis[tris(trifluoromethyl)hydrazide] $[(F_3C)_2NN(CF_3)]_2Hg$ [15] and mercury bis(trifluoromethylpentafluorothioamide) $[F_5SN(CF_3)]_2Hg$ [16], which, like *(I)*, are obtainable by addition of HgF_2 to appropriate fluorinated azomethines, and which also have similar properties. No measurements from which structural parameters could be deduced have been carried out in any of these cases.

Whereas the decrease in the electron density on the nitrogen was due to purely inductive effects in the above examples, the mesomeric effect predominates in mercury bis[bis(trimethylsilyl)amide] [8], in which $(p \rightarrow d)\pi$ bond components operate between the nitrogen and the silicon. This compound, which can be easily prepared at room temperature in ether by the reaction

$$2\,[(H_3C)_3Si]_2NNa + HgBr_2 \rightarrow 2\,NaBr + \{[(H_3C)_3Si]_2N\}_2Hg$$

was investigated by ^{1}H-NMR and vibration spectroscopy [8]. The vibration spectra are readily explained by a molecular model of point group D_{2h} or D_{2d}, with a linear N–Hg–N grouping and trigonal-planar coordination at the nitrogen. Force constant calculations indicate Si–N–Si bond angles of between 130 and 140 °, and the force constant k(Hg–N) is found to be between 2.4 and 2.2 mdyne/Å.

2.2. Mercury Carboxamides

Unlike the *N*-substituted mercury amides discussed so far, the many *N*-mercurated carboxamides are resistant to solvolysis.

A typical member of this group of compounds is mercury bis(acetamide) [17], which has been known since the turn of the century, and which was deduced from its reactions to contain Hg–N bonds [18]. A similar conclusion was drawn from the bathochromic shift found for the amide (I) absorption in relation to free acetamide in a brief IR spectroscopic study between 2.5 and 15 μm [19]. The Raman spectrum [20] and the IR spectrum between 4000 and 400 cm^{-1} [21], on the other hand, were interpreted as indicating chelate bonding of the acetamide to the mercury *via* the nitrogen and the oxygen. The true situation in the solid state is shown by X-ray structure analysis [22], according to which planar $(H_3CCONH)_2Hg$ molecules (point group C_{2h}) with collinear Hg–N bonds (d(Hg–N) = 2.06 Å) are linked by O · · · H · · · N bonds into ribbons (Fig. 1). In the observed space group C_{2h}^5, the molecules must have the site symmetry C_i [23], which implies mutual exclusion in the IR and Raman spectra. However, substantial coincidence is found in the published IR and Raman spectra. It would appear that thorough checking of the vibration spectra is necessary.

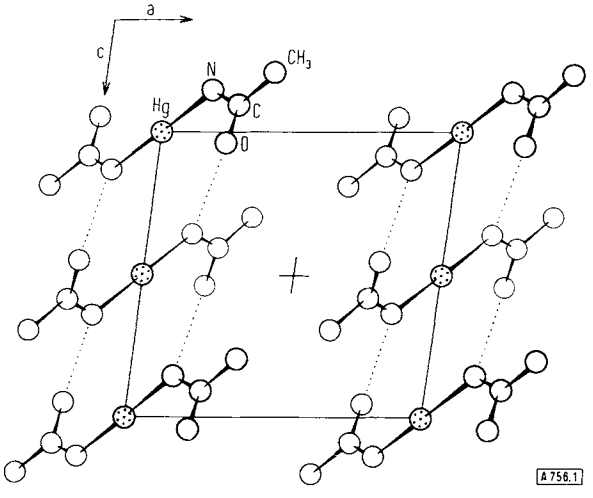


Fig. 1. Projection of the crystal structure of mercury bis(acetamide) in the *a*,*c* plane. H bonds are shown dotted [22].

The reaction of mercury bis(acetamide) with diacetohydrazide in water leads by transmercuration to insoluble mercury diacetohydrazide.

$$(H_3CCO)_2N_2H_2 + (H_3CCONH)_2Hg \rightarrow (H_3CCO)_2N_2Hg + 2\,H_3CCONH_2$$

On the basis of its properties, its IR spectrum, and the electron density distribution calculated from Debye-Scherrer diagrams, this product is assumed to have a

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polymeric chain structure with the structural groups $-Hg-N(OCCH_3)-N(OCCH_3)-$[24]. The structure of the colorless mercury bis(trifluoroaceto)hydrazide $(F_3CCO)_2N_2Hg$ that precipitates on reaction of mercury(II) acetate with bis(trifluoroaceto)hydrazide in aqueous solution[25], and which is stable up to 350 °C, has not been studied, but the compound is assumed to have a similar polymeric structure.

2.3. Mercury Sulfur Imides

A few preparative studies on ternary mercury-nitrogen-sulfur compounds have been reported. Heptasulfur imide reacts in a simple manner with mercury(II) acetate in methanol at −18 °C to give the yellowish-white labile derivative $(S_7N)_2Hg$[26].

$$2\ S_7NH + Hg(OOCCH_3)_2 \rightarrow (S_7N)_2Hg + 2\ HOOCCH_3$$

Tetrasulfur tetraimide $(SNH)_4$ reacts similarly with $Hg(OOCCH_3)_2$ in pyridine to give the yellow compound $(SN)_2Hg$, which is stable up to 160 °C; on alteration of the conditions, the reaction yields yellow-green $(SN)_8Hg_5$, which is thought to contain both Hg^{II} and Hg^{I}[27].

The sulfur diimide $S(NH)_2$ expected as an intermediate on ammonolysis of trithiazyl chloride has been intercepted as the greenish-yellow adduct $(SN_2)Hg \cdot NH_3$, which loses NH_3 on thermal degradation to give yellow, stable $(SN_2)Hg$[28].

$$N_3S_3Cl_3 \xrightarrow{NH_3(l)} 3\ S(NH)_2 \xrightarrow{HgI_2} (SN_2)Hg \cdot NH_3 \xrightarrow{-NH_3} (SN_2)Hg$$

No structural investigations have been carried out so far on any of these interesting compounds.

The crystal structure of mercury bis(sulfur difluoride imide) *(2)*, which was recently prepared[29] from *N*-fluoroformylimidosulfur difluoride and HgF_2 in accordance with

$$2\ FCONSF_2 + HgF_2 \rightarrow (F_2SN)_2Hg + 2\ COF_2 \qquad (1)$$

is, on the other hand, known[30]. In the isolated molecules, both the Hg–N bond length (2.05 Å) and the N–Hg–N bond angle (178 °, *i.e.* practically linear arrangement) lie in the expected region. The relatively large Hg–N–S angle (131 °) and the short N–S distance (1.44 Å), together with the high N–S bond force constant (9.90 mdyne/Å), point to strengthening of the N–S bond, so that the nitrogen, which is directly linked to only two neighboring atoms, tends distinctly toward an overall valence of 4. In the reactions studied so far (cleavage with halogens), *(2)* exhibits great similarity to *(1)*.

Corresponding to the preparation of *(2)*, $(F_2OSN)_2Hg$ probably occurs as an intermediate and in the solid residue in the reaction of *N*-fluoroformylimidosulfur oxide difluoride $FCONSF_2O$ with HgF_2 to form *N,N'*-carbonylbis(sulfur oxide difluoride imide)[31]. Mercury bis(sulfinylamide) is obtained from trimethylsilylsulfinylamine[32].

2.4. Mercury Amidosulfates

A series of Hg–N compounds can be obtained by mercuration of NH-acid aza-analogous sulfuric acid derivatives. Thus dipyridinium bis(amidosulfato)-mercurate $(C_5H_6N)_2[(O_3SNH)_2Hg]$ has been synthesized from esters of amidosulfuric acid and mercury(II) acetate[11] in methanol/pyridine; like the closely related bis(amidobissulfato)mercurate $M_4\{[(O_3S)_2N]_2Hg\}$[33], the above product probably contains a low molecular weight anion with a group structure. Special mention should be made of bis-(diamminemercury) bis(amidobissulfato)mercurate, $[(NH_3)_2Hg]_2\{[(O_3S)_2N]_2Hg\}$, in which mercury is linked to nitrogens having coordination numbers both of 3 and of 4.

According to studies by *Capestan et al.*[34,35], thermal degradation of bis(amidobissulfato)mercurates between 150 and 250 °C in the presence of water leads to pyrohydrolysis in which, irrespective of the cation M, mercury (amidosulfato)mercurate *(3)* is formed.

$$3\ M_4\{[(O_3S)_2N]_2Hg\} + 10\ H_2O \xrightarrow{150\,^\circ C} Hg[O_3SNHg]_2 + 10\ (0.6\ M,\ 0.2\ NH_4,\ 0.2\ H)_2SO_4 \qquad (3)$$

(3) is relatively stable, and decomposes above 380 °C into $HgSO_4$, Hg, SO_2, and N_2[36].

The mercuration of amidosulfates in the presence of strong bases yields (amidosulfato)mercurates $M[O_3SNHg]$ even with other cations[36,37]; these

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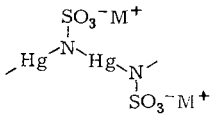
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products are assumed [11,38] to have a polymer chain structure in the anion.



The IR spectrum of $Na[O_3SNHg]$ in the region above 400 cm^{-1} has been briefly discussed on the basis of this assumption [39]. Thermolysis of these salts in the presence of moisture regenerates *(3)*

$$4\ M[O_3SNHg] + 2\ H_2O \xrightarrow{300\,^\circ C} (3) + 2\ M_2SO_4 + 4/3\ NH_3 + 1/3\ N_2 + Hg$$

which is also formed from mercury(II) oxide and ammonium sulfate above 200 °C [36],

$$3\ HgO + 2\ (NH_4)_2SO_4 \rightarrow (3) + 2\ NH_3 + 5\ H_2O$$

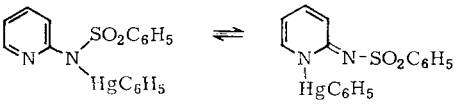
while bis(amidobissulfato)mercurates are formed under vacuum as intermediates [40] in accordance with

$$4\ M[O_3SNHg] \rightarrow M_4\{[(O_3S)_2N]_2Hg\} + 3\ Hg + N_2$$

Whereas the mercuration of the amidosulfates gives only one product, the reaction of sulfamide with mercury compounds in aqueous media yields complex mixtures whose compositions are strongly dependent on the mercuration reagent and on the reaction conditions [41]. This can be explained by incomplete mercuration, fluctuation of the degree of polymerization, and the possibility of two different monomer units in the polymer, *i.e.* [–NH–SO_2–NH–Hg–] and [–NH–SO(NH)–O–Hg–]. A simpler situation is found in the reaction of $Hg(ClO_4)_2$ with hydroxylamidosulfuric acid to form oxonium (hydroxylamidosulfato)mercurate $[H_3O][(O_3SNO)Hg]$, for which a chain structure consisting of [–O–N(SO_3)–Hg–] units is postulated [41]; this means that mercury is no longer bonded only to nitrogen, but is linked to both nitrogen and oxygen.

Alternative or simultaneous bonding of mercury to nitrogen or/and oxygen is conceivable for the mercury salt of trimeric sulfimide [42]. If the bonding found in the analogous silver salt on the basis of a preliminary X-ray analysis [43] is also valid here, Hg–N bonding should be favored.

Mention should also be made here of the interesting case of a "mercuriotropic" rearrangement with establishment of a tautomeric equilibrium between two different *N*-mercurated compounds, which was reported by *Kravcov* [44]. The results of a spectrometric study on the phenylmercuration of 2-phenylsulfonylaminopyridine in solution are interpreted by this author on the assumption of an equilibrium between an aminopyridine form and a dihydropyridinimine form:



the dihydropyridinimine form being favored by increasing polarity of the solvent. The rearrangement is thought to proceed *via* a four-membered ring chelate.

To close this section, we point out that there have been no published reports of attempts to prepare mercurated derivatives of oxoacid amides of other elements, such as nitroamine (*N*-methylnitroamine is reported to be mercurated on the oxygen [17]), phosphorus(V) acid amides, or chlorine(VII) acid amides.

3. Compounds Containing Nitrogen with a Coordination Number of 4 (Mercurioammonium Complexes)

The compounds discussed so far, apart from $(F_2SN)_2Hg$, $(F_2OSN)_2Hg$, and $(OSN)_2Hg$, contain N atoms having a total coordination number of 3 and Hg atoms having a coordination number of 2, and may therefore be regarded as dinuclear or polymeric complexes of formally uncharged nitrogen in which the coordination centers are linked by bidentate Hg ligand atoms. This metallocomplex character [45] becomes more distinct in the following section. All the coordination sites on formally monopositive nitrogen having a coordination number of 4 can be successively occupied by mercury, so that mercurioammonium complexes of various degrees of substitution are formed. The second bond of the mercury ligand may form a bridge to another ammonium nitrogen, and dinuclear and polynuclear complexes can be formed in this way. The formation of coordination polymers of this nature is prevented if one valence of the Hg^{II} is blocked by an inert, coordinately monodentate ligand; this leads to mononuclear, two-shell mercurioammonium complexes.

3.1. Mononuclear Complexes

The second valence of the Hg^{II} is most easily blocked with organic groups yielding organomercurioammonium complexes. Reports of such complexes have

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so far been sporadic[46–48]. In studies on the coordination chemistry of the methylmercury cation, the equilibrium constant for the reaction

$$H_3CHg^+ + NH_3 \rightleftarrows H_3CHgNH_3^+$$
(or more accurately: $H_3CHgOH_2^+ + NH_3 \rightleftarrows H_3CHgNH_3^+ + H_2O$)

was measured in aqueous solution[49].

To be able to collect structural data (X-ray data for single crystals and vibration-spectroscopic data also for solutions) with the aid of mononuclear model substances for the coordination-polymeric Hg–N compounds of the type ${}^{n-1}_{\infty}[NH_{4-n}Hg_{n/2}]^+X^-$, methylmercurioammonium complexes $[NH_{4-n}(HgCH_3)_n]^+$[50] and $[NH_{4-(m+n)}(CH_3)_m(HgCH_3)_n]^+$[51,52] have recently been systematically prepared in accordance with

$$[NH_{4-(m+n-1)}(CH_3)_m(HgCH_3)_{n-1}]^+ + H_3CHgOH \rightarrow [NH_{4-(m+n)}(CH_3)_m(HgCH_3)_n]^+ + H_2O$$

and studied.

A preliminary normal coordinate analysis was carried out for the series $[NH_{4-n}(HgCH_3)_n]^+ClO_4$ and $[ND_{4-n}(HgCH_3)_n]^+ClO_4$ (n = 1–4), ignoring the atoms that are not directly bonded to the nitrogen, and the result was compared with the IR and in part with the Raman spectra[53]. A calculation in accordance with the general valence force field model with constant parameters for the Hg–N bond [d(Hg–N) 2.07 Å, k(Hg–N) 3.00 mdyne/Å] gives vibration frequencies that show increasingly positive deviations from the observed frequencies with increasing values of n, both for the symmetrical (nondegenerate) and for the antisymmetrical (degenerate) vibrational modes. This trend of the frequencies can be interpreted as follows, taking into account the results of ^{1}H-NMR measurements on the series of compounds $[NH_{4-n}(HgCH_3)_n]^+ClO_4$[51]: As the degree of substitution n increases, the charge on the cation is increasingly spread over the coordinated highly polarizable Hg atoms. Thus the relative positive charge on a single Hg atom decreases, *i.e.* the electron density increases, with increasing n. This leads to increasing mutual repulsion of the Hg atoms. Since no appreciable deformation of the tetrahedral bond angles at the nitrogen is to be expected, this repulsion should lead to lengthening of the Hg–N bonds. This means a decrease in the Hg–N force constant and hence in the Hg–N vibration frequencies. X-ray structure analyses are being carried out to check this view[54].

3.2. Polynuclear Complexes

Complexes of the type $[(NH_3)_2Hg]^{2+}$ are usually regarded as having mercury as the central atom and ammonia as the ligands (diamminemercury complex). There are, however, arguments in favor of treating them as dinuclear, Hg-bridged ammonium complexes, and hence as metallocomplexes (μ-mercuriodiammonium complex). The second approach will be favored in the present context on systematic grounds.

3.2.1. Situation in Solution

The formation of ammine complexes of transition metals, and particularly of mercury, was studied by *Bjerrum*[55]. High and roughly equal complex formation constants are found for the first two steps of the addition of NH_3 to Hg^{2+} ($\log \beta_1$ = 8.8; $\log \beta_2$ = 8.7); the constants for the third and fourth steps, which are again very similar to each other, are about eight orders of magnitude smaller than β_1 and β_2. At medium NH_3 concentrations and pH values, therefore, practically the only complexes present in aqueous solution are $[(NH_3)Hg]^{2+}$ and $[(NH_3)_2Hg]^{2+}$; it is only at very high NH_3 concentrations and pH values that triammine and tetrammine complexes become important. *Bjerrum*'s results were confirmed and extended in studies by *Wirth* and *Davidson*, who also found a linear relation between the first formation constants for ammine-mercury complexes and the dissociation constants of the protonated amines[56,57].

3.2.2. Situation in Solids of the Type ${}^{n-1}_{\infty}[NH_{4-n}Hg_{n/2}]^+X^-$

The most thorough structural investigations using the greatest variety of methods have been carried out on dinuclear (n = 1) and coordination-polymeric (n = 2, 3, 4) mercurioammonium complexes ${}^{n-1}_{\infty}[NH_{4-n}Hg_{n/2}]^+X^-$ as solids. The structure of these complexes are well understood, though a few details still remain to be clarified. Diammine complexes with ammonia or simple alkylamines[58,59] are usually formed as the only products on reaction of a binary or quasibinary mercury salt with the pure amine, possibly in organic solvents of low polarity. Compounds of this

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type can be obtained from aqueous solution under the simultaneous action of the amine and the corresponding ammonium salt in certain concentrations [11, 58–60]. The influence of the ammonium salt concentration can be seen on dilution of an ammonium chloride solution that has been adjusted to the equilibrium concentration over solid $(NH_3)_2HgCl_2$ [61]:

$$(NH_3)_2HgCl_2 \rightarrow NH_2HgCl + NH_4Cl$$

The thermolysis of the diammine complex occasionally leads uniquely to the monoammine stage [58, 59], but this can also be reached by other routes, as is shown by the example of $(NH_3)HgSO_4$ [62]:

$$HgO + NH_4HSO_4 \rightarrow (NH_3)HgSO_4 + H_2O$$

Whereas the crystal structures of the monoammine complexes are not yet known, those of the diamminemercury halides $(NH_3)_2HgX_2$ (X = Cl, Br) appear to have been established [1, 9, 67]. Linear $^+H_3N-Hg-NH_3^+$ groups are arranged along the axes of a primitive cubic halide lattice with statistical orientation such that four halide ions are identically coordinated in a plane normal to the N–Hg–N line. The mercury thus has an effective coordination number of 6 (Fig. 2). The same structure is assigned to $(NH_3)_2HgI_2$ [60].

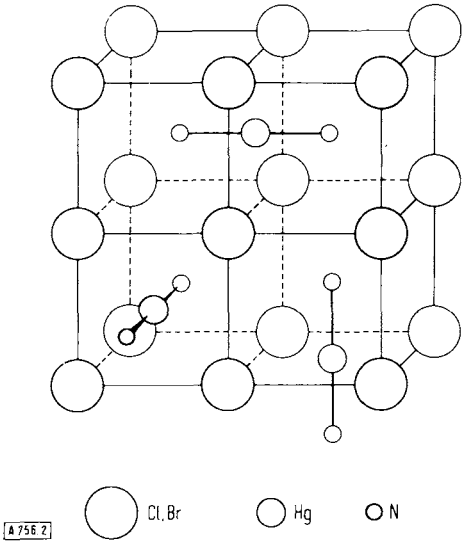


Fig. 2. Section of the structure of $[(NH_3)_2Hg]X_2$ with randomly oriented $^+H_3N-Hg-NH_3^+$ groups [1, 9, 67].

Numerous spectroscopic studies have been carried out on the diamminemercury halides on the basis of the knowledge of their structures. An early and important finding from the broad-line proton resonance is the free rotation of the coordinated NH_3 ligands about the Hg–N bond [5].

Partly on the basis of false structural assumptions [63] and partly without [6, 64] or with consideration of the rotation of the NH_3 ligands [65, 66], IR spectra alone as well as IR and Raman spectra [7] have been interpreted and the assignments confirmed in many cases by normal coordinate analyses. However, site symmetry effects were not considered in any of these cases. Comparison of the Urey-Bradley force constants for the metal-nitrogen bond in various amminemetal complexes shows [66] that the Hg–N bond has the highest force constant, $k(Hg-N) = 2.05$ mdyne/Å, and the strongest covalence, and so heads the series

$$Hg^{II} > Co^{III} > Cr^{III} > Cu^{II} > Ni^{II} > Co^{II}$$

Thus the vibration-spectroscopic behavior of the diamminemercury halides is largely elucidated; there is still some uncertainty due to the fact that the asymmetric stretching vibration of the N–Hg–N group is very weak, and is often completely absent.

On the basis of IR studies, dihydrazinemercury dichloride is assumed to contain cationic complexes $[(N_2H_4)_2Hg]^{2+}$ analogous to the diammine complexes $[(NH_3)_2Hg]^{2+}$, while coordination-polymeric chains $(-\overset{+}{N}H_2-\overset{+}{N}H_2-Hg-)$ or $^1_\infty[(N_2H_4)Hg_{2/2}]^{2+}$ are assumed for monohydrazinemercury halides $(N_2H_4)HgX_2$ (X = Cl, Br) [68].

The "infusible precipitates" formed directly or from the diamminemercury dihalides at lower ammonium salt concentrations and higher pH values have been thoroughly investigated in the form of the chlorides and bromides, and identified as coordination-polymeric mercurioammonium halides $^1_\infty[NH_2Hg_{2/2}]^+X^-$.

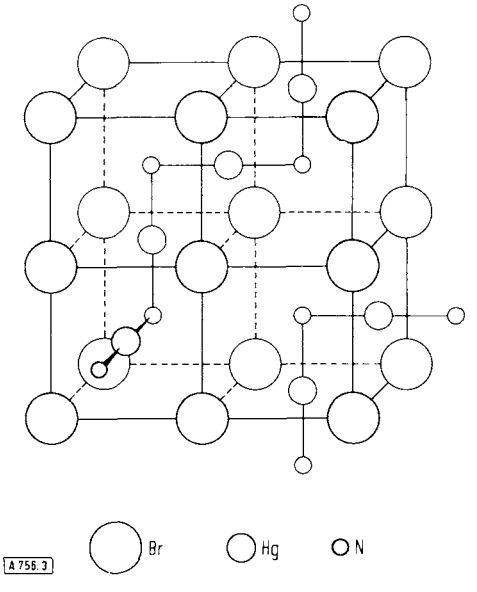


Fig. 3. Section of the structure of the cubic $[NH_2Hg]Br$ with randomly oriented $^1_\infty[NH_2Hg_{2/2}]^+$ chains [4, 67].

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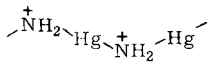
[66] *I. Nakagawa* and *T. Shimanouchi*, Spectrochim. Acta *22*, 759 (1966).

[67] *W. Rüdorff* and *K. Brodersen*, Z. anorg. allg. Chem. *270*, 145 (1952).

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The crystal structure of the cubic NH_2HgBr is very similar to that of $(NH_3)_2HgBr_2$, which is also cubic; this similarity is also shown by the formation of solid solutions of these two compounds [4,67].

Chains that bend at the nitrogens



thread their way through the primitive cubic bromide lattice with no preferred orientation; mercury has effectively octahedral coordination in this lattice (Fig. 3). The incorporation of small quantities of $HgBr_2$ into NH_2HgBr leads to stabilization of a rhombic mixed phase in which the chains are oriented parallel to the crystallographic c axis [69,70]. Pure NH_2HgCl forms a similar oriented rhombic structure [3] (Fig. 4).

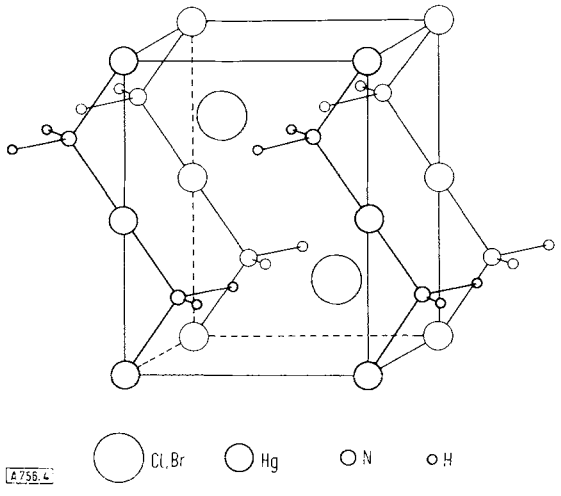


Fig. 4. Structure of rhombic $[NH_2Hg]X$ [69,70].

On the basis of the IR spectra a bond angle of 90° at the ammonium nitrogen was assumed for the cubic NH_2HgBr [6]. Normal coordinate analyses for the polymer chains in NH_2HgCl [71] and in NH_2HgBr [72] show that the observed and calculated frequencies agree well, largely irrespective of any deviation from the tetrahedral bond angle. However, the value deduced from the ^{1}H-NMR spectrum of NH_2HgCl for the distance between the protons in the NH_2 group points to the tetrahedral angle [5]. The question of the bond angle in the cubic NH_2HgBr thus cannot yet be definitely answered.

Mention should be made of the existence of a mercuriomethylammonium bromide $NHCH_3HgBr$ isotypic with the cubic NH_2HgBr [73]; with the aid of *N*- and *C*-deuterated derivatives, it has been possible to achieve a substantially definite assignment of the IR spectrum in the region 4000–200 cm^{-1} [74].

A remarkable structural relationship between NH_2HgCl and "mercury hydrazinochloride" (dimercuriohydrazinium dichloride) $[(N_2H_2)Hg_2]Cl_2$, which is also rhombic, has been demonstrated by X-ray and IR studies [68,75]. The compounds have unit cells with very similar dimensions, in which the mercury atoms occupy the same positions. In NH_2HgCl, the chains are held together in the b direction mainly by hydrogen bonds $H\cdots Cl\cdots H$, whereas $[(N_2H_2)Hg_2]Cl_2$ has covalent N–N bonds in the same lattice direction; this leads to the formation of puckered $^2_\infty[(N_2H_2)Hg_{4/2}]^{2+}$ layers parallel to the b,c plane.

This provides a connection with the layer structure of the hexagonal "mercury imidobromide" (trimercuriodiammonium tribromomercurate bromide) $NHHg_2Br_2$, which is better formulated as $^2_\infty[(NH)_2Hg_3]^{2+}Br^- \cdot HgBr_3$ on the basis of X-ray structure analysis [76,77] and as $^2_\infty[(NH)Hg_{3/2}]^+ \cdot 0.5\ Br^- \cdot 0.5\ HgBr_3^-$ when the coordination in the cation is taken into account. An interesting feature here is the presence of two structurally different types of Hg atoms. Mercury in the cationic layer forms a very distorted, effectively octahedral coordination polyhedron; linear polymer chains $^2_\infty[HgBr_3Br_{2/2}]^{2-}$ with effectively trigonal-bipyramidal coordination of the mercury pass through the lattice normal to the layers and along the c axis (Fig. 5).

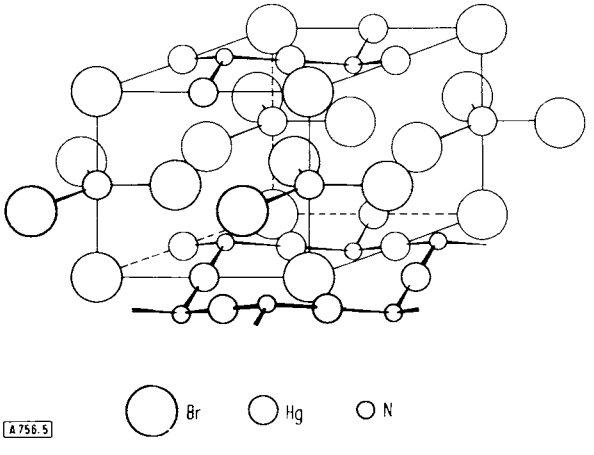


Fig. 5. Unit cell of "mercury imidobromide" $NHHg_2Br_2$ with completed mesh of the $^2_\infty[(NH)Hg_{3/2}]^+$ network [76,77].

Compounds having analogous compositions, such as $NHHg_2Cl_2$ and $(NR)Hg_2X_2$ were synthesized by *Meuwsen* and *Weiss* [78]; their structures have not yet been established. They are insoluble in water and in organic solvents; as solid phases in the presence of the solvents, they give up HgX_2 reversibly into the solvent, the composition $[(NR)_2Hg_3]X_2$ being reached in the

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limiting case. $[(NR)_2Hg_3]X_2$ can be obtained directly by reaction of amines and mercury halides in alkaline media at high temperatures [58]. Studies of the structure of these polymeric substances seem desirable. A start has been made by the definite assignment of the IR spectra of $[(NCH_3)_2Hg_3]Br_2$ and its deuterium analogs [74].

Complete substitution of the H atoms of the ammonium ion by Hg leads to derivatives of Millon's base, $NHg_2OH \cdot 2\,H_2O$. All compounds of this type have a bulky, three-dimensional coordination-polymeric, cationic skeleton ${}^3_\infty[NHg_{4/2}]^+$. The mutual arrangement of the NHg_4 tetrahedra, which are joined by their vertices, is influenced by the ability of the anions to coordinate with the Hg atoms of the skeleton; the symmetry of the three-dimensional cation thus depends on the anion. From observations made so far it appears that oxo anions with lower tendencies to coordinate, such as nitrate and chlorate(VII) [79,80], lead mainly to the development of cubic modifications, in whose cavities water can be reversibly accommodated with no change in structure. In the cubic $[NHg_2]HPO_4 \cdot H_2O$, however, thermal dehydration is accompanied by a transition to a tetragonal modification [80]. The existence of a cubic form of the dihydrate of Millon's base $[NHg_2]OH \cdot 2H_2O$ [2] is doubtful [11]. The oxo anions situated in the lattice passages can also be replaced, in some cases reversibly, particularly by halide ions. Though the cubic structure is retained, however, lattice imperfections are evidently produced [9,79]; under the action of heat, these distorted cubic forms change into denser, more stable, hexagonal modifications [11], which are also formed directly under suitable conditions. X-ray structure analyses of the hexagonal modifications [81,82] show that the Hg atoms effectively achieve a distorted octahedral coordination. The high coordinating power of the anions Cl^-, Br^-, I^-, and OH^- apparently plays an important part in the structure of the hexagonal lattice.

Weber has presented his views on the formation and degradation of Millon's base in several publications [83].

3.2.3. Comparison with Silicate Structures

The structural relationship of the Millon salts with the silicon dioxide modifications β-cristobalite (cubic) [79] (cf. Fig. 6) and β-tridymite (hexagonal) [81] (cf. Fig. 7) was quickly recognized. The two possibilities for the mutual orientation of two joined NHg_4 tetrahedra in the ${}^3_\infty[NHg_{4/2}]$ skeleton are also found in principle in the linkage of the SiO_4 groups in the three-dimensional ${}^3_\infty[SiO_{4/2}]$ network. Owing to the bond angle of 130 to 140 ° at the oxygen [84], the number of possibilities for the arrangement of the SiO_4 tetrahedra is greater (quartz modifications) than in the derivatives of Millon's base, in which the bonds at the mercury are collinear. Checks should be made to establish whether coesite-like high pressure modifications [85] can exist for Millon salts. Since the coordination number of nitrogen, unlike that of silicon, cannot exceed 4, no analogs of stishovite are to be expected.

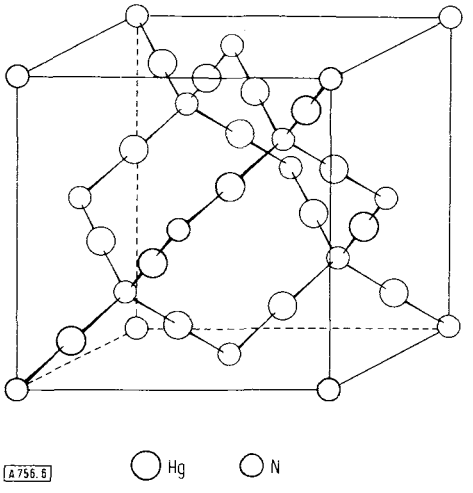


Fig. 6. Skeleton structure of the cation of cubic Millon salts ${}^3_\infty[NHg_{4/2}]^+X^-$ [79].

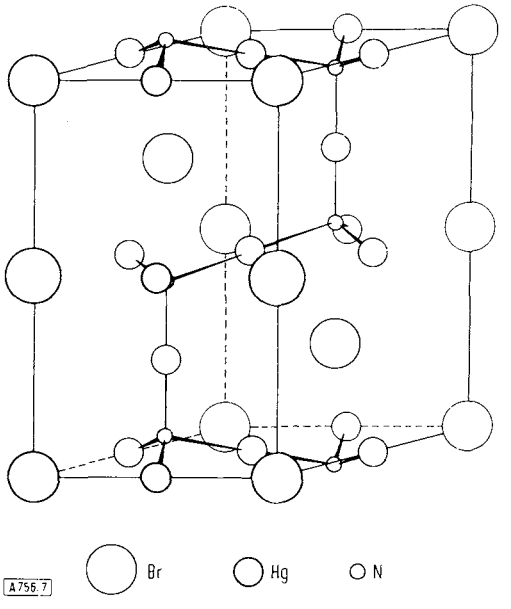


Fig. 7. Unit cell of hexagonal Millon salts [81].

The comparison of the structures of mercurioammonium salts and silicates may be carried still further. The relationships become clear on comparison of the general coordination formulas for mercurioammonium ions ${}^{n-1}_\infty[NH_{4-n}Hg_{n/2}]^+$ and for silicate ions ${}^{n-1}_\infty[SiO_{4-n}O_{n/2}]^{(4-n)-}$, with mercury corresponding to coordinately bidentate oxygen and protons to coordinately monodentate oxygen.

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Table 1. Structural units of mercurioammonium and silicate ions.

n	4	3	2	1
$^{n-1}_{\infty}[NH_4-nHg_{n/2}]^+$	$^{3}_{\infty}[NHg_{4/2}]^+$	$^{2}_{\infty}[NHHg_{3/2}]^+$	$^{1}_{\infty}[NH_2Hg_{2/2}]^+$	$^{0}[NH_3Hg_{1/2}]^+$
$^{n-1}_{\infty}[SiO_4-nO_{n/2}]^{(4-n)-}$	$^{3}_{\infty}[SiO_{4/2}]$	$^{2}_{\infty}[SiOO_{3/2}]^-$	$^{1}_{\infty}[SiO_2O_{2/2}]^{2-}$	$^{0}[SiO_3O_{1/2}]^{3-}$
Silicate type	tecto-	phyllo-	ino-	soro-

While for $n = 4$, as described earlier, a correspondence exists between Millon salts and three-dimensional silicon dioxide modifications (tectosilicates), parallels can also be drawn between the layer structure of the polymeric cation in $NHHg_2Br_2$ and the two-dimensional phyllosilicates, the chain structure in NH_2HgX and one-dimensional inosilicates, and the group structure of $(NH_3)_2HgX_2$ and zero-dimensional sorosilicates.

Differences between mercurioammonium and silicate structures are due to the fact that in the Hg–N compounds, for $n \leq 3$, the anions can form N–H $\cdots$ X^- bridges, and also coordinate to the bridge Hg atoms. Silicates exhibit pronounced coordination of the cations M to terminal O atoms, which changes the strength of the Si–O(–M) bond, depending on the field strength of the cation, but also affects the bond parameters of the SiO(–Si) group, and hence the structure [86]. In layer silicates, this type of coordination leads to a cation-dependent infrastructure (layer folding) [87]. Such coordination effects undoubtedly determine the structure of Hg–N compounds, but still require systematic elucidation.

4. Comparison of the Parameters for Hg-C, Hg-N, and Hg-O Bonds

The bond system between mercury and hetero atoms is influenced by the positive charge acquired by the Hg atom, which depends in turn on the electronegativity of the bonding partner and its charge. If the Hg atom is strongly positive (formally treated as Hg^{2+}), a transition between the electronic configurations $5d^{10}$ and $5d^96s^1$ is possible with a relatively low energy requirement (5.3 eV), with subsequent $d_{z^2}s$ hybridization [88]; this explains the formation of two strong bonds along the z axis; weaker coordination of further ligands is possible in the xy plane, limited only by electrostatic and geometric factors. If the Hg is only weakly positive (formally treated as Hg^+ having the configuration $5d^{10}6s^1$), the energy required for the transition $5d^{10}6s^1 \rightarrow 5d^{10}6p^1$ is relatively large ($\approx$ 6eV). The most favorable economy occurs on formation of a linear sp hybrid system using only an energetically higher p state [89]. Owing to the weaker positive charge acquired by the Hg atom, little or no coordination tendency is now observed in a plane perpendicular to the direction of the sp hybrid.

An idea of the influence of the electronegativity of the bonding partner is provided by the Hg–C bond lengths found by microwave spectrometry for the methylmercury halides $H_3C-Hg-X$ (Table 2).

Table 2. Hg–C bond lengths in methylmercury halides.

X	Cl	Br	I
d(Hg–C) (Å)	2.061	2.074	2.087
Ref.	[90]	[90]	[91]

By contrast, equal Hg–C bond lengths are found for dimethylmercury (d(Hg–C) 2.094 Å [92]) and diphenylmercury (d(Hg–C) 2.092 Å [93]), despite the difference in the hybridization states of the carbons, which should lead to different electronegativities.

Finally, the influence of the ligands attached to the positively charged mercury in excess of the characteristic coordination number of 2 must also be taken into account.

It is against this background that the still problematic comparison of parameters for the Hg–C, Hg–N, and Hg–O bonds must be seen. The simplest solution appears to be a comparison of the isosteric groups $H_3C-Hg-CH_3$, $H_3\overset{+}{N}-Hg-\overset{+}{N}H_3$, and $H_2\overset{+}{O}-Hg-OH_2$, with the bond lengths d(Hg–C) = 2.094 Å [92] and d(Hg–N) = 2.05 (X = Cl) [7,66] or 2.11 Å (X = Br) [67] (coordination effect); in $HgSO_4 \cdot H_2O$ (highly distorted octahedral oxygen coordination), $d(Hg-\overset{+}{O}H_2)$ is 2.24 Å [94]. No structural data are available for diaquo complexes.

Let us compare the Hg–N distances in $(NH_3)_2HgCl_2$ (2.05 Å) and $(H_3CCONH)_2Hg$ (2.06 Å) [22], though the validity of such a comparison is questionable in view of the change in both the formal charge and hybridization state ($sp^3 \rightarrow sp^2$) of the nitrogen and the effective coordination number of the mercury. Without knowing the contribution due to each change individually, it can however be stated that the changes roughly balance each other out. A better comparison should be possible in the series $H_3C-Hg-CH_3$, $H_3C-Hg-\overset{+}{N}H_3$, $H_3C-Hg-\overset{+}{O}H_2$, since the positive

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charge on the Hg atom is smaller. The normal coordinate analysis for $H_3C-Hg-\overset{+}{N}H_3$, with d(Hg–N) = 2.07 Å and k(Hg–N) = 3.00 mdyne/Å in the general valence force field, gives good agreement between the calculated and the measured data [53]; though the $Hg-\overset{+}{O}H_2$ stretching vibration has been observed in the Raman spectrum, however, the Hg–O bond parameters have not yet been calculated [95].

Structural data are known for geminally dimercurated nitrogen and oxygen compounds, but not for carbon compounds of this type. For the polymeric cation $^1_\infty[NH_2Hg_{2/2}]^+$ in NH_2HgCl, d(Hg–N) is 2.05 Å [3], while for $^1_\infty[OHHg_{2/2}]^+$ in $OHHgXO_3$ (or $Hg(XO_3)_2 \cdot HgO \cdot H_2O$, X=Cl, Br), d(Hg–O) is 2.29 and 2.32 Å [96]. Both modifications of mercury(II) oxide have been found to have d(Hg–O) = 2.03 Å [97,98]. The weakening of the Hg–O bond by protonation of the oxide oxygen to oxonium oxygen can also be demonstrated in the pair $O(HgCH_3)_2$ (ν_s(Hg–O–Hg) = 487 cm^{-1}) and $[OH(HgCH_3)_2]^+$ (ν_s(Hg–O–Hg) = 415 cm^{-1}) [95].

Trimercurio onium groups are found in $NHHg_2Br_2$ and $O_2Hg_3SO_4$ ($HgSO_4 \cdot 2HgO$). For the nitrogen compound, it was deduced from IR data, using a simple mechanical model, that d(Hg–N) = 2.26 Å [11]; this value seems relatively high. Distances d(Hg–O) = 2.03 Å were found by X-ray studies for the cation $^2_\infty[OHg_{3/2}]^+$ [99]. Tris(chloromercurio)oxonium chloride $[O(HgCl)_3]^+Cl^-$ is found from neutron [100] and X-ray diffraction [101] to have Hg–O bond parameters of d(Hg–O) = 2.04 and 2.06 Å, Hg–O–Hg = 118.9 and 117.9 °, respectively.

The vibration spectra of the ion $[O(HgCH_3)_3]^+$ [102], which, unlike $[O(HgCl)_3]^+$, is evidently planar, have not yet been quantitatively evaluated. In view of the strength of the Hg–O and Hg–N bonds, it is interesting to note that the totally symmetrical stretching vibrations for the $[O(HgCH_3)_3]^+$ and $[N(HgCH_3)_4]^+$ groupings appear in the Raman spectrum with only slightly different frequencies (132 and 141 cm^{-1} respectively [53]).

Finally, mention should be made of the "mercarbides" having the idealized molecular formula $C_2Hg_6O_2X_2$, which, as apparently three-dimensional polymers, exhibit a certain similarity to Millon salts [103]. A distance d(Hg–N) = 2.07 Å has been reported for the cubic form of Millon's base and its salts, irrespective of the anion [79]; values ranging from 2.04 (dihydrate of the base) to 2.09 Å (Millon iodide), depending on the coordinating power of the anions, have been found, on the other hand, for the hexagonal forms [11,81]. The overall ranges of the bond lengths d(Hg–X) are thus

d(Hg–C): 2.06 – 2.10 Å
d(Hg–N): 2.05 – 2.11 (2.26) Å
d(Hg–O): 2.03 – 2.32 Å

5. Existence of Mercury(I)-Nitrogen Compounds

The supposed formation of mercury(I)-nitrogen compounds on reaction of Hg(I) salts with ammonia or amines of higher basicity has been definitely refuted [9, 79, 104, cf. 105]. The reaction leads by disproportionation to mercury and the mercury(II)-nitrogen compounds that are also formed from the corresponding Hg^{II} salts. Hg^I–N complexes can however be formed with amines of lower basicity, as has been shown for the system Hg_2^{2+}/aniline [56]. The potentiometrically and spectrometrically determined formation constant for the complex $[(C_6H_5NH_2)Hg_2]^{2+}$ ($\beta = 5.1 \times 10^3$ l $mole^{-1}$) is almost one order of magnitude lower than that of the Hg^{II} complex $[(C_6H_5NH_2)Hg]^{2+}$ ($\beta = 4.0 \times 10^4$ l $mole^{-1}$). It was assumed that the difference between $\beta_{Hg^{II}}$ and β_{Hg^I} would increase with increasing basicity; this would be compatible with the disproportionation of Hg^I and the formation of Hg^{II}–N compounds at higher basicities, but would also lead one to expect the existence of stable Hg^I–N compounds at lower basicities. This expectation is verified not only by the aniline complexes, which have been detected in solution [56] and isolated as $[(C_6H_5NH_2)_2Hg_2](NO_3)_2$ [106], but also by a few other Hg^I–N compounds. Shortly after it had been shown [27] that the products obtained in the reaction of mercury(II) acetate with NH-acid tetrasulfur tetraimide were probably Hg^I–N compounds, relatively stable mercury(I) derivatives of $(SNH)_4$ and S_7NH, *i.e.* the yellow $[(SN)Hg]_x$ and the light yellow $(S_7N)_2Hg_2$, were obtained [107], *e.g.*:

$$Hg_2(NO_3)_2 + 2\ S_7NH \xrightarrow{DMF,\ 20\,^\circ C} (S_7N)_2Hg_2 + 2\ HNO_3$$

Diacetohydrazide, which is also an NH-acid compound, reacts similarly in weakly acidic aqueous solution to give orange $(H_3CCO)_2N_2Hg_2$; the properties of this product and the Hg–Hg distance of 2.9 Å deduced from a calculated radial electron density distribution seem to establish conclusively that this is a Hg^I–N compound [108]. However, the Hg–Hg

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vibration, which appears with high intensities for other Hg^I derivatives, could not be detected in the Raman spectrum of this compound [109].

In the meantime, further Hg^I derivatives of bis(fluorosulfonyl)amine, *N,N*-bis(fluorosulfonyl)urea, and fluorosulfonylcarbamates have been prepared [110] and investigated by vibrational spectrometric methods along with mercury(I) diacetohydrazide. All compounds exhibit intense Raman lines caused by Hg–Hg vibrations. From the observed frequencies Hg–Hg distances ranging from 2.44 to 2.47 Å have been calculated [111] using an appropiate Badger formula (cf. [109]).

However further preparative work and structural studies are necessary for a more profound understanding of the problem of Hg^I–N compounds.

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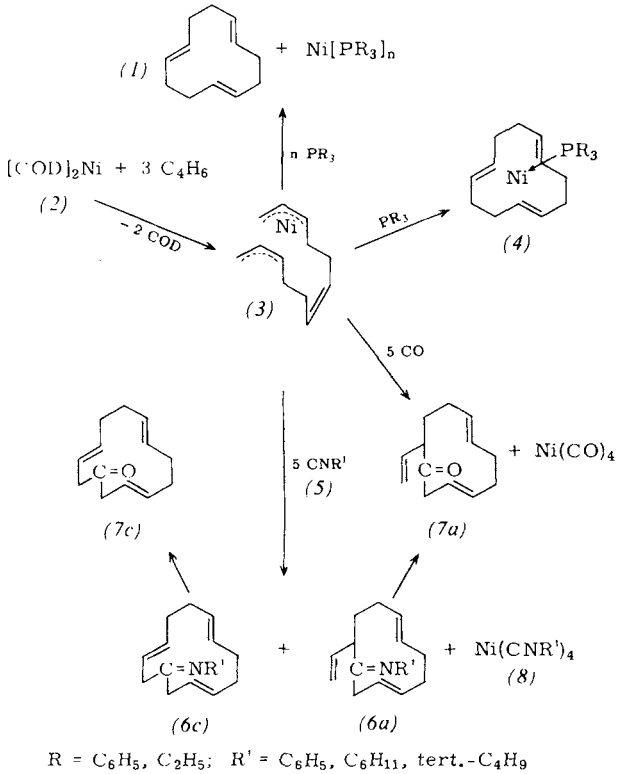
COMMUNICATIONS

3,7,11-Cyclotridecatrien-1-one and 11-Vinyl-3,7-cycloundecadien-1-one

By *Heinz Breil* and *Günther Wilke* [*]

Butadiene is cyclotrimerized to 1,5,9-cyclododecatriene *(1)* (at 20–100 °C) by "naked nickel" [1,2]. On refluxing (below 0 °C) with butadiene, bis(1,5-cyclooctadiene)nickel(0) *(2)* forms a complex $C_{12}H_{18} \cdot Ni$ *(3)*, which is isolable in crystalline form and in which a $C_{12}H_{18}$ chain is bonded to nickel by two terminal π allyl groups [1,2]. On reaction of compound *(3)* with electron donors such as phosphines (PR_3) in the molar ratio 1 : 1, C–C linkage occurs to give 1,5,9-cyclododecatrienephosphinenickel(0) *(4)*; reaction with an excess of phosphine affords *(1)* and $Ni(PR_3)_n$, $n = 2$–4 [1,2]. At –40 to –60 °C *(3)* undergoes an insertion reaction with carbon monoxide to give 11-vinyl-3,7-cycloundecadien-1-one [1,2] *(7a)*.

We have now found that reaction of compound *(3)* with isocyanides *(5)* proceeds *via* insertion to give the imines *(6a)* and *(6c)* of vinylcycloundecadienone *(7a)* and cyclotridecatrienone *(7c)*, and is accompanied by formation of tetrakis(isocyanide)nickel(0) complexes *(8)*.



R = C_6H_5, C_2H_5; R' = C_6H_5, C_6H_{11}, tert.-C_4H_9

The readily accessible [3] complex *(2)* is treated with liquid butadiene until all the crystals have disappeared. The deep red liquid reaction product is then allowed to react with isocyanide (Ni: *(5)* = 1 : 5) at 0 °C, precipitated *(8)* is filtered off, and the mixture of isomers *(6a)* and *(6c)* is isolated. The yields of *(6)* lie between 40 and 70% (based on *(2)*).

The isomers *(6)* can be hydrolyzed by 30% CH_3COOH/3.5 N H_2SO_4 (1 : 1) to yield the four ketones *(7a–d)* which were almost completely separated by distillation. We were able to identify *(7a)*, 11-ethylidene-3,7-cycloundecadien-1-one *(7b)*, and 3,7,11-cyclotridecatrien-1-one *(7c)* by their IR, ^{1}H-NMR, and mass spectra. Compound *(7b)* appears to be formed from *(7a)* on acid hydrolysis of *(6)*; *(7d)* is probably an isomer of *(7c)* having a *cis* double bond. The isomeric distribution (gas chromatography) varies according to the isocyanide used: *tert*-C_4H_9NC and $C_6H_{11}NC$ give *(7a)* : *(7b)* : *(7c)* : *(7d)* = 2 : 1 : 90 : 7 and 42 : 41 : 13 : 4, respectively — *i.e.* the bulky *tert*-butyl group causes preferential linkage of the terminal C atoms of *(3)* with the isocyanide C atom, while C-3 and C-12 of *(3)* react in the case of cyclohexyl isocyanide; the ratio C_{11}-ring/C_{13}-ring amounts to about 3 : 97 and 83 : 17, respectively.

Catalytic hydrogenation of *(7c)* yields cyclotridecanone, m.p. 32 °C (literature value).

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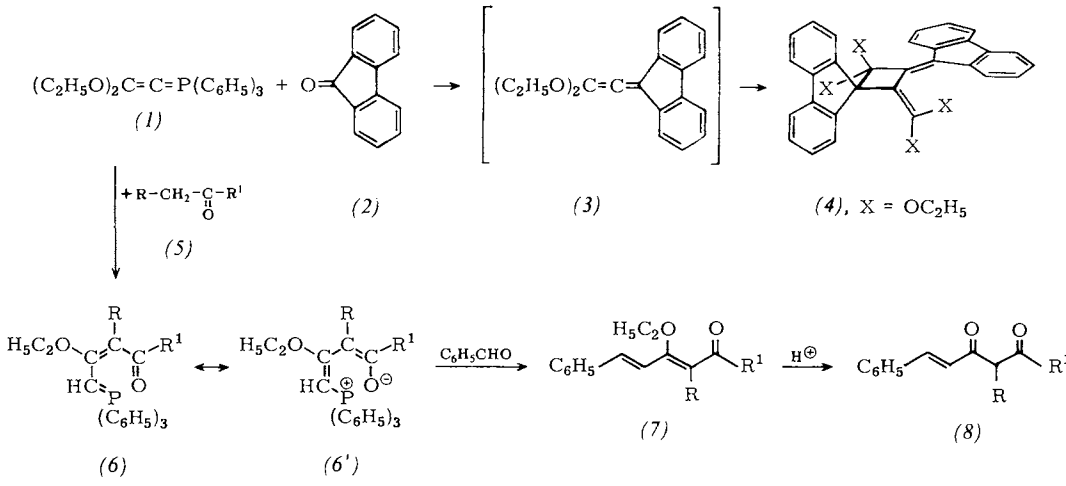
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Reactions of 2,2-Diethoxyvinylidenetriphenylphosphorane with Ketones. Synthesis of 1,3-Dioxo-4-pentenes and Their Enol Ethers

By *Hans-Jürgen Bestmann* and *Rolf W. Saalfrank* [*]

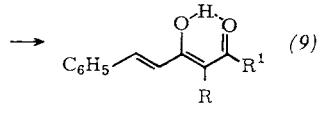
2,2-Diethoxyvinylidenetriphenylphosphorane *(1)* [1] undergoes a Wittig reaction with fluorenone *(2)* to give the allene *(3)* which immediately dimerizes to *(4)* (m.p. 184 °C, yield 65 %). The structure of *(4)* was confirmed by degradation.



	R	R¹	(6) m.p. (°C)	(6) yield (%)	(7) m.p. (°C)	(7) yield (%)	(8) m.p. (°C)	(8) yield (%)
(a)	H	C_6H_5	174	65	85	57	111	95
(b)	H	CH_3	146	55	50	53	86	94
(c)	—$(CH_2)_4$—		177	69	51	51	93	81
(d)	H	OC_2H_5	166	74	55	66		

Reaction of *(1)* with ketones *(5)* having a methylene group α to the carbonyl is quite different: The stable ylides *(6)* are formed by Michael addition and subsequent loss of ethanol. The shift of the carbonyl band to 1582—1597 cm^{-1} in *(6a)*—*(6c)* and to 1645 cm^{-1} in *(6d)* indicates a large contribution by the resonance structure *(6')*. When R = H, this proton signal is split into a doublet by long-range coupling with the phosphorus ($^4J_{PH}$ = 6.5 Hz). Coupling between the phosphorus and the α-H atom is temperature dependent [2].

The alkylidenetriphenylphosphoranes *(6)* react with aldehydes, *e.g.* benzaldehyde, to give the enol ethers *(7)* of 1,3-dioxo-4-pentenes (C_6H_5—CH=CH: J_{HH} = 15.9 Hz), which can be cleaved by acids to give the free dicarbonyl compounds *(8)*. According to the ^{1}H—NMR spectra, compounds *(8)* are present almost exclusively as enols *(9)* [τ = —5.37 to —6.72 (OH/s)]. Scission of *(7d)* under the above conditions results in hydrolysis and decarboxylation to give benzylideneacetone.



Experimental:

An equivalent amount of ketone is added dropwise to a salt-free benzene solution of ylide [3] prepared from 2,2-diethoxyvinyltriphenylphosphonium tetrafluoroborate [1] by the sodium amide method. After 20 hours' stirring at room temperature the benzene is distilled off under vacuum and the residue recrystallized from ethyl acetate.

The resulting red-brown to yellow compound *(6)* is dissolved in anhydrous benzene, treated with an equivalent amount of benzaldehyde, and refluxed for 4 hours. The solvent is subsequently distilled off and the residue extracted with light petroleum; undissolved triphenylphosphine oxide is filtered off and the light petroleum is distilled off from the filtrate. Recrystallization of the residue from ethanol at —30 to —40 °C furnishes compound *(7)*. The enol ether *(7)* is stirred with hot 25% sulfuric acid for 30 min. The crystalline residue isolated by filtration is dissolved in methylene chloride, the solution dried over $MgSO_4$, and the solvent evaporated off. Compound *(8)* is then recrystallized from ether or ethanol at —60 °C.

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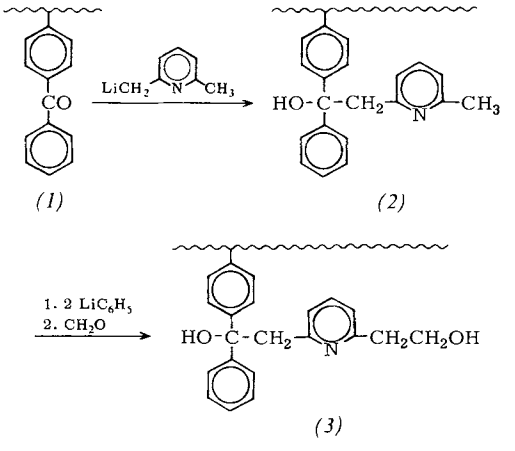
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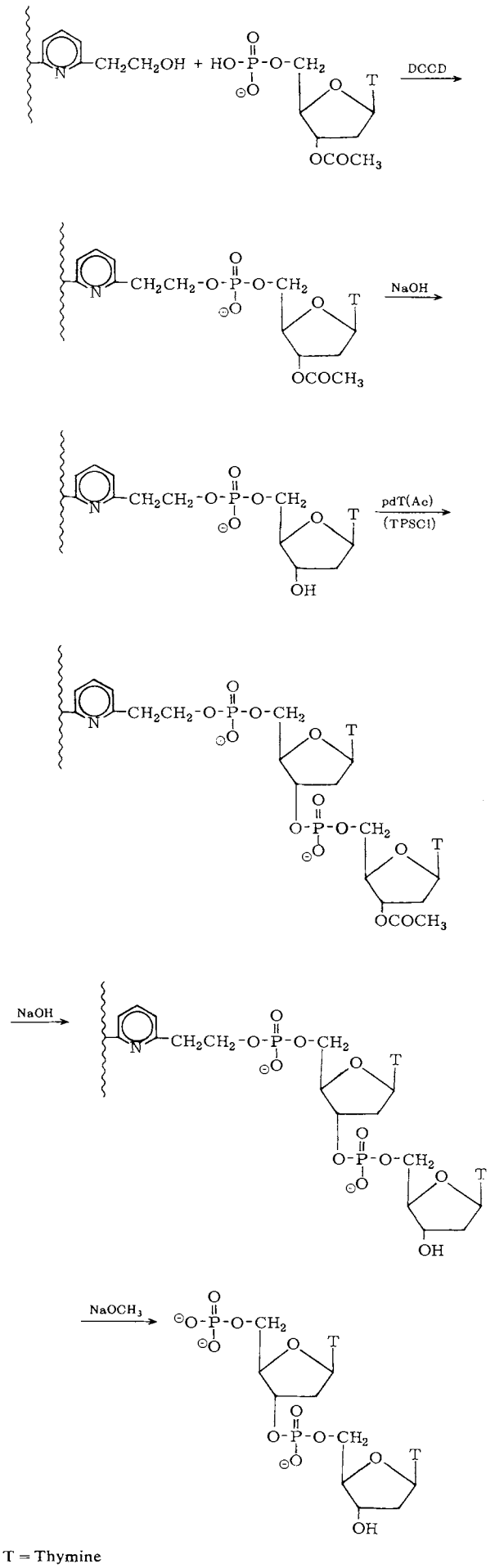
Synthesis of Oligonucleotide 5′-Phosphates on a Polymeric Carrier Containing 2-Pyridineethanol as Functional Group

By *Wolfgang Freist* and *Friedrich Cramer* [*]

In syntheses of oligonucleotides on polymeric carriers the nucleotide is usually attached to the polymer by the 5′-OH group, so that removal from the carrier affords oligonucleotides with a free 5′-OH group [1]. Synthesis of oligonucleotide 5′-phosphates has been effected only on one carrier up to the trinucleotide [2].

We have prepared a new polymeric carrier for the synthesis of oligonucleotide 5′-phosphates, wherein the 2-pyridineethanol group is attached as "phosphate trap" (cf. [3]) to a 6% crosslinked, macroporous polystyrene. 23% benzoylated polystyrene *(1)* is first treated with a mixture of equivalent amounts of phenyllithium and 2,6-lutidine, whereupon lutidyllithium adds to the CO group, giving *(2)*. Then two equivalents of phenyllithium are added to this product, so





that not only the H atom of the hydroxyl group but also one hydrogen atom in the side chain of the pyridine ring is replaced by lithium. Finally formaldehyde is added to give product *(3)*[**]. About 20% of the phenyl groups of the carrier are thus converted into functional groups.

For synthesis of oligothymidylic acids the carrier was loaded with 0.2 mmole of nucleotide per g of polymer by reaction with 3′-*O*-acetyldeoxythymidine 5′-phosphate and dicyclohexylcarbodiimide (DCCD)[***], the 3′-*O*-acetyl group was removed by 2 N-NaOH and pyridine (1 : 1), and the product was condensed with 3′-*O*-acetyldeoxythymidine 5′-phosphate by means of 2,4,6-triisopropylbenzenesulfonyl chloride (TPSCl)[***]. The nucleotide was removed from the carrier by 2 N-$NaOCH_3$ in methanol/pyridine (1 : 1).

Oligothymidylic acids were thus synthesized up to the hexanucleotide.

Table 1. Yields in individual steps [a] based on the preceding step.

$(pdT)_2$	$(pdT)_3$	$(pdT)_4$	$(pdT)_5$	$(pdT)_6$
35%	50%	78%	33%	38%

[a] Reaction time 15 h; five- to ten-fold excess of the phosphate component.

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[**] We assume that the methyl group reacts preferentially.

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Electron Transfer from Solvent to a Triplet Excited Acceptor Molecule

By *Günther Briegleb* and *Helmut Schuster*[*]

We have studied the effect of electron donor-acceptor (EDA) complex formation on both the triplet-triplet (TT) absorption spectrum and the phosphorescence spectrum of the electron donor component in the complexes |DA| of the donors (D) naphthalene *(1)* and phenanthrene *(2)* with the acceptors (A) tetrachlorophthalic anhydride *(3)* and pyromellitic dianhydride *(4)* at $T = 96$ to 118 °K in solution in dipropyl ether (PE) glass[1].

After production of triplet (T) excited molecules of the donors *(1)* and *(2)* respectively in the complex $|D_T^* \cdots A|$ by flash excitation in the charge transfer (CT) absorption band of the dissolved complexes at $T \approx 100$ °K and at a concentration ratio $q = c_D/c_A = 1$ we recorded the TT absorption spectrum, the phosphorescence spectrum, and the mean lifetime τ of the T-excited state of complexed *(1)* and *(2)* respectively. Complex formation is seen to modify the spectra and τ[1].

At higher temperatures, T = 105—118 °K, and/or an excess of donor ($q = 100$) distinct changes were observed in the TT absorption, the phosphorescence spectrum, and the lifetime of the T-excited donor as a result of excimer formation $D \cdot D_T^* \cdots A$.

In addition, new relatively intense and broad unstructured absorption bands were observed between 12×10^3 and 20×10^3 cm^{-1} outside the typical spectral range of donor-TT

absorption of *(1)* (23—27 × 10^3 cm^{-1}) and of *(2)* (20—24 × 10^3 cm^{-1}). These new bands constitute the first evidence for CT* absorption bands of an electron transfer from a T-excited donor to an unoccupied energy level of an acceptor [2].

In the present communication we wish to report the results of studies on an electron transfer from the solvent dipropyl ether (PE) as n-donor to the dissolved T-excited acceptors *(3)* or *(4)* [3].

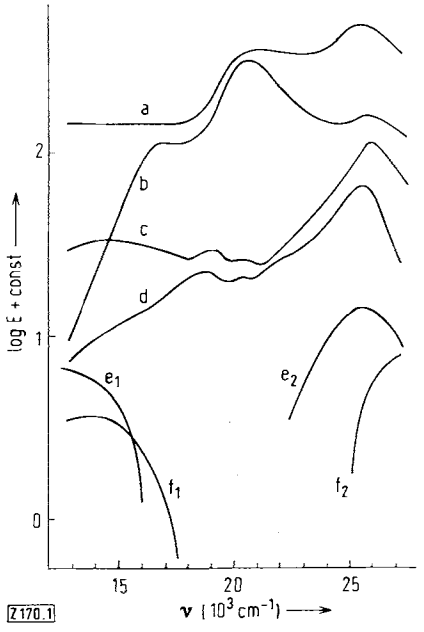


Fig. 1. Absorption spectra of triplet excited pyromellitic dianhydride *(4)* and tetrachlorophthalic anhydride *(3)* in solvent glass.

a) *(4)* in PE (3 × 10^{-5} M), T = 100 °K; b) *(4)* in BA (1.6 × 10^{-4} M), T = 115 °K; c) *(3)* in PE (6 × 10^{-5} M), T = 100 °K; d) *(3)* in BA (1.4 × 10^{-4} M), T = 115 °K. e) difference between the spectra of *(4)*, a—b; f) difference between the spectra of *(3)*, c—d. Band width: 70 (short wave region) to 200 cm^{-1} (long wave region).

We compared the TT absorption spectra of *(4)* and *(3)* in a solvent glass composed of 75 % butyl acetate, 19 % methylcyclohexane, and 6 % isopentane (BA) in the 12—27 × 10^3 cm^{-1} region (Fig. 1: b,d) with the corresponding spectra of solutions in (PE) glass (Fig. 1: a,c): The main difference is observed at $\tilde{\nu} < 17 \times 10^3$ cm^{-1} in a new, broad absorption band (Fig. 1: a,c). Assuming that the spectra a,b and c,d are equal, to a good approximation, in the TT absorption region 17—21 × 10^3 cm^{-1} of *(4)* and 18—25 × 10^3 cm^{-1} of *(3)* the subtraction of the spectra in (PE) and (BA) affords two broad unstructured absorption bands exhibiting no fine structure (Fig. 1: e,f). The red shift of the maxima of these new double bands in (PE) on going from *(3)* to *(4)* corresponds to an increase in the electron affinity of the acceptor from 0.55 to 0.85 eV [4].

If it is considered that the electron affinity of a T-excited acceptor molecule is higher than that in the ground state by an amount equal to the T-excitation energy [5], the longwave absorption band (Fig. 1, e_1, f_1) of T-excited *(3)* and *(4)* in (PE) can be interpreted as a CT* band of electron transfer from (PE) as electron donor to T-excited *(3)* and *(4)* respectively:

$$D + A_T^* \rightarrow |DA_T^*| \xrightarrow{h\nu_{CT^*}} |\dot{D}^+\dot{A}^-|$$

This would be the first observation of a CT absorption band due to an *electron transfer from a donor to a triplet excited acceptor molecule* [6].

The energy of the CT* absorption can be estimated from:

$$h\nu_{CT^*} \approx IE(D) - EA(A_T^*) - E_C \qquad (1)$$

where IE(D) is the ionization energy of the solvated donor; EA(A) and $EA(A_T^*)$ are the electron affinities of the solvated acceptor in the ground state and the triplet excited state respectively; E_C is the coulombic interaction energy in the ion pair $[\dot{D}^+ \cdots \dot{A}^-]_{solv}$; E_{00} ($S_0 \rightarrow T_1$) is the T-excitation energy of the acceptor; $EA(A_T^*) = EA(A) + E_{00}(S_0 \rightarrow T_1)$.

IE(PE) = 9.3 eV [7]; $EA(3)$ = 0.55 eV and $EA(4)$ = 0.85 eV [4]; $E_{00}(S_0 \rightarrow T_1)$ = 23 × 10^3 cm^{-1} = 2.85 eV for *(3)* and *(4)*; $EA(3)_T^*$ = 3.4 eV; $EA(4)_T^*$ = 3.7 eV.

With $\tilde{\nu}_{CT}$ = 29 × 10^3 cm^{-1} (3.6 eV) for the n,π complex (PE)-tetracyanoethylene *(5)*, the relationship $E_C \approx IE(PE) - EA(5) - h\nu_{CT}$ with $EA(5)$ = 2.0 eV [4] gives E_C = 3.7 eV. Insertion of these values into eq. (1) yields $\tilde{\nu}_{CT_1^*}(PE) \cdot (3)_T^* \approx$ 17.7 × 10^3 and $\tilde{\nu}_{CT_1^*}(PE) \cdot (4)_T^* \approx$ 15.3 × 10^3 cm^{-1}.

The $\tilde{\nu}_{CT_1^*}$ values calculated in this manner lie — within the limit of errors of such an estimation — in the range of the *long wave* CT* absorption band (Fig. 1: e_1, f_1).

The energy difference of the absorption bands (Fig. 1: e_1, e_2 and f_1, f_2) show good agreement with the excitation energy $E_{00}(T_1 \rightarrow T_2)$ of the acceptor (≈ 15 × 10^3 cm^{-1}). Thus it may be supposed that the second absorption band (Fig. 1: e_2, f_2) at shorter wavelength is also a CT* absorption band, which can be calculated from

$$h\nu_{CT_2^*} = h\nu_{CT_1^*} + E_{00}(T_1 \rightarrow T_2)$$

However, in view of the great errors of such rough estimations a further detailed experimental study (*e.g.* polarization measurements) will be necessary.

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[3] For further details see *G. Briegleb* and *H. Schuster*, Z. Naturforsch. *a*, to be published.

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[6] Studies connected with fluorescence quenching provided evidence for a direct electron transfer without any need of *hν via* intermolecular complex formation

$$D_S^* + A \rightarrow |D_S^*A| \searrow$$
$$|\dot{D}^+\dot{A}^-|$$
$$D + A_S^* \rightarrow |DA_S^*| \nearrow$$

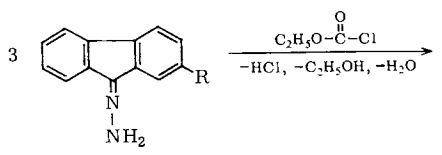
of a singlet excited donor or acceptor molecule with an acceptor or donor molecule in the ground state. Cf., *e.g.*, *H. Knibbe, D. Rehm*, and *A. Weller*, Ber. Bunsenges. physik. Chem. *73*, 839 (1969).

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An Unusual Reaction of Fluorenone Hydrazones

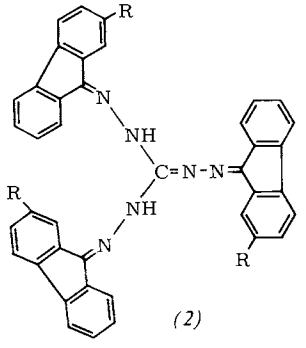
By *Joachim Gante* and *Günther Mohr* [*]

Reaction of fluorenone hydrazone *(1a)* [1] and 2-chlorofluorenone hydrazone *(1b)* [2] with ethyl chlorocarbonate in anhydrous ethyl acetate in the presence of triethylamine (molar ratio 1 : 1 : 1) did not yield the expected carbazates but, instead, *N,N',N''*-tris(fluorenylidenamino)guanidine *(2a)* (yield 46%, decomp. pt. 300 °C, brownish red crystals) and *N,N',N''*-tris(2-chlorofluorenylidenamino)guanidine *(2b)* (yield 25%, decomp. pt. 340 °C, brownish red crystals).



(1)

(a), R = H
(b), R = Cl



(2)

(2a) and *(2b)* are insoluble in almost all the usual organic solvents. They may be recrystallized from dimethylformamide. The composition of *(2a)* and *(2b)* follows from analysis and the IR spectrum. Chemical evidence for the structure was obtained by heating triaminoguanidine hydrochloride[3] with fluorenone (molar ratio 1 : 3) in ethanol/conc. hydrochloric acid (7 : 1) to give a product that was identical with *(2a)* according to its IR spectrum and analysis.

Attempts to prepare compounds corresponding to *(2a)* and *(2b)* by the same route from other hydrazones, such as benzaldehyde-, *p*-nitrobenzaldehyde-, and benzophenone hydrazone, proved unsuccessful; complicated mixtures were obtained instead.

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[1] *H. Wieland* and *A. Roseeu*, Liebigs Ann. Chem. *381*, 231 (1911).

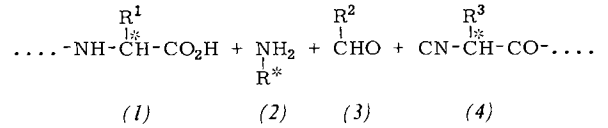
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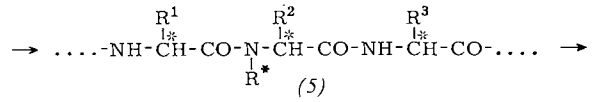
Stereorelating Syntheses of Planar Chiroids

By *Dieter Marquarding*, *Hans Klusacek*, *George Gokel*, *Peter Hoffmann*, and *Ivar Ugi*[*]

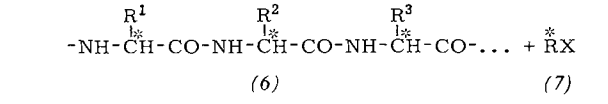
The success of asymmetrically induced four component peptide syntheses[1–3]



(1) *(2)* *(3)* *(4)*



(5)



(6) *(7)*

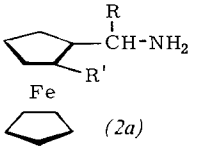
depends appreciably upon the amine component *(2)*[3] which, in this context, has to meet the following requirements:

a) The condensation of *(2)* with *(1)*, *(3)*, and *(4)*, if necessary *via* the Schiff base of *(2)* and *(3)*, should take place rapidly and in high overall yield[2].

b) As a component of the condensation, *(2)* must also have the effect of an asymmetrically inducing steric matrix and provide for a highly stereoselective synthesis of the newly formed amino acid unit in the desired configuration.

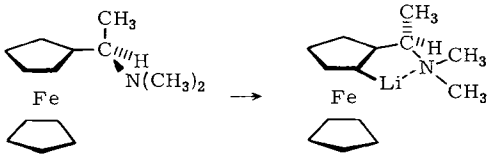
c) The residue R* must be readily cleaved from *(5)* under mild conditions, *e.g.* in cold formic or trifluoroacetic acid, preferably in such a manner that *(2)* can be regenerated from *(7)*.

Of all previously tested[2] amines *(2)* only those of type *(2a)* meet all the specifications (a)–(c)[4,5].

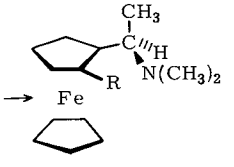


(2a)

Optically pure chiral ferrocene derivatives[**] with planar and central chirality can be obtained *via* the *stereorelating*[6] metalation of chiral tertiary α-ferrocenylalkylamines, as is illustrated by the example of the synthesis of *(10a)*–*(10e)* from *(8)*. Both antipodes *(8)* can be readily obtained by resolution of the racemate by (*R*)-(+)-tartaric acid [*(8)*-(*S*)-(*R*)-tartrate from methanol, *(8)*-(*R*)(*R*)-tartrate from the residue of the mother liquor by crystallization from acetone-water (10 : 1)].



(8)-(*R*) *(9)*-(*R*)(*R*)



(10a)-*(10e)*

The metalation of *(8)*-(*R*)[5] by *n*-butyllithium in ether leads almost exclusively (Q_{pn} = 96 : 4[7], by quantitative chromatography) to *(9)*-(*R*)(*R*)[6]. The methyl group of the side chain has to point "downward" when the (*R*)(*S*)-diastereomer of *(9)* is formed by a chelate mechanism[8,9] with the consequence that an appreciable repulsive interaction with the ferrocene system is witnessed.

The reactions of *(9)*-(*R*)(*R*) with alkylating agents (methyl and ethyl iodide[9], trimethylsilyl chloride[6]) or carbonyl compounds (formaldehyde, benzophenone[6]) produce *(10a)* to *(10e)*.

(10a): R = CH_3 (after treatment of the reaction mixture with dimethylamine), yield 66%, chromatography on Al_2O_3-acetone/hexane (1 : 4), b.p. 104–105 °C/0.2 torr, $[\alpha]_D^{20}$ = +32.9 °, *c* = 2.4 (ethanol).

(10b): R = C_2H_5 (after treatment of the reaction mixture with dimethylamine), yield 47%, b.p. 106–107 °C/0.2 torr, $[\alpha]_D^{20}$ = –16.2 °, *c* = 1.7 (ethanol).

(10c): R = $(CH_3)_3Si$, yield 61%, R_f = 0.55 [NH_3-treated SiO_2-ligroin/isopropanol (20 : 1)] b.p. 103–104 °C/0.04 torr, $[\alpha]_D^{20}$ = +15.5 °, *c* = 1.5 (ethanol).

(10d): R = $HOCH_2$, yield 58%, m.p. 109–110 °C (cyclohexane), $[\alpha]_D^{20}$ = +121.5 °, *c* = 1.4 (chloroform).

(10e): R = $HO(C_6H_5)_2C$, yield 52%, m.p. 118–119 °C (methanol), $[\alpha]_D^{20}$ = –191.6 °, *c* = 0.5 (ethanol).

Since the amines of type *(10)* are easily transformed (*e.g.* by retentive S_N1[4,5] or eliminations[4,9]) into other ferrocene

derivatives with planar or planar and central chirality, the asymmetrically induced metalation of chiral tertiary α-ferrocenylalkylamines provides a general basis for sterically predesignated syntheses and configurational assignments for optically pure compounds of the above mentioned classes[10].

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[**] In this and further papers by the present authors, the following procedure will be used with regard to the (*R*)(*S*)-nomenclature for the metallocenes [10, 11]: (a) The (*R*)(*S*)-nomenclature is confined to metallocenes with not more than two substituents per ring (*Ruch*'s class *a* [12]). Metallocenes with more than two substituents per ring represent chiroids of class *b* [12] and are therefore not subject to a right-left-classification like the (*R*)(*S*)-nomenclature (see also ref. [10]). (b) The observer looks upon the disubstituted ring along the main (C_5) axis of the metallocene framework. If the sequential priority [10] of the substituents decreases (or increases, respectively) on the shortest clockwise arc (*e.g.* 1→2 or 1→3), the configuration is termed an (*R*) (or an (*S*), respectively). (c) In the case of chiroids with several different types of classes of chirality elements, these are designated in the order: central axial, planar.

For example, in (*10c*)-(*R*)(*S*) the (*R*) refers to the side chain center of chirality and the (*S*) to the ligand sequence of the chirality plane of the ferrocene nucleus.

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New Method for the Preparation of 1,3-Diazetidinediones[1]

By *Herbert Helfert* and *Egon Fahr*[*]

1,3-Diazetidinediones *(3)* have hitherto been prepared by dimerization of isocyanates *(1)*. We have now found that these industrially important compounds can also be synthesized by cyclization of allophanyl chlorides *(2)*. The

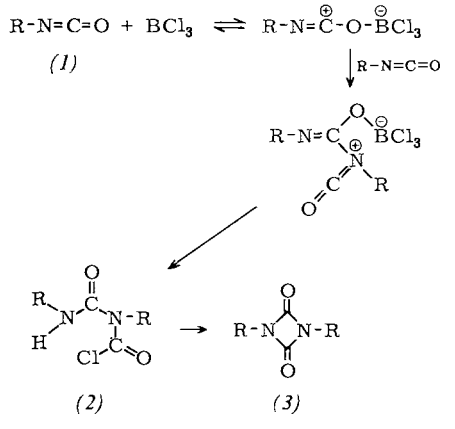
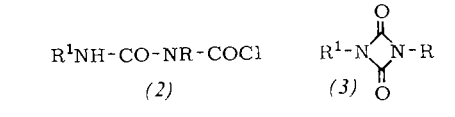


Table. Allophanyl chlorides *(2)* [4, 5] and diazetidinediones *(3)* [5].



No.	R	R^1	*(2)* [a] m.p. (°C)	*(2)* [a] yield (%)	*(3)* [c] temp. (°C)	*(3)* [c] time (h)	*(3)* [c] m.p. (°C)	*(3)* [c] yield (%) [d] [6]
(a)	C_6H_5	C_6H_5	120–122	70	20	12	176–177	95
(b)	o-CH_3–C_6H_4	o-CH_3–C_6H_4	100–102	55	−16	18	131–132	43
(c)	m-CH_3–C_6H_4	m-CH_3–C_6H_4	[b]	60	20	18	163–164	65
(d)	p-CH_3–C_6H_4	p-CH_3–C_6H_4	117–119	57	20	18	180–181	70
(e)	o-Cl–C_6H_4	o-Cl–C_6H_4	99–101	70	−16	10	141–142	35
(f)	m-Cl–C_6H_4	m-Cl–C_6H_4	86–88	53	20	10	173–174	66
(g)	p-Cl–C_6H_4	p-Cl–C_6H_4	138–139	54	20	10	176–177	63
(h)	o-NO_2–C_6H_4	o-NO_2–C_6H_4	170–171	36				
(i)	m-NO_2–C_6H_4	m-NO_2–C_6H_4	134–135	42	50	0.1	183–185	45
(j)	p-NO_2–C_6H_4	p-NO_2–C_6H_4	170–171	24	50	0.1	203 (dec.)	52
(k)	p-biphenylyl	p-biphenylyl	168–169	55	20	4	240–241	78
(l)	α-naphthyl	α-naphthyl	135–136	60	20	6	181–182	42
(m)	β-naphthyl	β-naphthyl	152–153	31	20	4	210–211	75
(n)	C_6H_5–CH_2	C_6H_5			20[e]	≈150	63–64	43
(o)	CH_3	CH_3						

[a] *(2a)*–*(2g)* were prepared in toluene, *(2h)*–*(2m)* in $CHCl_3$.

[b] *(2c)* could not be crystallized and isolated in analytically pure state.

[c] A number of diazetidinediones *(3)* have already been described in the literature (prepared by "dimerization" of isocyanate), albeit with melting points deviating from our values. Since the isocyanate reaction, unlike allophanyl chloride cyclization, can lead, *e.g.*. to trimeric isocyanates, it may be assumed that the respective authors had obtained products of higher molecular weight or mixtures of such products with *(3)*.

[d] Optimum yields are most readily obtained by following the decrease in intensity of the allophanyl chloride band at *ca.* 1740 cm^{-1}.

[e] Reaction of 2.8 mmoles of *(2n)* in 50 ml of water- and alcohol-free $CHCl_3$ with 10 ml of 2,6-lutidine.

previously inaccessible allophanyl chlorides *(2)* bearing aromatic substituents[2] were obtained by reaction of *(1)* with BCl_3[3].

Allophanyl chlorides (2)

An excess of gaseous BCl_3 (N_2 stream) is passed into a solution of isocyanate *(1)* (100 mmoles) in anhydrous toluene (200 ml) or water- and alcohol-free $CHCl_3$ (200 ml) at −60 °C. After 4 hours' stirring at 0 °C the reaction mixture is treated with ice-water (100 ml) and filtered to remove boric acid[4]. The aqueous phase is repeatedly extracted with solvent (see Table).

Diazetidinediones (3)[6]

Pyridine (10 ml) is added to *(2a)*–*(2g)* (2.5 mmoles) in anhydrous toluene (60 ml) or *(2i)*–*(2m)* in water- and alcohol-free $CHCl_3$ (100 ml) and the reaction mixture is worked up by pouring into ice-water, acidifying with conc. HCl, and extracting the aqueous phase with $CHCl_3$ (2 × 30 ml). Reaction of allophanyl chlorides bearing aliphatic [*e.g. (2o)*] or aliphatic and aromatic substituents [*e.g. (2n)*[7]] with pyridine yields complex products[1]. If 2,6-lutidine, which is blocked in the *o*-position, is used in place of pyridine for reaction with *(2n)* then the diazetidinedione *(3n)* is formed; with *(2o)* no reaction occurs.

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[1] Part of the Dissertation by *H. Helfert*, Universität Würzburg 1969.

[2] Allophanyl chlorides bearing aliphatic and aliphatic/aromatic substituents can be prepared by reaction of urea derivatives with phosgene: *H. Ulrich*, *J. N. Tilley*, and *A. A. R. Sayigh*, J. org. Chemistry *29*, 2401 (1964); *H. Ulrich* and *A. A. R. Sayigh*, Angew. Chem. *78*, 761 (1966); Angew. Chem. internat. Edit. *5*, 704 (1966).

[3] For the structure of the isocyanate/BCl_3 adducts and their reaction to give allophanyl chlorides, see *E. Fahr* and *L. Neumann*, Liebigs Ann. Chem. *715*, 15 (1968); *721*, 14 (1969), and ref. [1].

[4] In the case of *(2h)*–*(2j)* and *(2m)* a mixture of boric acid and *(2)* is precipitated; *(2)* is extracted with hot toluene.

[5] Satisfactory elemental analyses were obtained for the compounds.

[6] On cylization of *(2)*, isocyanates *(1)* are formed as by-products, both by monomerization of *(3)* and also directly from *(2)*. Compound *(2h)* gave only *(1h)*.

[7] Prepared from benzylphenylurea by a method based on that given in ref. [2] (yield 50%, m.p. 86–88 °C [5]).

Condensation of Dialkyl Sulfone Diimines with Malonic Esters

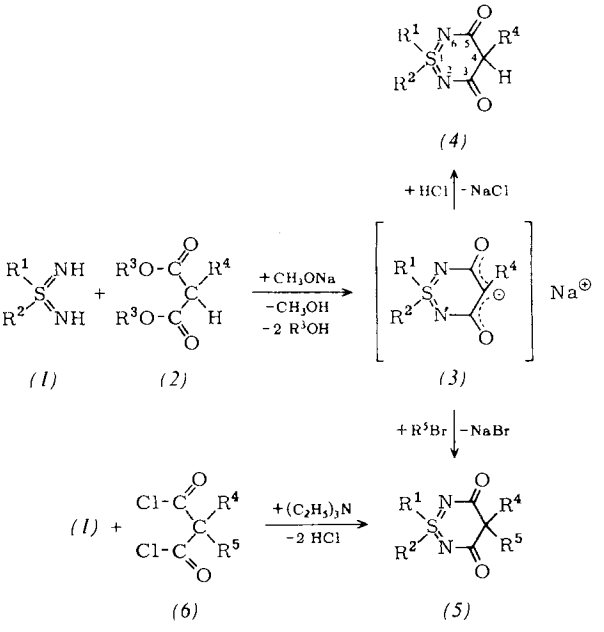
By *Manfred Haake*[*]

Dialkyl sulfone diimines *(1)*, which are accessible by chloroamination of thioethers[1], can be condensed with unsubstituted and monosubstituted malonic esters *(2)* in the presence of sodium methoxide to give novel 3,5-dioxo-3*H*-4,5-dihydro-1,2,6-thia$^{(IV)}$diazines *(4)*.

After dissolution of an equivalent amount of sodium in anhydrous methanol and addition of components *(1)* and *(2)* the reaction mixture was refluxed for one day. On prolonged standing, a portion of the sodium salt *(3)* crystallized from the cool solution. Compounds *(4)* were isolated by neutralization of the reaction mixture with dilute hydrochloric acid and extraction of the residue with boiling isopropanol, from which they crystallize on cooling.

Dialkyl malonates do not react with *(1)*. However, the 4,4-dialkylated compounds *(5)* can be prepared by alkylation of the salts *(3)*. Thus *(5a)* was obtained by reaction of ethyl methyl sulfone diimine[2] with ethyl malonate to give the salt *(3)* which was allowed to react with a slight excess of ethyl bromide.

Reaction of *(1)* with dialkylmalonyl dichloride *(6)* in the presence of triethylamine also yields compounds of type *(5)*. Thus *(5b)* was prepared by stirring equivalent amounts of dimethyl sulfone diimine and dimethylmalonyl dichloride with a five-fold excess of triethylamine in dry benzene for one day.



	R^1	R^2	R^3	R^4	R^5	M.p. (°C)	Yield (%)
(4a)	CH_3	CH_3	C_2H_5	C_2H_5	H	190	52
(4b)	CH_3	CH_3	CH_3	H	H	206	67
(4c)	CH_3	CH_3	C_2H_5	C_6H_5	H	245	34
(4d)	CH_3	C_2H_5	C_2H_5	C_2H_5	H	181	55
(5a)	CH_3	C_2H_5	C_2H_5	C_2H_5	C_2H_5	195	44
(5b)	CH_3	CH_3	–	CH_3	CH_3	215	42

(4) and *(5)* are colorless, hygroscopic substances that readily dissolve in water (with the exception of *(4a)*) and decompose at their melting points. Their structures were established by elemental analysis and spectroscopic data.

In addition to a strong band at 1640 cm^{-1} (ν_{CO}), the IR spectra (KBr) contain intense bands at 1330 and 1050 cm^{-1} (possibly due to ν_{NSN}[3]).

In the NMR spectra ([D_6]-DMSO, TMS as internal standard), all the *S*-methyl groups appear at δ = 3.6 (s) and the *S*-ethyl groups of *(4d)* and *(5a)* at 3.7 (q) and 1.3 (t) ppm, resp. The signals of the protons attached to C-4 are observed at 3.0 [(t) for *(4a)* and *(4d)*, (s) for *(4b)*] and 4.3 ppm [(s) for *(4c)*], those of the ethyl groups on C-4 in *(4a)* and *(4d)* and in *(5a)* at 2.0 (m) and 0.8 (m), resp., that of the phenyl group on C-4 in *(4c)* at 7.6 (s), and that of the methyl group on C-4 in *(5b)* at 1.3 (s) ppm.

On addition of D_2O, the protons on C-4 are seen to undergo rapid exchange; a gradual exchange of the *S*-alkyl protons in the α position may also be observed.

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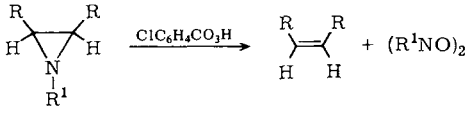
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Stereospecific Deaminations of Some *N*-Alkylaziridines by *m*-Chloroperbenzoic Acid[1]

By *Harold W. Heine, Jay D. Myers*, and *Edward T. Peltzer III*[*]

When *cis*-1-benzyl- [*cis-(1a)*] or *cis*-1-cyclohexyl-2,3-dibenzoylaziridine [*cis-(1b)*][1a,2] was treated with an equivalent quantity of *m*-chloroperbenzoic acid in benzene in the dark at room temperature for 24 h and the reaction mixture worked up by extracting with aqueous sodium carbonate, drying the benzene layer over anhydrous magnesium sulfate, filtering, and evaporating the benzene in the dark, 85—90% yields of a mixture of the known *cis*-dibenzoylethylene [*cis-(2)*][3] and known nitroso dimer [either *(3a)* or *(3b)*, respectively][4] were obtained. Similar treatment of *trans-(1a)* and *trans-(1b)* gave 90% yields of *trans-(2)* and nitroso dimer.



cis-(1) *cis*-(2) (3)

(a), $R^1 = C_6H_5CH_2$

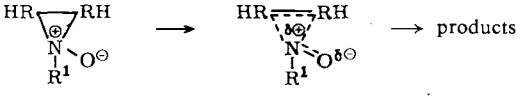
(b), R^1 = 

R = C_6H_5CO

The dimer of α-nitrosotoluene *(3a)* could be separated from *cis-(2)* or *trans-(2)* by dissolving the crude reaction products in a very small quantity of hot ethyl acetate, cooling, and filtering. Authentic samples of the *cis*- and the *trans*-dibenzoylethylenes[3] and the dimer of α-nitrosotoluene[4] were prepared by known procedures for purposes of comparison.

The deamination reaction and the work-up of the reaction mixture must be carried out in the dark to avoid extensive isomerization of *trans-(2)* to *cis-(2)*.

The stereospecific course of the reaction suggests a concerted mechanism for the deamination. The products probably arise *via* an intermediate such as *(4)*.



(4)

The results are to be compared with the reaction of 1,2,3-triphenylaziridine with *m*-chloroperbenzoic acid in methylene chloride. In this case, a non-stereospecific deamination occurred with the formation of 7% *cis*-stilbene, 7% *trans*-stilbene, 14% nitrosobenzene, 16% benzaldehyde, 8% benzylideneaniline, and 19% of a mixture of *cis*- and *trans*-stilbene oxides[5].

The reaction was also successfully extended to 3-benzyl-1,5-diphenyl-9,3-oxazatricyclo[3.3.1.$0^{2,4}$]nonan-7-one[6]. Treatment of the latter compound with at least a two-fold excess *m*-chloroperbenzoic acid afforded a 64% yield of 1,5-diphenyl-3,9-dioxatricyclo[3.3.1.$0^{2,4}$]nonan-7-one (m.p. 124 to 126 °C), which was characterized by elemental analyses and NMR and mass spectroscopy. Here the deamination reaction to the corresponding alkene was followed by an epoxidation.

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Determination of Halide Ions by Gas Chromatography[1]

By *H. A. Rüssel*[*]

One method of converting hydrophilic, non-volatile halide ions in aqueous solution into readily volatile compounds lies in their reaction with 1,2-olefin oxides to give halogeno alcohols[2].

The reaction proceeds at a satisfactory rate, but leads to uniform products only with ethylene oxide. The reaction solution must be acidic; since addition of sulfuric or phosphoric acid promotes the already inevitable formation of glycol it is advisable to convert the halide ions into the hydrohalic acids in a strongly acidic ion exchanger. After passage of ethylene oxide and prolonged standing the sample is subjected to gas chromatography, whereupon the resulting compounds 2-chloro-, 2-bromo-, and 2-iodoethanol proved readily separable (Fig. 1). Conversions were practically quantitative; an interpretable signal was obtained at concentrations as low as 0.5×10^{-4} M hydrochloric acid.

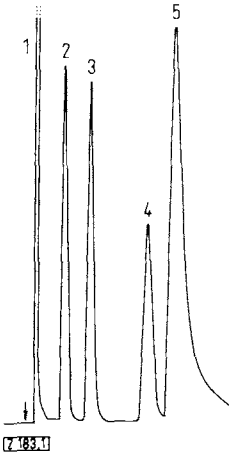


Fig. 1. Gas chromatogram: 1, ethylene oxide; 2, 2-chloroethanol; 3, 2-bromoethanol; 4, 2-iodoethanol; 5, ethylene glycol.

Experimental:

Solutions of the halides are converted into the corresponding acids by reaction with a strongly acidic ion exchanger. Ethylene oxide is passed (2 bubbles/s) into the ice-cooled acid (10.0 ml) for 15 min; alternatively, liquid ethylene oxide (1 ml) is added to the acid. After 1 hour, the volume is made up to 15.0 ml and 1 μl of the solution is injected into the gas chromatograph.

Conditions: 2 m column, 12% EGS on Gaschrom P, 100 °C (determination of very small amounts of chloride is best carried out at 80 °C), 60 ml N_2, FID; gas chromatograph: Packard 7839.

Example: A solution that was 0.1 N in hydrochloric, hydrobromic, and hydriodic acid was analyzed (cf. Fig. 1) and the

gas chromatogram compared with those of solutions containing known amounts of 2-chloro-, 2-bromo-, and 2-iodoethanol.

	Peak area (mm^2)	Conversion (%)
HCl	894	95
HBr	909	96
HI	934	99

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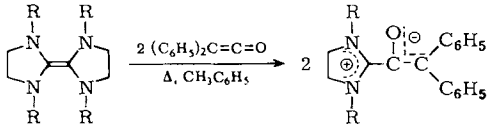
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Stable Dipoles from 1,1',3,3'-Tetraaryl-2,2'-biimidazolidinylidenes and Ketenes[1] [**]

By *Manfred Regitz*, *Jürgen Hocker*, and *Bernd Weber* [*]

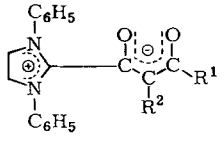
The exceptional reactivity of electron-rich olefins[2] is also evident in the reaction of the 1,1',3,3'-tetraaryl-2,2'-biimidazolidinylidenes *(1a)* and *(1b)* with diphenylketene, which proceeds *via* scission of the double bond to give the stable dipoles *(2a)* and *(2b)*. They are characterized by the extreme readiness with which they undergo (3 + 2)-cycloaddition with, *e.g.*, phenyl isothiocyanate and dibenzoylacetylene.



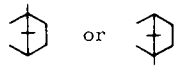
(1) *(2)*

(a), R = C_6H_5 *(b)*, R = p-$CH_3OC_6H_4$

Acylated ketenes, formed by Wolff rearrangement from 1,3-dioxo-2-diazo compounds, dimerize very rapidly. If the Wolff rearrangement is carried out in the presence of *(1a)*, however, the dipoles *(3a)*–*(3d)* derived from the monomeric



(3)

(a), $R^1 = R^2 = C_6H_5$
(b), $R^1 = OC_2H_5$, $R^2 = CH_3$
(c), R^1, R^2 = 
(d), R^1, R^2 = 

ketenes are obtained. As β-diketone enolates, they give a reddish-brown color on reaction with iron(III) chloride; a 1 : 1 complex (m.p. 210 °C) was isolated in the case of *(3a)*.

Owing to electron delocalization in the anionic part of the molecule, a long-wave CO absorption is observed in the IR spectrum of all the dipoles; compared with imidazolidines[3] the NMR signals of the CH_2 protons in the cationic part are shifted downfield as a result of decreased shielding (see Table).

Cpd.	Yield (%)	M.p. (°C)	NMR in $CDCl_3$ δCH_2 (ppm)
(2a)	74	178	3.98
(2b)	80	181	3.98
(3a)	95	228–230	4.08
(3b)	60	208–210	4.36, 4.39
(3c)	37	205–208	4.38–4.44
(3d)	78	211	4.23–4.64

2,2-Diphenyl-1-(1,3-diphenyl-4,5-dihydro-2-imidazolio)-vinylate (2a)

Phenylbenzoyldiazomethane (6.66 g, 30 mmoles) in absolute toluene (90 ml) is refluxed under nitrogen for 30 min, allowed to cool and, after addition of *(1a)* (6.66 g, 15 mmoles), again heated for 20 min. Pecipitation of *(2a)* starts while the red solution is still hot. On cooling, 9.3 g (74%) of the red compound *(2a)* is obtained (recrystallized from chloroform/ether).

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Xenon(II) Fluoride Pentafluoroorthotellurate as Fluoride Donor: $[XeOTeF_5]^+$ $[AsF_6]^-$

By *Friedrich Sladky* [*]

Xenon difluoride reacts with stoichiometric amounts of pentafluoroorthotelluric acid with loss of HF to give xenon(II) fluoride pentafluoroorthotellurate *(1)*[1] and xenon(II) bis(pentafluoroorthotellurate)[2]. With fluoride acceptors of type EIF_5 (*e.g.* El = As or noble metal), the salts $[XeF]^+$ $[EIF_6]^-$, $[XeF]^+$ $[El_2F_{11}]^-$, and $[Xe_2F_3]^+$ $[EIF_6]^-$ are formed[3].

Two routes are feasible for a reaction of *(1)* with equimolar amounts of EIF_5:

$$FXeOTeF_5 + EIF_5 \quad (1) \quad \begin{cases} \nearrow [XeF]^+ [F_5EIOTeF_5]^- \\ \searrow [XeOTeF_5]^+ [EIF_6]^- \end{cases}$$

The behavior of *(1)* towards BF_3, PF_5, and AsF_5 has been investigated; in the case of BF_3 or PF_5 no reaction takes place. Gentle warming of a mixture of *(1)* (which is a liquid at room temperature) and an excess of AsF_5 results in immediate formation of a bright yellow 1:1 adduct, m.p. 160 °C (in a glass capillary, partial decomposition), which can be sublimed very slowly and without decomposition in an oil-pump vacuum (10^{-3} torr).

The Raman spectrum of the product (He-Ne laser) is characteristic of a hexafluoroarsenate — AsF_6^- (O_h): ν_1 = 668 (vs), ν_2 = 596 (w), ν_5 = 385 (m) cm^{-1} — and in good agreement with the spectrum of the hexafluoroarsenate *(3)* (ν_1 = 683 (vs), ν_2 = 575 (w), ν_5 = 369 (m) cm^{-1})[3], whose structure has been confirmed by single crystal X-ray structure analysis[4]. The band ν_{Xe-F} that appears at 520 cm^{-1} in the Raman spectrum of *(1)* is absent. Consequently, the 1:1 adduct has to be formulated as the salt $[XeOTeF_5]^+$ $[AsF_6]^-$ *(2)*.

With increasing electronegativity of the second ligand in F_5TeO-substituted xenon(II) compounds, *i.e.* with increasing cationic character of the $XeOTeF_5$ group, a shift of the XeO

stretching vibration to higher wave numbers is observed [ν_{Xe-O} (cm^{-1}): $Xe(OTeF_5)_2$ 434; $FXeOTeF_5$ 457; $XeOTeF_5^+$ 477]. This tendency is already apparent to a greater extent in the transition $XeF_2 \rightarrow XeF^+$; the XeF valence force constant is about 30 % greater in the cation [3].

$Xe(OTeF_5)_2$ does not react with AsF_5, even above the melting point.

$$Xe(OTeF_5)_2 + AsF_5 \not\rightarrow [XeOTeF_5]^+ [F_5AsOTeF_5]^-$$

The fluoride donor strengths of *(1)* and XeF_2 appear to be similar. Both compounds donate F^- to AsF_5, but not the weaker acceptors BF_3 and PF_5. XeF_2, however, can displace *(1)*:

$$\underset{(2)}{} + 2\ XeF_2 \rightarrow \underset{(3)}{[Xe_2F_3]^+ [AsF_6]^-} + \underset{}{(1)}$$

The reaction is quantitative at 60 °C. Salt *(3)*, which crystallizes monoclinically, was identified from Debye-Scherrer photographs; compound *(2)*, on the other hand, is orthorhombic according to preliminary powder- and Buerger precession photographs.

Present results indicate the relative order of the fluoride donor strengths of xenon compounds to be:

$$XeF_4 \ll FXeOTeF_5 < XeF_2 < XeF_6$$ [5].

Experimental:

All reactions were followed tensimetrically in a Monel system and gravimetrically in easily weighable reaction vessels (Kel-F).

$FXeOTeF_5$ (2.319 g, 5.96 mmoles) was allowed to react with an excess of arsenic pentafluoride ($\approx$ 1400 torr) at 60 °C over a period of several hours. After pumping off the excess of AsF_5, 3.333 g of $[XeOTeF_5]^+ [AsF_6]^-$ could be isolated, yield 90 %.

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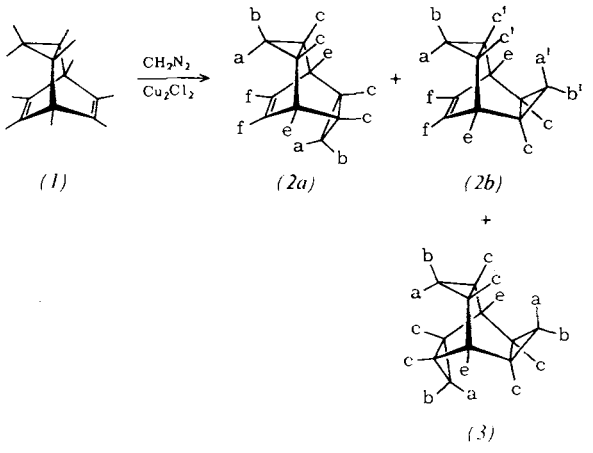
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"Trishomobarrelene" and "Trishomobullvalene"

By *Armin de Meijere* and *Christian Weitemeyer* [*]

The stabilization of a carbonium ion by α-cyclopropyl groups has been verified in many cases [1]. In this connection the highly symmetric compounds "trishomobarrelene" *(3)* [2a] and "trishomobullvalene" *(7)* [2b] are of interest since they are rigid tricyclopropylmethyl ring systems [3]. Their bridgehead reactivities should, therefore, play a special role [4]. We wish to report here on the synthesis of these novel hydrocarbons [5].

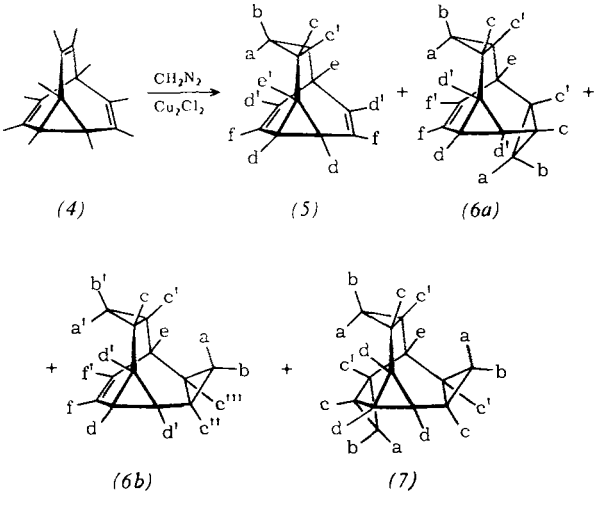
"Homobarrelene" *(1)* [6] was treated with diazomethane in the presence of copper(I) chloride. The following products were isolated from the reaction mixture by preparative gas chromatography: the isomeric "bishomobarrelenes" *(2a)* (46 %) and *(2b)* (25 %), the "trishomobarrelene" *(3)* (27 %), and unreacted *(1)* (1 %).



(1) *(2a)* *(2b)* *(3)*

The analogous reaction of bullvalene *(4)* [7] with diazomethane in the presence of copper(I) chloride afforded a mixture of *(4)* (14 %), "homobullvalene" *(5)* (33 %), the two isomeric "bishomobullvalenes" *(6a)* (15 %) and *(6b)* (27 %), and "trishomobullvalene" *(7)* (10 %).

Assignment of structures was based mainly on spectroscopic findings. A distinction between *(2a)* and *(2b)* is possible by NMR spectroscopy because of the long range shielding effect of the cyclopropane rings on the olefinic protons [8]. In *(2a)* two cyclopropane rings act in this way on the olefinic protons; consequently their signal is shifted to $\tau = 4.73$ compared to $\tau = 4.06$ in the case of *(2b)* and $\tau = 3.54$ for the olefinic protons in *(1)* which are not additionally shielded [6].



(4) *(5)* *(6a)* *(6b)* *(7)*

"Homobullvalene" *(5)* [9], because of its homotropylidine system, is a molecule with fluctuating bonds; this is confirmed by the NMR spectrum. The isomers *(6a)* and *(6b)* can be distinguished in the same way as the isomers *(2a)* and *(2b)*. Compared to the barrelene system, the structure of these molecules is extended at one bridgehead and consequently the two cyclopropane rings in *(6a)* have a shielding effect on only one of the two olefinic protons ($\tau = 5.00$ for H^f and $\tau = 4.32$ for $H^{f'}$); this effect is less pronounced in the case of *(6b)* ($\tau = 4.32$—4.72 for H^f and $H^{f'}$).

The unidirectional arrangement of all three cyclopropane rings in *(3)* [9] and *(7)* [9] is suggested by an examination of molecular models. It is confirmed by the ratio of the NMR signal intensities [*(3)*: H^a:H^c:H^b = 3:6:3; *(7)*: H^a:(H^c+ H^d): H^b = 3:9:3] and also, in the case of *(3)*, by the relatively small number of absorptions in the IR spectrum, which is

consistent only with the highly symmetrical structure [point group C_{3h} for *(3)*].

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[1] See references given in [4a].

[2] Systematic name: a) pentacyclo[3.3.3.$0^{2,4}$.$0^{6,8}$.$0^{9,11}$]undecane; b) hexacyclo[4.4.3.$0^{2,4}$.$0^{5,7}$.$0^{8,10}$.$0^{11,13}$]tridecane.

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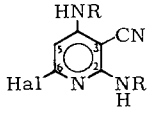
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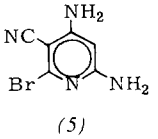
[9] Satisfactory C,H analyses were obtained for this compound.

Simple Synthesis of 2,4-Diaminopyridines[1]

By *Peter Boldt*, *Wilfried Thielecke*, and *Jürgen Oberdörfer*[*]

Malononitrile can be *C-tert*-alkylated by tertiary alkyl halides in the presence of Lewis acid catalysts[2]. We have now tried to introduce secondary alkyl groups in the same way. Reaction of isopropyl bromide/aluminum chloride with malononitrile, however, did not yield the expected product but — as was shown by elemental and spectroscopic analyses — 2,4-bis(isopropylamino)-6-bromo-3-cyanopyridine *(1)*.

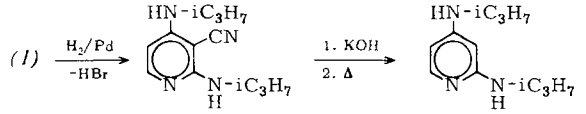




(5)

	R	Hal
(1)	*i*-propyl	Br
(2)	*i*-propyl	Cl
(3)	*cyclo*-C_6H_{11}	Cl
(4)	H	Br

The position of the substituents in *(1)* was established from the NMR spectra of the compounds *(6)* and *(7)*, which are accessible from *(1)* by hydrogenolytic removal of bromine (Pd-$BaSO_4$/H_2, 55 % yield) followed by hydrolysis of the nitrile group (10 %) and finally decarboxylation (100 %).



(6) *(7)*

Similarly, reaction of malononitrile/aluminum chloride with isopropyl chloride or cyclohexyl chloride affords pyridine derivatives, which, on the basis of analytical data and by analogy with *(1)*, could be assigned the structures *(2)* and *(3)*. Reaction of malononitrile with hydrogen bromide in benzene yields compound *(5)* (72%, as hydrobromide) and not *(4)*, as was assumed in earlier reports[3]: replacement of bromine by hydrogen (Pd-$BaSO_4$/H_2, 60 %) gives a product whose ring protons are, according to the NMR spectrum, *para* to each other, and which affords 2,4-diaminopyridine[4] after hydrolysis (60 %) and decarboxylation.

2,4-Bis(isopropylamino)-6-chloro-3-cyanopyridine (2)

An ice-cold solution of malononitrile (26.5 g, 0.4 mole) in nitromethane (80 ml) is treated successively with solutions of aluminum chloride (53.3 g, 0.4 mole) in nitromethane (80 ml) and isopropyl chloride (41 g, 0.52 mole) in nitromethane (20 ml), and, after 45 hours at +3 °C, with aqueous sodium bicarbonate (ice-cold). The reaction mixture is then filtered and the residue and filtrate are extracted with ether (Soxhlet in the case of the residue). Both extracts are combined, evaporated to dryness, and the resulting residue [17.5 g *(2)*, 35 % w. r. t. malononitrile] is purified by recrystallization from ethanol followed by sublimation (120 °C/12 torr); m.p. (after sublimation) 144—145 °C (corr.). [*(1)*: m.p. 161 to 161.5 °C, 20 %; *(3)*: m.p. 127—127.5 °C, 33 %].

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[1] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the State of Niedersachsen.

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[3] *W. J. Middleton*, US.-Pat. 2790806 (April 30, 1957), Du Pont; Chem. Abstr. *51*, P. 14829 (1957).

[4] We thank Prof. Dr. *J. den Hertog* for supplying us with a comparison sample of 2,4-diaminopyridine.

The Equilibrium "Azepine ⇌ Benzene Imine"[1][**]

By *Horst Prinzbach*, *Dieter Stusche*, and *Rainer Kitzing*[*]

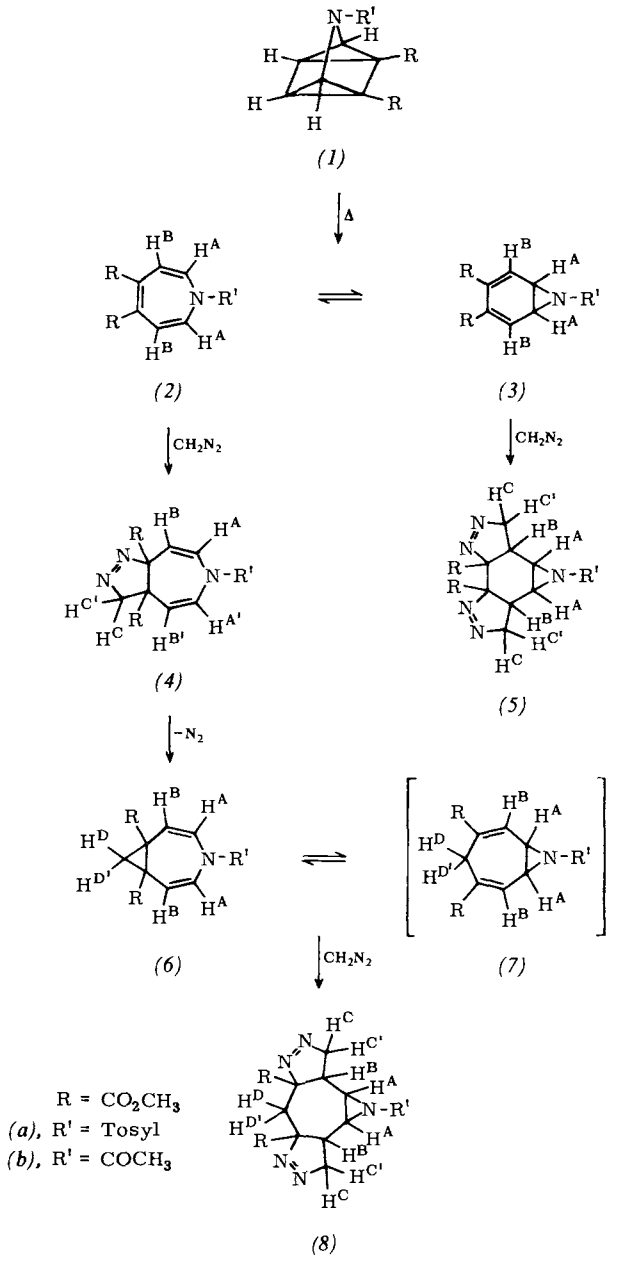
Although existence of the equilibrium oxepin ⇌ benzene oxide has been confirmed on many occasions[2] by NMR measurements and adduct formation, a tautomerism azepine ⇌ benzene imine has not hitherto been established by the same criteria. Aromatization to aniline derivatives or aromatization with elimination of nitrogen have so far been the only indications of such a tautomerism[3].

We have now found evidence for the equilibrium azepine ⇌ benzene imine in that we have been able to isolate *(5a)* as a product of the reaction of *N*-tosyl-4,5-bis(methoxycarbonyl)-azepine *(2a)*[4] with diazomethane [1 g (2.8 mmoles) of *(1a)* or *(2a)*[5] and *ca.* 0.32 g (7.6 mmoles) of CH_2N_2 in CH_2Cl_2 (50 ml), 72 h, 20 °C; after concentration the pyrazoline is precipitated by addition of ether].

In our opinion, the way the diazomethane molecules are oriented in *(5a)* rules out an attack on *(2a)* and subsequent isomerization.

In addition to *(5a)* smaller yields of *(8a)* were isolated whose presence we explain as being due to competitive addition of CH_2N_2 to *(2a)* to give *(4a)* followed by loss of nitrogen to give the homoazepine *(6a)*, Cope rearrangement to give *(7a)*, and addition of CH_2N_2 to the CC double bonds, which are now activated by ester groups, to give *(8a)*.

Results in the *N*-acetyl series are in agreement with these hypotheses. Both *(1b)* and *(2b)* react with diazomethane [1 g (4.0 mmoles) of *(1b)* in ether (100 ml) and 0.64 g (15 mmoles) of CH_2N_2, 48 h, 20 °C] to give the labile monopyrazoline *(4b)*, which loses nitrogen on standing to give the homoazepine *(6b)*. At temperatures between +60 and —50 °C the NMR spectrum shows a temperature



R = CO_2CH_3
(a), R' = Tosyl
(b), R' = $COCH_3$

dependence for H^A and H^B (weak, acetyl rotation), but not for H^D. Reaction of *(6b)* with an excess of diazomethane, however, affords a bisadduct *(8b)* that is obviously derived from *(7b)*. Addition of a large excess of CH_2N_2 to *(2b)* (ratio *ca.* 4 : 1) results in direct formation of *(8b)*; *(5b)* could not be detected.

By analogy with the substitution-dependence of the equilibrium cycloheptatriene ⇌ norcaradiene[3] it can be reasoned that strongly electron attracting groups on the nitrogen favor the bicyclic form *(3)*. According to preliminary measurements, the NMR spectrum of *(2a)*, unlike that of *(2b)*, is temperature-dependent in the range +40 to −68 °C ($CDCl_3$).

The structures of the new compounds are established by elemental analyses and by UV-, IR-, and NMR spectra (see Table). The coupling constants of the methylene protons and the $n\rightarrow\pi^*$ transitions are typical of 1-pyrazolines. The *cis* configuration of the pyrazoline rings in the case of *(5a)*, *(8a)*, and *(8b)* follows from the NMR spectra; the structure of *(5a)* is further confirmed by the fact that azatrishomobenzene is formed on photolysis[6]. The coupling constant $J_{H^AH^B}$ of *ca.* 5 Hz determined for this compound by spectrum simulation[7] indicates the probability of an all-*cis* configuration of the pyrazoline and aziridine rings in *(5a)*.

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[7] We thank Dipl.-Chem. *H. H. Limbach* for his assistance.

Cpd. m.p. (°C)	NMR (τ) [a] H^A	H^B	N–R'	$-CO_2CH_3$	H^C	H^D	UV [b] λ_{max} (nm; ε)
(4b)	2.89 (1, br. D) 4.50 (1, D)		7.68 (3, S)	6.32 (3, S)	5.33 (1)		
	3.13 (1, br. D) 4.80 (1, D)			6.18 (3, S)	4.86 (1)		
132	$J_{AB} = J_{A'B'} = 10.5$ Hz				$J_{C/C'} = 17.0$ Hz		
(5a)	6.65 (2, M)	7.30 (2, M)	2.26 (2, A_2)	6.20 (6, S)	5.25 (2)		322 (405)
			2.60 (2, B_2)		5.85 (2)		272 (510)
116			7.50 (3, S)		$J_{C/C'} = 17.0$ Hz		262 (740)
					$J_{B/C'} = 7.5$ Hz		254 (680)
					$J_{B/C} = 5.5$ Hz		
(6b)	3.18 (2)	4.67 (2)	7.68 (3, S)	6.28 (6, S)		7.52 (1)	248 (13700)
						8.77 (1)	
109	$J_{AB} = 9.5$ Hz					$J_{D/D'} = 4.0$ Hz	
(8a)	6.70–7.10 (4, M)		2.29 (2, A_2)	6.23 (6, S)	5.16 (2)	7.77 (1)	
			2.58 (2, B_2)		5.60 (2)	6.20 (1)	
			7.51 (3, S)		$J_{C/C'} = 18.0$ Hz	$J_{D/D'} = 15.0$ Hz	
140					$J_{B/C} = 5.5$ Hz		
					$J_{B/C'} = 8.0$ Hz		
(8b)	7.20–7.45 (2, M)	6.7–7.1 (2, M)	8.00 (3, S)	6.16 (6, S)	4.94 (2)	6.12 (1)	323 (330)
					5.14 (2)	7.50 (1)	
136					$J_{C/C'} = 18.0$ Hz	$J_{D/D'} = 15.0$ Hz	
					$J_{B/C} = 6.0$ Hz		
					$J_{B/C'} = 7.5$ Hz		

[a] In $CDCl_3$. [b] In CH_3OH.

Structure of Cycloheptasulfur

By *Isao Kawada* and *Erwin Hellner*[*]

We are engaged in the structural elucidation of the first sulfur ring known to contain an uneven number of atoms, *i.e.* cycloheptasulfur, which was recently prepared by *Max Schmidt et al.*[1,2].

The substance forms pale yellow needles that rapidly decompose at room temperature. It was therefore necessary to fit the Weissenberg camera with a low-temperature device[3] (cooling to −80 ± 1 °C with a stream of N_2) in order to carry out an X-ray study on a single crystal (length *ca.* 3 mm, thickness 0.2 mm). A photograph of the layers *hk*0 to *hk*5 with $Cu_{K\alpha}$ radiation afforded the following crystallographic data: a = 21.77 ± 0.04, b = 20.97 ± 0.04, c = 6.09 ± 0.01 Å; $\alpha = \beta = \gamma = 90°$; d_{exp} (20 °C) = 2.090, $d_{X\text{-ray}}$ (−80 °C) = 2.144 g cm^{-3}; Z = 16.

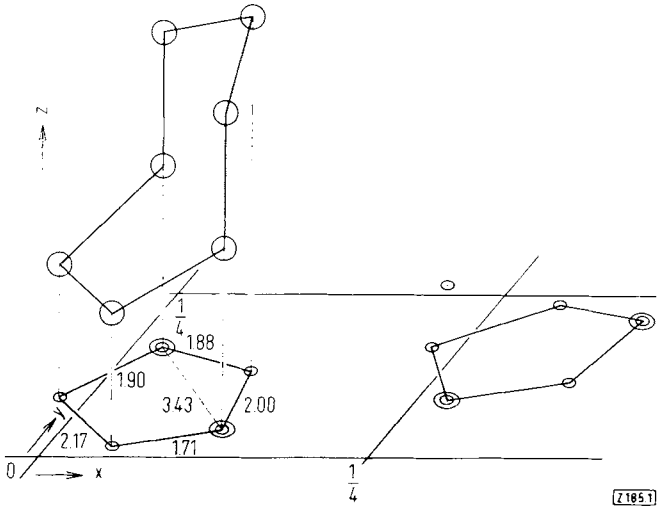


Figure. Perspective diagram of a cycloheptasulfur molecule and projection on the *xy* plane (distances given in Å).

C..a was found as extinction symbol; the space group could not, however, be determined unequivocally. The initially studied *xy* projection belongs to the planar pgg group with $a' = a/2$ and $b' = b/2$. The intensities of 137 independent *hk*0 reflections were estimated visually and the phases of the 40 strongest reflections ($E \geq 1.0$) determined unambiguously by the method of symbolic addition. A Fourier synthesis calculated with these values shows five maxima arranged in the form of a ring, two of which are doubly weighted, *i.e.* a projection of a seven-membered ring.

The x and y parameters were refined by the method of least squares. For the two double maxima we inserted twice the structure factor of sulfur. After six cycles the R factor was 20.9 % for all 137 reflections and 12.7 % for the observed reflections only.

The projection indicates a seven-membered ring in a chair configuration; in the projection on the *xy* plane two sets of atomic coordinates overlap (see Figure).

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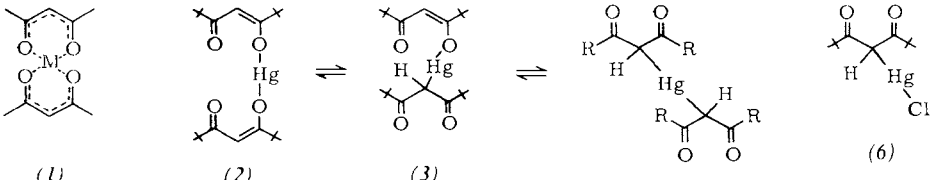
[3] We are grateful to Dipl.-Phys. *U. Sondermann* for fitting the low-temperature cooling device.

The Structure of Mercury Compounds of 2,4-Pentanediones[1]

By *Karsten Flatau* and *Hans Musso*[*]

All metals so far investigated[2,3] react with 2,4-pentanedione to give soluble chelate complexes of type *(1)* in which the metal atom is equidistant from both oxygen atoms and the bonds are symmetrically delocalized. Since mercury tends to coordinate linearly with two organic ligands[4] an elucidation of the structure of Hg derivatives of 2,4-pentanedione appeared to be of interest. The chelates *(1)* show a characteristic broad long wavelength C—O band at 1580 cm^{-1} in the IR spectrum[5]. The mercury complex of 2,2,6,6-tetramethyl-3,5-heptanedione, however, exhibits a sharp C=O absorption band at 1678 cm^{-1}. *Nonhebel* has, therefore, suggested the open enolate structure *(2)* for this compound[6]. In this communication we present evidence that mercury is bonded to the central carbon atom of such β-ketones.

At room temperature the ^{1}H—NMR spectrum of the complex prepared according to the method given in ref.[6] consists of a sharp signal at −1.18 ppm (TMS, internal) for the two equivalent *tert*-butyl groups and a broad signal at −5.05 ppm for the proton on the central C atom. At −40 °C this latter signal splits into four sharper components. The most intense signal is at −4.86 ppm and is flanked by two symmetrical satellites whose intensities are about 10 % of the total, thus indicating a H—C—Hg coupling of J = 221 Hz (^{199}Hg is about 18 % abundant in natural mercury, and possesses a nuclear spin of $I = 1/2$). The weakest signal at −5.75 ppm is assigned to the olefinic protons of the



enolates *(2)* or *(3)*, which are present in about 3 % in equilibrium with *(4)*. A splitting is also visible on the downfield side of the *tert*-butyl singal (d in the Figure). On addition of 2,2,6,6-tetramethyl-3,5-heptanedione *(7)*, the intensities of the signals assigned to structure *(2)* and *(3)* increase. When mercuric chloride is added the H—C—Hg coupling vanishes and signals of the complex *(6)*, which can also be isolated, appear at −5.16 and −1.20 ppm, thus indicating the equilibrium *(4)* + $HgCl_2$ ⇌ 2 *(6)*. In the spectrum of the complex, no signals are observed in the region of the enol proton of *(7)* at −10.89 ppm.

The half-width and coalescense of the −5 ppm signal depends on the method of preparation of *(4)* and, of course, on the trace amounts of mercury salts present[7]. The best way to prepare *(4)* and *(5)* not contaminated by mercury salts is by

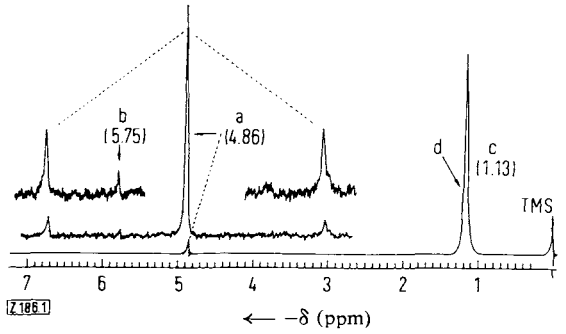
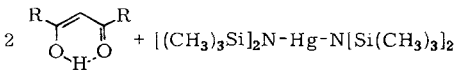
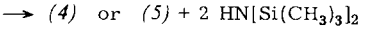


Figure. ^{1}H—NMR spectrum of bis(dipivaloylmethyl)mercury(II) *(4)* in $CDCl_3$ at −40 °C. a: HC (ketone); b: HC (enol); c: $(H_3C)_3C$ (ketone); d: $(H_3C)_3C$ (enol).

reaction of the β-diketones *(7)* and *(8)* with bis(hexamethyldisilylamido)mercury *(9)* [8,9] in dry ether. In this manner it was possible to prepare for the first time the sparingly soluble compound *(5)* in analytically pure form.



(7), R = $C(CH_3)_3$ *(9)*
(8), R = CH_3



(4) or *(5)* + 2 $HN[Si(CH_3)_3]_2$

The methods given in the literature [10,11] always lead to products which contain OH, acetate, or Cl as ligands, and which are *ca.* 3 % deficient in carbon, and exhibit several intense bands in the C=O region of the IR spectrum [12]. Since pure *(5)*, like *(4)* (in KBr), shows only one sharp C=O band at 1678 cm^{-1}, the metal in mercury(II) acetylacetonate *(5)* must also be bonded to the central C atom.

Bis(diacetylmethyl)mercury(II) (5)

A solution of acetylacetone *(8)* (12.02 g) in ether (50 ml) is added with stirring to a solution of *(9)* (3.24 g) in absolute ether (30 ml). A finely crystalline, colorless precipitate is formed immediately, yield 2.51 g (100 %). After recrystallization from acetylacetone, compound *(5)* decomposes at temperatures above 254 °C. The compound is very sparingly soluble in all common solvents.

Bis(dipivaloylmethyl)mercury(II) *(4)* has been prepared in the same way; yield 91 %, m.p. 195—197 °C (dec.). Its IR spectrum can be superimposed on that of the compound prepared from *(7)* and mercury(II) acetate according to the method given in ref. [6].

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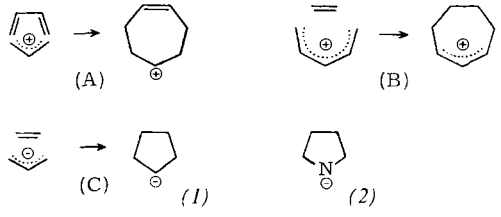
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[12] *Note added in proof*: *F. Bonati* and *G. Minghetti*, J. organometallic Chem. *22*, 5 (1970), also tried to prepare pure compound *(5)* by the usual methods but without success.

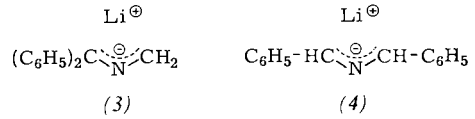
Anionic 3 + 2 Cycloaddition [1] [**]

By *Thomas Kauffmann*, *Heike Berg*, and *Edgar Köppelmann* [*]

According to the principles of conservation of orbital symmetry the ionic one-stage $[_\pi4 + _\pi2]$ cycloadditions (A)—(C) are allowed [3]. Although there are examples for the two cationic types [3], no reaction is apparently yet described for anionic $[_\pi4 + _\pi2]$-cycloaddition (C) in accord with this principle [4].



We started from the consideration that cycloaddition of the general type (C) should be favored energetically and be accompanied by fewer undesired secondary reactions if an amide anion *(2)* were formed in place of a carbanion *(1)*, and we therefore treated the 2-azaallyllithium compounds *(3)* and *(4)* in tetrahydrofuran/ether (10 : 1) with unsaturated hydrocarbons that should be readily susceptible to nucleophilic attack. We obtained the azaallyl compounds by the action of one molar equivalent of lithium diisopropylamide in the same solvent mixture on, respectively, *N*-(diphenylmethylene)-methylamine and *N*-benzylidenebenzylamine at −60 °C (cf. [2]).



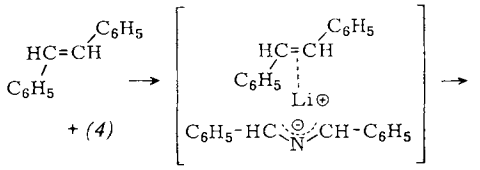
(3) *(4)*

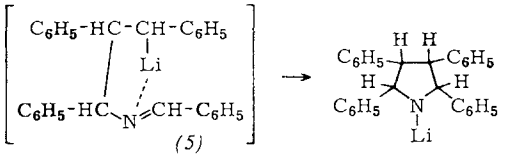
Li cpd.	Alkene or alkyne	Temp. (°C)	Product	Yield (%) [a]	M.p. (°C)
(3)	Styrene	20 [b]	2,2,3-Triphenylpyrrolidine	85	86—87
(3)	Tolan	20 [b]	2,2,3,4-Tetraphenylpyrroline	43	138—139
(4)	Styrene	0	2,3,5-Triphenylpyrrolidine	75	68
(4)	*trans*-Stilbene	0	2,3,4,5-Tetraphenylpyrrolidine	39	110—111
(4)	Tolan	40 [c]	2,3,4,5-Tetraphenylpyrrole	73	215—217[d]

[a] Yields not optimized.
[b] The alkene or alkyne was added to a solution of the lithium compounds at −60 °C and the mixture was then warmed to +20 °C.
[c] No reaction at 0 °C.
[d] *G. Magnanini* and *A. Angeli*, Ber. dtsch. chem. Ges. *22*, 855 (1889), give m.p. 214.5 °C.

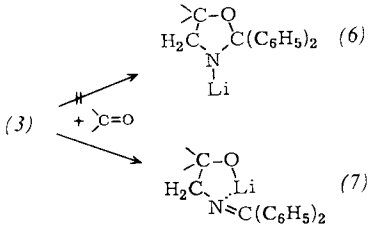
As shown in the Table, hydrolysis of the reaction mixtures usually gives the expected cycloaddition products. The 2,3,4,5-tetraphenylpyrrole produced is, however, a dehydrogenated cycloaddition product. The products isolated appear homogeneous on thin-layer chromatography and NMR spectroscopy, and their structures follow from analyses, molecular-weight determinations, NMR and mass spectra, and from the mode of preparation.

In these reactions the unsaturated hydrocarbon presumably forms a π-bond to the lithium ion. The question whether the subsequent 3 + 2 cycloaddition (*Huisgen*'s nomenclature[5]) occurs in one stage or in two stages [by way of an intermediate of type *(5)*] is under present study.





As expected, the electronegativity of the atoms participating in the multiple bonding plays a significant part in the course of addition of 2-azaallyllithium compounds. Thus reaction of *(3)* with carbonyl double bonds leads to open-chain compounds of type *(7)* and not to oxazole derivatives of type *(6)*.



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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

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[2] *Th. Kauffmann, E. Köppelmann*, and *H. Berg*, Angew. Chem. *82*, 138 (1970); Angew. Chem. internat. Edit. *10*, 163 (1970).

[3] *R. B. Woodward* and *R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. internat. Edit. *8*, 781 (1969).

[4] 1,3-Dipolar cycloadditions are, it is true, related to anionic [π4 + π2]-cycloaddition [3] but differ therefrom in non-participation of the anions.

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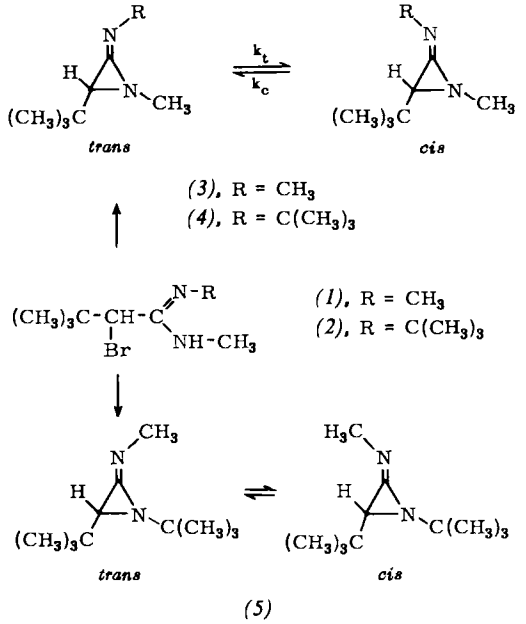
Aziridine Imines[**]

By *Helmut Quast* and *Edeltraud Schmitt*[*]

Although aziridones (α-lactams)[1] have already been known for some years, attempts to prepare aziridine imines have so far failed[2]. In connection with our investigations on the valence isomerization of heteromethylenecyclopropanes[3] we report here on a stereoselective synthesis of such compounds.

By treating the α-bromoamidines *(1)* and *(2)* (which can be prepared in the usual way from the corresponding *N*-methylamide) with potassium *tert*-butoxide in ether we were able to obtain compounds in 70—80% yield which, according to elemental analyses, molecular weight determinations (osmometric in benzene), mass spectra, and IR spectra [extremely high C=N frequency (see Table 2) and absence of NH bands], have an aziridine imine structure.

At low temperatures the 1,3 elimination of α-bromoamidines proceeds with both *high regio- and high stereo-selectivity;* at −40 °C, compound *(2)* yields predominantly *(4)* [(4) : (5) = 86 : 14], while at room temperature a mixture of about equal amounts of *(4)* and *(5)* is obtained. IR and NMR spectra permit unequivocal assignment of structure (see Table 2).



(3), b.p. <15 °C/0.001 torr *(5)*, m.p. −3 to −2.5 °C
(4), m.p. 19–20 °C (pentane) (pentane)

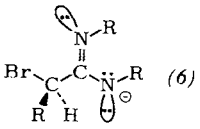
At −40 °C, both *(1)* and *(2)* yield almost exclusively the *trans* isomers (stereoselectivity > 90%), which are in equilibrium with their thermodynamically more stable *cis* isomers at room temperature.

In order to distinguish between inversion of the ring nitrogen[4] and *syn-anti* isomerization of the imino group, the rate of this isomerization was followed by NMR spectroscopy. The data given in Table 1 are only consistent with a slow *syn-anti* isomerization of the imino group.

Table 1. Equilibrium and rate constants of the *syn-anti* isomerization of *(3)* and *(4)* at 36 ± 1 °C.

Starting compound	$K = k_t/k_c$ (±0.05)	$10^5 \times (k_t + k_c)$ (s^{-1})	$\Delta G^{\neq}$ (kcal/mole)
trans-(3)	2.33	5.95 ± 0.02	23.3
trans-(4)	4.49	138.0 ± 0.6	21.4

The configuration of *trans-(3)* and *trans-(4)* is proved by the observed coupling of the H on C-3 with the methyl group on the imino nitrogen[5]; *cis-(3)*, *(4)*, and *cis-(5)* show only singlets. The NMR spectra in benzene support the assignment of configuration: as expected, the upfield shift of the signals for all *cis* protons was larger than for those *trans* to the alkyl groups on the imino nitrogen[5].



(6)

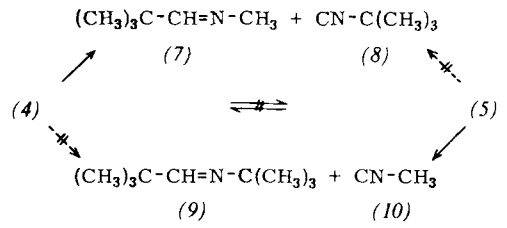
The kinetically preferred formation of *trans*-aziridine imines in the intramolecular S_N reaction *via* a semi W-like transition state[6] can be explained by the greater stability of the configuration *(6)* of the intermediate amidine anion, in which mutual repulsion of the lone pairs is at its lowest[7].

Table 2. IR and NMR data of the aziridine imines.

Cpd.	IR, νC=N (cm^{-1})	NMR, δ (ppm) in CCl_4			
		C-3-*t*-Bu	C-3-H	N-1-R	=N—R
trans-(3)	1805	0.95	1.92 [a]	2.69	3.10 (d, J = 0.6 Hz)
cis-(3)		0.96	1.83	2.61	3.08
trans-(4)	1780	0.95	1.66	2.71	1.23
cis-(4)		1.00	1.78	2.55	1.18
trans-(5)	1800	0.93	2.16 (q, J = 0.7 Hz [b])	1.15	3.08 (d, J = 0.7 Hz)
cis-(5)		0.95	2.15	1.13	3.05

[a] Broad signal.
[b] Measured in the absence of solvent.

Compound *(4)* starts to decompose at 50 °C [→*(7)* + *(8)*, halflife about 17 h at 60 °C]; *(5)*, on the other hand, only decomposes above 120 °C [→*(9)* + *(10)*] to afford isocyanide and imine in quantitative yield (cf.[1–3]). This decomposition serves as independent proof of the structure of *(4)* and *(5)* and permits a simple preparation of pure *(5)* by fractional thermolysis of a mixture of *(4)* and *(5)* at 100 °C.



We have not yet been able to detect a valence isomerization *(4)*⇌*(5)* either directly or indirectly (by identification of isomeric thermolysis products).

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[**] This work was supported by the Deutsche Forschungsgemeinschaft

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CONFERENCE REPORTS

Problems of Modern Silicone Chemistry

By *Walter Noll*[*]

The diversity of this subject, particularly as regards industrial aspects, is illustrated by three selected topics.

1. *Synthesis of silanes*

Little use has been made of the many recommendations based on laboratory work in the technical development of the direct synthesis of methylchlorosilanes (use of η-phase Cu_3Si; other metallic catalysts in place of, or in addition to, copper; pretreatment of the silicon; *etc.*). The process has reached a high level of development owing to process-engineering measures and particularly to the use of fluidized beds. Apart from the usual addition reactions of the Si—H bond, substitution reactions of bromomethylsilanes (or siloxanes) have proved useful for the production of organo-functional silanes. Bromo-(sometimes also chloro-)methylsilanes have assumed a key role in the preparation of amino-, hydroxy-, mercapto-, or carboxy-substituted derivatives; they also permit ring-closure reactions (silamorpholine).

2. *Chain polymers*

Recent publications have paid detailed attention to mechanisms of "self crosslinking" of silicone rubber. Chain polymeric polydimethylsiloxanes having terminal OH groups are made into pastes with crosslinking agents of the type CH_3SiX_3, fillers, and other additives; these pastes may be stored unchanged in the absence of moisture. When exposed to the air, they react with the water vapor present to give crosslinked soft-elastic materials. Crosslinking agents having X = carboxy, amino, *N*-alkylacylamide, or ketoxime are of industrial interest. The products are used as sealants in the building industry.

The properties of polydimethylsiloxanes are modified considerably by anionic copolymerization with diphenylsiloxanes to give regular polymers of high crystallinity. Introduction of amino or hydroxymethyl groups or co-condensation with polyethers increases the hydrophilic character of the molecules; in both cases interesting surface activity results from the increase in polarity of the molecules.

3. *Surface chemistry*

This generally plays an important role in the uses of silicones. Force/area isotherms of monomolecular siloxane films, which were registered on a continuously operating, automatically recording film balance, show variations depending upon the nature of the substituents. The molecules of those siloxanes that are of industrial interest because of their surface activity lose their coil or helical form and are converted into "spreading chains" that are bonded to the water *via* their Si—O—Si bonds and can be converted into a two-dimensional close packing on compression (*e.g.* dimethyl-, methyl-*H*-, methyl-γ-trifluoropropylsiloxanes). Under such conditions, dimethylsiloxanes form surface layers in which only hydrocarbon groups are directed toward the gas phase. An increase in the size of the aliphatic groups, introduction of diphenylsiloxane

units, or presence of other bulky substituents results in loss of this orientation capacity; moreover, such siloxanes spread considerably more slowly than those mentioned above. Siloxanes bearing hydrophilic groups, *e.g.* hydroxymethyl or aminomethyl substituents, exhibit a capacity for orientation and a particularly high affinity for water. They are excellent agents for forming extremely thin, water-repellent, detergent-resistant, brilliant films on solid surfaces to which they are held by an adsorbed layer of water.

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Chemistry of the Lanthanides in Liquid Ammonia

By *James C. Warf*[*]

Europium and ytterbium in liquid ammonia: Europium and ytterbium, *i.e.* the two lanthanides that most readily form doubly charged cations, dissolve in liquid ammonia to give deep blue solutions[1]. The enthalpy of the reaction

$$Eu_{(s)} \rightarrow (Eu^{2+})_{NH_3} + (2e)_{NH_3}$$

is found (Born-Haber cycle) to be approximately −26 kcal/mole: the change in free energy is −7 kcal/mole (240 °K). Europium is the only metal that dissolves in ammonia to give paramagnetic cations. Samarium is insoluble, as is also americium. Element 101, mendelevium, which readily forms Md^{2+} ions in aqueous solution, may also be soluble in liquid ammonia.

Magnetic properties of the hexammine compounds: The five compounds $Ca(NH_3)_6$, $Sr(NH_3)_6$, $Ba(NH_3)_6$, $Eu(NH_3)_6$, and $Yb(NH_3)_6$ form golden crystals that are excellent electronic conductors. $Eu(NH_3)_6$ fulfills all the prerequisites of ferromagnetic behavior. *Sienko et al.*[2] have found that it follows the Curie-Weiss law down to 47 °K. At this temperature the compound becomes ferromagnetic. Solid solutions of $Eu(NH_3)_6$ in diamagnetic $Yb(NH_3)_6$ or $Sr(NH_3)_6$ exhibit the same behavior and almost the same Weiss constant; thus the ferromagnetic behavior is not affected by the increase in the Eu—Eu distances. In $Eu_{0.085}\ Yb_{0.915}\ (NH_3)_6$, the Eu—Eu distance is 18.8 Å; nevertheless, coupling of the magnetic moments does occur, doubtless *via* the conductivity electrons.

Reactions of europium and ytterbium in liquid ammonia: Reaction with phosphine yields $Eu(PH_2)_2$ and $Yb(PH_2)_2$[3]. Benzene is reduced to cyclohexadiene and cyclohexene[4]. As expected, $Eu(C_5H_5)_2$ is obtained with cyclopentadiene in liquid ammonia. In contrast, ytterbium gives not only $Yb(C_5H_5)_2$ but also $Yb(C_5H_5)_3$ and the sublimable compound $Yb_2(C_5H_5)_3(NH_2)_2$ whose structure is unknown[5].

Amides of europium and ytterbium: Solutions of europium in liquid ammonia decompose to $Eu(NH_2)_2$[6] at 50 °C; on the other hand, ytterbium, whose ammonia solution is considerably less stable, gives a mixture of $Yb(NH_2)_2$ (≈ 30 %) and $Yb(NH_2)_3$ (≈ 70 %), as shown by IR spectra and magnetic measurements[7].

Formation of electrons solvated with ammonia: A remarkable reaction was observed during attempts to prepare $Yb(NH_2)_2$ from YbI_2 and KNH_2 in liquid NH_3[8]: The solution turns deep blue and a white precipitate appears. The spectrum of the solution is identical with that of a solution of electrons solvated with NH_3 (at 24 °C asymmetric curve, maximum at 5400 cm^{-1}) prepared by a different method. The reaction thus proceeds according to

$$(Yb^{2+})_{NH_3} + 3\ NH_2^- \xrightarrow[NH_3]{\text{liquid}} Yb(NH_2)_3 + (e^-)_{NH_3}$$

Yb^{2+} in liquid ammonia is therefore a stronger reducing agent than potassium. In fact, elemental potassium is found in the residue left on evaporation of the ammonia. The reductive power is further increased by the extreme insolubility of $Yb(NH_2)_3$ in liquid ammonia. The same reaction occurs with the iodides of Eu(II) and Sm(II). Within certain limits, $ZrBr_3$ behaves similarly to Eu^{II}, Yb^{II}, and Sm^{II}[9].

Recent experiments have shown that the equilibrium

$$Yb(NH_2)_2 + NH_2^- \underset{NH_3}{\overset{\text{liquid}}{\rightleftharpoons}} Yb(NH_2)_3 + (e^-)_{NH_3}$$

is shifted far to the right-hand side.

Lecture at Saarbrücken on February 13, 1970 [VB 235 IE]
German version: Angew. Chem. *82*, 397 (1970)

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Configurational and Conformational Selectivity in Catalytic Oxidations on Platinum Catalysts

By *Kurt Heyns*[*]

The selective oxidations of polyhydroxy compounds, and of mono- and oligosaccharides in particular, with atmospheric oxygen on a platinum catalyst in solution — with conversion of primary hydroxyl groups into formyl and carboxy groups — have led to an efficient method for the preparation of uronic acids, aminouronic acids, uronosides, aldonic acids, and intermediates used in the synthesis of ascorbic acid. Further investigations on cyclitols of the inositol and conduritol type have shown that only secondary hydroxyl groups in axial positions are selectively dehydrogenated to keto groups. In the case of the 1H and H1 conformations of the half-chair structures of the six-membered ring the selectivity of dehydrogenation was found to decrease in the order: quasiaxial OH > quasiequatorial OH with vic. axial OH > quasiequatorial OH with vic. equatorial OH > axial OH > equatorial OH. These findings were successfully utilized in the preparation of keto sugars from the pyranosides of pentoses and hexoses.

Other substitution rules were obtained for the catalytic oxidation of secondary hydroxyl groups attached to cyclobutane, cyclopentane, cyclohexane, and tetrahydrofuran rings; different reaction rates could be ascribed to preferred conformations in which no eclipsing of neighboring ring members occurs. Specific selective dehydrogenations, *e.g.*, of the preferred *cis*-1,4-(a,e)-, *trans*-1,3-(a,e)-, and *cis*-1,2-(a,e)-conformations were possible in the case of the *cis*- and *trans*-1,2-, -1,3-, and -1,4-cyclohexanediols.

A similar series of decreasing rates could be established for the bicyclic [3.3.0], [3.2.1], and [2.2.1] ring systems. *Endo*

groups prove to be much more susceptible to dehydrogenation than do *exo* substituents. In the norbornanols the order is *endo* OH > *exo* OH > 7-OH. An *endo* OH in the presence of vicinal *exo* OH is dehydrogenated at a considerably slower rate than other *endo* groups. Furthermore, in the[2.2.1] system *exo* groups are dehydrogenated much faster in the presence of a 7-*syn* OH group than in the presence of a 7-*anti* OH group. The behavior of the isomeric bicyclo[2.2.2]-octane-2,6,7-triols illustrates unequivocally that intramolecular hydrogen bonds considerably increase the rate of catalytic oxidation.

Lecture at Freiburg, February 6, 1970 [VB 234 IE]
German version: Angew. Chem. *82*, 363 (1970)

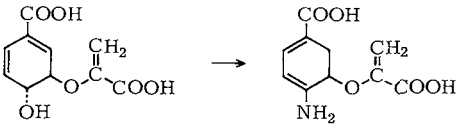
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Biosynthesis of Vitamins; Allosteric Enzymes – Recent Results

By *Franz Lingens*[*]

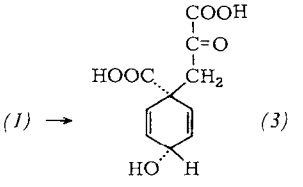
Studies of vitamin biosynthesis in microorganisms employ deficiency mutants having genetic blocks in their biosynthetic pathways. *N*-Methyl-*N'*-nitro-*N*-nitrosoguanidine (MNNG) has proved a particularly effective mutagen for the production of such mutants. Treatment of DNA with *N*-trideuteriomethyl-*N'*-nitro-*N*-nitrosoguanidine at pH 6 yields 7-trideuteriomethylguanine, thus ruling out exchange of deuteron with solvent proton and hence the intermediacy of diazomethane in the methylation.

Action of MNNG on a polyauxotrophic mutant of *Aerobacter aerogenes*, which produces large amounts of chorismic acid *(1)*, yielded a *p*-aminobenzoic acid$^-$-mutant. This latter mutant releases a nitrogen-containing intermediate into the medium which is readily converted by acids into *p*-aminobenzoic acid. Structure *(2)* (3-enolpyruvic acid ether of 2,3-dihydro-*p*-aminobenzoic acid) has been proposed for the intermediate. Chorismic acid *(1)* can be converted into *(2)* in the presence of glutamine by an enzyme extract from the mutant.



(1) *(2)*

Allosteric enzymes of the multiple-branched aromatic amino acid biosynthetic pathway have been enriched from the yeast *Saccharomyces cerevisiae* and from the fungus *Claviceps paspali*. Chorismate mutase from *C. paspali*, which converts *(1)* into prephenic acid *(3)*, is inhibited by phenylalanine and tyrosine, and is activated by tryptophan. This activation effect can be exploited for affinity chromatography of the enzyme. Sepharose was activated with cyanogen bromide and treated with tryptophan to give a carrier that absorbs chorismate mutase. The enzyme is eluted with tryptophan.



(1) → *(3)*

Activation of chorismate mutase with typtophan can be used as a sensitive analytical tool for the determination of this amino acid. It must, however, be borne in mind that tryptophan homologs and analogs also display an activating effect.

Lecture at Wuppertal on March 11, 1970 [VB 236 IE]
German version: Angew. Chem. *82*, 398 (1970)

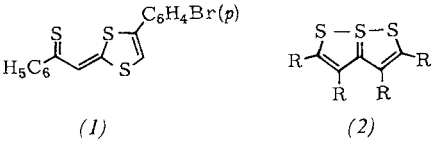
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SELECTED ABSTRACTS

The reactions of atomic and molecular halogens with silver have been compared by *R. J. McIntyre* and *F. K. McTaggart*. Atomic chlorine, bromine, and iodine were produced in a flow system by an electric discharge; the walls of the apparatus were prepared with phosphoric acid to minimize early recombination of the halogen atoms. The rate of growth of silver halide film was followed by means of an interference method. The halide film was found to inhibit further attack of molecular halogens, whereas film thickness has no influence on the reaction rate with atomic halogens. Low activation energies (around 5 kcal mole^{-1}) and high reaction probabilities (0.73 for I, 0.52 for Br, 0.25 for Cl) were found for the halogen atom reactions. / J. physic. Chem. *74*, 866 (1970)/ —Hz. [Rd 164 IE]

The molecular structure of an "isothiathiophthene" *(1)* has been established X-ray crystallographically by *R. J. S. Beer* and *D. Frew*. The data support formulation of *(1)* as α-(4-*p*-bromophenyl-1,3-dithiol-2-ylidene)thioacetophenone rather than as a bicyclic system analogous to the thiathiophthene *(2)*. This is surprising since a number of isothiathiophthenes and thiathiophthenes resemble each other chemically and spectroscopically.

(1), m.p. 200–203 °C, crystallizes as purple triclinic needles, $a = 17.775$, $b = 7.190$, $c = 6.474$ Å, $\alpha = 90°55'$, $\beta = 110°1'$,

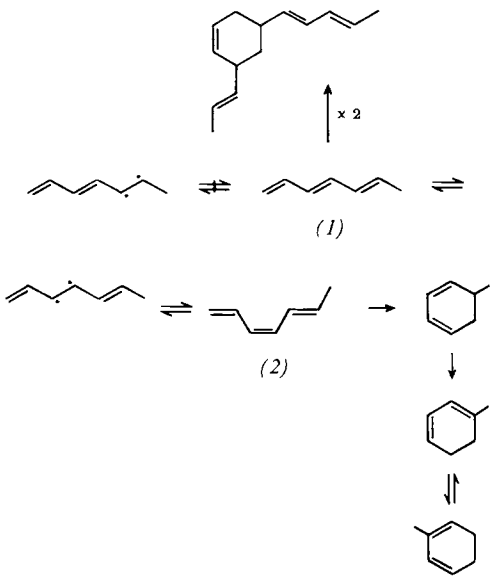


(1) *(2)*

$\gamma = 89°6'$, space group $P\bar{1}$. The exocyclic S—S distance is 2.91 Å. In the thiathiophthenes *(2)* the first and third of the almost linearly arranged S atoms are *ca.* 4.7 Å apart. / Chem. Commun. *1970*, 154 / —Kr. [Rd 173 IE]

Neutron energy-loss spectrometry is used by *M. F. Collins*, *B. C. Haywood*, and *G. C. Stirling* for a study of the vibrational frequencies of hydrogen bonds. The instrument described allows the detection of resonances in the 400 to 1400 cm^{-1} range. Because of the mass similarity, the technique preferentially observes hydrogen motions, thus providing an advantage over IR and Raman spectroscopy. Coincidence of results with those of optical spectroscopy is demonstrated for KHF_2, $CsHCl_2$, and $CsDCl_2$. For $NaHCO_3$ and the acid potassium trifluoro- and trichloroacetates, the hitherto unknown bending modes of the hydrogen bridges are identified. / J. chem. Physics *52*, 1828 (1970). / —Hz. [Rd 170 IE]

The gas phase isomerization of 1,*trans*-3,*trans*-5-heptatriene *(1)* was followed by *K. W. Egger* and *T. L. James* at 247 to 332 °C and 1.6—22 torr with product analysis by gas chromatography. The primary product is 1,*cis*-3,*trans*-5-heptatriene *(2)*, which undergoes fast cyclization to 5-methyl-1,3-cyclohexadiene and further isomerization to 1- and 3-methyl-1,3-cyclohexadienes. The reaction is clean under the conditions used, only the Diels-Alder reaction contributing measurably to the overall conversion at lower temperatures and



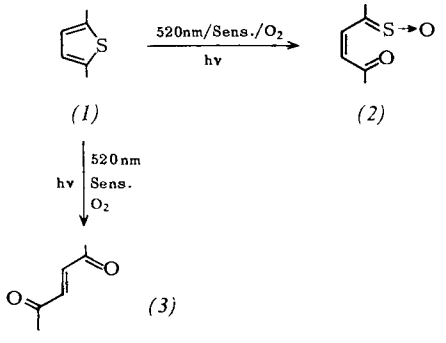
(1)

(2)

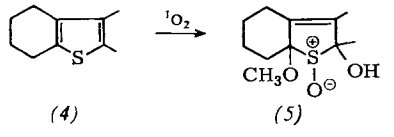
higher pressures. The observed rate parameters agree with those expected for a 3,4-biradical transition state, with the planes of the two radical ends perpendicular to each other. The isomerization about the 5,6-bond does not contribute to the reaction. / Trans. Faraday Soc. *66*, 410 (1970) / —Hz.

[Rd 168 IE]

The reaction of singlet oxygen with thiophenes has been studied by *C. N. Skold* and *R. H. Schlessinger* and by *H. H. Wasserman* and *W. Strehlow*. The first named authors irradiated 2,5-dimethylthiophene *(1)* in $CHCl_3$ and in CH_3OH in presence of methylene blue. The sulfine *(2)* and the diketone *(3)* were formed, obviously *via* different routes. Under similar conditions *Wasserman et al.* obtained the thiophene oxide *(5)*



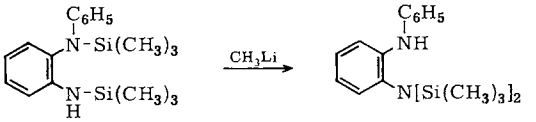
(1) *(2)* *(3)*



(4) *(5)*

from a solution of 2,3-dimethyl-4,5,6,7-tetrahydrobenzo[*b*]-thiophene *(4)* in CH_3OH with participation of the solvent. / Tetrahedron Letters *1970*, 791, 795 / —Kr. [Rd 174 IE]

New rearrangements of bis(organosilyl)-*o*-phenylenediamines have been described by *H. F. Stewart*, *D. G. Koepsell*, and *R. West*. In the presence of methyllithium, compounds such as *(1)* undergo anionic rearrangement in ether at room temperature to give *(2)*. Rearrangement appears to be intramolecular and to proceed *via* a planar transition state. Equilibrium is set up between compounds of type *(2)* and *(1)* as a

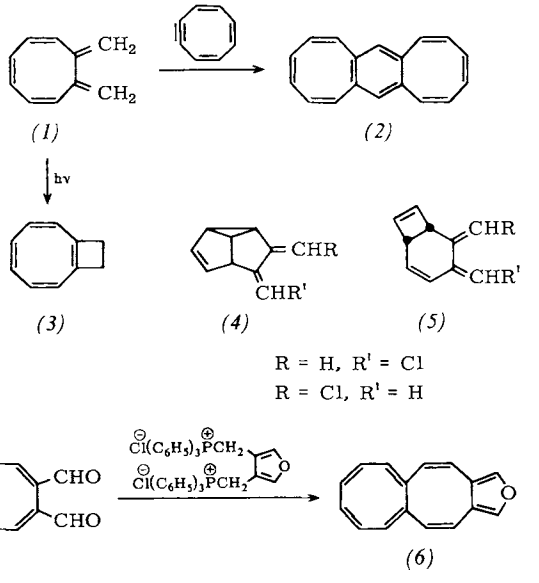


(1) *(2)*

result of the novel thermal intermolecular rearrangement occurring at 275 °C. / J. Amer. chem. Soc. *92*, 846 (1970) / —Kr.

[Rd 179 IE]

7,8-Dimethylene-1,3,5-cyclooctatriene *(1)* is, according to *J. A. Elix*, *M. V. Sargent*, and *F. Sondheimer*, a key substance for the synthesis of a great variety of novel polycyclic compounds. Compound *(1)*, which the authors obtained from 1,3,5,7-cyclooctatetraene-1,2-dimethanol *via* the dibromide, undergoes Diels-Alder reaction of its exocyclic double bonds. With dehydrocyclooctatetraene generated *in situ* it affords the pale yellow dicycloocta[*a*,*d*]benzene *(2)*, m.p. 179—181 °C, which is nonplanar and therefore unrelated to [18]annulene.



(1) *(2)* *(3)* *(4)* *(5)* *(6)*

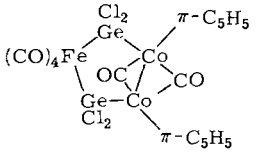
On UV irradiation, compound *(1)* is converted into dihydrocyclobutaoctene *(3)*, while in the reaction of α-chloro-*(1)* to give *(4)* and *(5)* the exocyclic double bonds are retained. The authors also obtained octalenofuran *(6)* by reaction of the dicarbaldehyde with a phosphonium salt of furan. The eight-membered rings in *(6)* have a tub-like configuration. / J. Amer. chem. Soc. *92*, 962, 969, 973 (1970) / —Kr.

[Rd 180 IE]

A novel five-membered metal-metal heterocycle *(2)* has been synthesized by *M. J. Bennett*, *W. Brooks*, *M. Elder*, *W. A. G. Graham*, *D. Hall*, and *R. Kummer*. The Ge-Co compound *(1)* was heated with $Fe(CO)_5$ under nitrogen for 2 h without solvent in a bath at 110 °C. On extraction of the residue with CH_2Cl_2, dark green crystals were obtained (yield 40 %) which were stable for many months to light and air; $[Cl_2GeFe(CO)_4]_2$ remains in solution. The spectroscopic data are consistent only with a cyclic structure; this has been confirmed by a

π-$C_5H_5(CO)Co(GeCl_3)_2 + Fe(CO)_5 \longrightarrow$

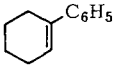
(1)

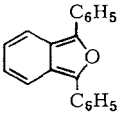


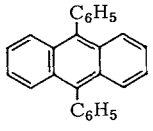
(2)

single-crystal X-ray structure determination. *(2)* crystallizes in the orthorhombic space group $P2_12_12_1$; the five-membered metal ring is almost planar. / J. Amer. chem. Soc. *92*, 208 (1970) / —Kr. [Rd 177 IE]

Oxygenation of organic molecules in the solid state by singlet oxygen produced in a microwave discharge has been accomplished on a preparative scale by *J. R. Scheffer* and *M. D. Ouchi*. The apparatus was based on that used by *Ogryzlo*[1]. The substrate was adsorbed on microcrystalline cellulose or silica gel and treated with the singlet oxygen at about 5 torr and room temperature in the dark. Examples: *(1)*→*(2)*, 33% yield; *(3)*→*(4)*, 91%; *(5)*→*(6)*, 79%. / Tetrahedron Letters *1970*, 223 / —Kr. [Rd 184 IE]

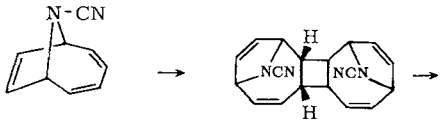
(1)  *(2)*

(3)  *(4)*

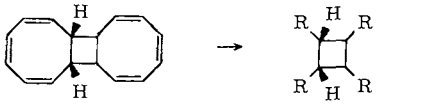
(5)  *(6)*

[1] *E. A. Ogryzlo*, Proc. New York Acad. Sci., in press.

The unknown *anti*-3+2 dimer of cyclooctatetraene *(3)* has been prepared by *A. G. Anastassiou* and *R. M. Lazarus*. Sensitized irradiation of 9-cyano-9-azabicyclo[4.2.1]nona-2,4,7-triene *(1)* in benzene in the presence of benzophenone at room temperature afforded the dimer *(2)*, m.p. 220—221 °C yield 70%. Treatment of *(2)* with hot methanolic KOH gave the diamine (65%) which was converted into a bis(nitroso) derivative (100%) by $NaNO_2$/dilute mineral acid. Reaction of this derivative with warm alkaline $Na_2S_2O_4$ was accompanied by evolution of N_2 and gave the dimer *(3)*, m.p. 98—99 °C. Ozonization of *(3)* followed by oxidative work-up and methylation with CH_2N_2 led to *(4)*. / Chem. Commun. *1970*, 373 / —Ma. [Rd 186 IE]



(1) *(2)*



(3) *(4)*, R = CO_2CH_3

Metallic berkelium, element 97, has been prepared by *J. R. Peterson*, *J. A. Fahey*, and *R. Baybarz* [a] and independently by *D. K. Fujita* [b]. 8—10 μg of berkelium(III) fluoride was reduced with lithium vapor at 10^{-6}—10^{-7} torr and 1025 to 1050 °C in a micro tungsten spiral which served as a crucible. The resulting metal was recrystallized by annealing for several minutes at 900 °C. Metallic berkelium is silver-white and malleable. It exists predominantly in a face-centered cubic modification with the lattice constant $a = 4.987 \pm 0.001$ Å [b] or 4.99 ± 0.01 Å [a] but there also appears to be a hexagonal modification having $a = 3.41 \pm 0.01$ Å and $c = 11.05 \pm 0.01$ Å [a]. The melting point of Bk is approx. 1000 °C. The atomic radius is calculated from the lattice constants to be 1.76 Å in the cubic phase and 1.74 Å in the hexagonal phase [b]. Susceptibility measurements by *Fujita* [b] yielded a magnetic moment of $\mu_{eff} = 8.23\ \mu_B$ for the cubic modification and $\mu_{eff} = 8.52\ \mu_B$ for the hexagonal modification. The cubic modification becomes ferromagnetic below 140 ± 15 K, and the hexagonal modification antiferromagnetic below 35 ± 3 K. The magnetic data indicate that more than three electrons per atom are in the bonding orbitals and that the metal valence is about 3.4. / [a] Oak Ridge National Laboratory Chemistry Division Progress Report for Period Ending May 20, 1969, ORNL-4437 (Sept. 1969); [b] Dissertation, Berkeley 1969, UCRL-19507 (Nov. 1969) / —FW. [Rd 187 IE]

BOOK REVIEWS

Lehrprogramm Chemie. (Programmed Learning: Chemistry.) By *J. Nentwig*, *K. Kreuder*, and *K. Morgenstern*. Verlag Chemie, Weinheim/Bergstr. 1969, Vol. 1, 29 Programs with 32 Ill., 1st Edit., xiii, 675 pp., paperback, DM 22.—.

In this book of programs the team of authors makes use of the experience they have themselves gained in training chemical laboratory assistants at Farbenfabriken Bayer. The material to be taught is divided into small "easily digestible bits" and is skilfully so arranged that the pupil reaches his objective in the optimal manner, which is an aim not achieved through a "search-and-find" book or through a formal lecture. "Programmed Learning: Chemistry" is characterized by its use of both the linear and the branched programming technique. In the linear method the pupil must formulate the answers himself; the questions are usually easy and the pupil sees at once from the next step whether he has answered correctly or not. Since his answer will usually be correct his success stimulates pleasure in active work; his confidence is strengthened and he is positively motivated for further problems. The disadvantage of the linear method is that when he gives the wrong answer the pupil does not learn why he went wrong. This and other didactic considerations induced the authors to build branches into the program. At each step in a branched program the student is faced with a large amount of information, but of a type that passes into associative memory; this material ends with a question for

which various, mutually exclusive answers are offered; if the pupil chooses the correct answer he is at once led further through the program as fast as his knowledge and intelligence allow; if he chooses the wrong answer he is led to an exposition especially designed to correct the error; and individual correction is thus achieved.

The first volume of "Programmed Learning: Chemistry" deals almost exclusively with the chemistry of materials. The contents are arranged according to the well tested principle of "from easy to difficult". An introductory program explains changes of phase as physical processes and changes of material as chemical processes; the differences between mixtures and chemical compounds are set out clearly. Then follow one chapter each on "Air", "Water", and "Hydrogen": they include descriptions of experiments that are already familiar to the laboratory assistants for whose use this book is primarily intended.

Among the programs dealing with materials are scattered six further program son "Theoretical Principles" such as the concept of an atom, valency, Avogadro's hypothesis, and quantitative analysis; the advantages of this procedure are obvious. Two programs on organic chemistry, on a purely practical basis, complete the volume.

The range of each program is restricted so that in general it can be worked through at one sitting without undue strain on the pupil.

Programs for chemistry are a rarity; indeed the 1968 bibliography, compiled by *J. Lorenz*, of programmed learning in German does not contain a single one. So the authors may be forgiven for occasionally faltering in their programming technique and for steps that, in the reviewer's opinion, are not of much use. Isolated steps such as the definition of a catalyst, and steps with too many gaps in the question or with implausible or trivial alternative answers at branch points should be avoided as far as possible.

The arrangement as a "scrambled textbook" explains the astonishingly low price but it also leads to diversions during the continuous cross-referencing; in a new edition it would be desirable to use a printing technique that leads to sharper separation of the individual programs since it is only too easy to turn to the wrong program during the forward- and back-referring.

In spite of these criticisms this book of programmed learning can be recommended for all those who want to build up a basic knowledge of chemistry quickly and effectively.

There is a companion volume to the programs, designed for the instructor, that explains in detail the connections between the various programs, isolating the main route and all the branches.

Siegfried Nöding [NB 871 IE]

The Thermal Properties of Transition Metal Ammine Complexes. By *W. W. Wendlandt* and *J. P. Smith*. Elsevier Publishing Company, Amsterdam-London-New York 1967, 1st Edit., x + 235 pp., numerous figures, bound, Dfl. 47.50.

This book deals with the results of the thermal decomposition of ammine complexes of the transition metals and also of gallium, indium, and thallium. It is principally concerned with kinetic methods.

First of all, the problem of thermodynamic stability is explained with some specific examples. This is followed by a comprehensive survey of kinetic breakdown techniques such as thermogravimetry, differential thermal analysis, mass spectrometry, thermomagnetic methods, and high-temperature reflectance spectroscopy, and of their applications. In a special section a systematic treatment is given of the thermal properties of the individual ammine complexes, taking full account of recent literature. Complexes with organic amines, and also aquo- and acido-ammine complexes are considered.

Only the results of the kinetic methods are given in detail, these methods having the advantage of being less time-consuming than the static methods (isothermal or isobaric tensiometric decomposition). They relate principally to differences in the rates of decomposition of the phases under consideration. This involves crystal formation, particle size, nucleation, growth, and diffusion processes. A very critical evaluation of the degradation curves is thus required, particularly where the number and the thermodynamic stability of the intermediates are concerned. The authors emphasize that one should never be satisfied with a single method. An X-ray study of the solids is absolutely indispensable, and yet it is performed all too rarely.

The value of this book lies predominantly in the following points: 1. All available kinetic methods and their uses are dealt with. 2. Comprehensive factual material is provided. 3. The book reveals the existing gaps in our knowledge which require further experimental treatment. We can also see that the theoretical treatment of the stability problem is still very much in arrears. For example, it is still not generally possible to say on theoretical grounds where the stability of ammine complexes will increase in the order chloride, bromide, iodine, and in which cases it will decrease. There are also still a number of gaps in the X-ray determination of the crystal structures of ammine complexes. Thus in many cases the proposed structures are still uncertain, and this is also true for the structural formulas given on pp. 170 and 172 for the adducts of *o*- and *p*-phenylenediamine with Cd salts. From the stereochemical viewpoint, these formulas are unsatisfactory.

The chemist working in the field of coordination chemistry will find this very clearly written book to be stimulating reading; its publication is therefore greatly welcomed.

Otto Schmitz-DuMont [NB 866 IE]

Comprehensive Chemical Kinetics. Edited by *C. H. Bamford* and *C. F. H. Tipper*. Vol. 1: The Practice of Kinetics. Elsevier Publishing Company, Amsterdam-London-New York 1969. 1st Edit., 450 pp., numerous figures, Dfl. 95

This is the first in a planned series of 25 volumes. It should be said at the outset that the authors have succeeded in collating and presenting in a thoroughly accessible form the widely scattered literature on the subject. This achievement is particularly welcome in the light of the explosive development in experimental techniques in certain branches of kinetics.

The chapters devoted to the experimental methods used in the study of slow (*L. Batt*), fast (*D. N. Hague*), and heterogeneous (*D. M. Shooter*) reactions, and the one on the detection of intermediates (*R. P. Wayne*), are well equipped with useful diagrams and descriptions of the apparatus used, including, where applicable, electronic instrumentation. The accent is placed on thermal, photochemical, and radiochemical systems, while biochemical and electrochemical systems have obviously been deliberately neglected.

Naturally, all classical and modern chemical and physical methods of studying chemical reactions are also discussed, though the treatment accorded to some of the modern methods is somewhat curtailed. The editors are to be complimented on the fact that overlapping between individual chapters has been reduced to a minimum. On the other hand, they have clearly failed to persuade the authors of the first three chapters to maintain uniformity of arrangement.

The concluding chapter on the treatment of experimental data (*D. Margerison*) is in particular of inestimable value to all those working in kinetics. It is illustrated with a number of examples and tables and constitutes an unsurpassed aid to the analysis of experimental results, even for the most complex systems.

This volume will provide invaluable help in planning, carrying out, and analyzing kinetic experiments, both to those who are occasionally concerned with kinetics and to those constantly dealing with this field.

Oskar Friedrich Olaj [NB 863 IE]

The Biochemistry of Viruses. Edited by *H. B. Levy*. Marcel Dekker, Inc., New York-London 1969, 1st Edit., xiv + 657 pp., numerous figures, bound $ 28.50.

The molecular biology of virus infections is currently receiving an increasing amount of attention. A large number of laboratories throughout the world are engaged in studying both the structure of viruses and the mode of replication of a number of types of virus, and also the effect of viral multiplication on the infected cell. In particular, it is known that a virus infection can lead not only to death of the infected cell but also to a malignant modification of the cell. This has resulted in the tumor viruses, thanks to the limited extent of their genetic information, becoming an excellent model for carcinogenesis. It is thus hardly surprising that the literature on the biochemistry of viruses has recently grown to such an extent that even the subject specialist finds it difficult to keep abreast of the latest developments.

It is therefore all the more gratifying to find that the present book, edited by *Levy* and written by a number of competent authors, provides a survey of the recent literature. The two opening chapters describe the chemical composition of animal viruses and the structure of viruses. After these general chapters, which contain a wealth of useful information, the biochemistry of the main virus groups is systematically discussed. Particular emphasis is placed on the mode of multiplication of the different types of viruses. In addition, one chapter deals with the genetic analysis of the polio virus. The final chapter is concerned with the biochemistry of interferon. In the introduction it is said that the work was intended as a textbook for advanced students and as a source of reference for the virologist. For this purpose it is certainly well equipped, particularly since the literature is covered up to 1968. It is a pity that the compilation of the chapters gives the impression of a certain degree of incompleteness. The value of the book would be increased if Arboviruses and Rhabdoviruses were also dealt with. The omission of any reference to RNA phages and DNA tumor viruses leaves the book incomplete.

Gerhard Sauer [NB 861 IE]

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Cooperative Conformational Transitions of Linear Biopolymers

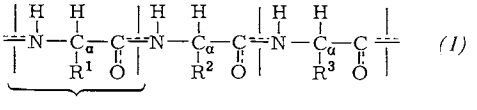
By Jürgen Engel and Gerhard Schwarz[*]

Conformational transitions in proteins, nucleic acids, and other biopolymers evidently play a decisive role in many biological processes, particularly in control processes. They often proceed cooperatively, i.e. the elementary process of the transition of an individual segment of these macromolecules is influenced by the state of other segments via intramolecular interactions. In general, the segments favor the same state as their neighbors. The resulting equilibrium properties of cooperative systems, e.g. the sharpness of the transitions and their dependence on the chain length, can be quantitatively explained for linear systems by the linear Ising model. The molecular causes of the cooperativity can be explained for simple model polymers.

1. Introduction

Macromolecules are important structural units of organisms, each by itself often exercising surprisingly complicated functions. These biological macromolecules consist chemically of chains built up from a relatively small number of types of monomer units. The most important of these macromolecules are the proteins, which include the enzymes that catalyze and regulate the metabolism, and the nucleic acids, which carry genetic information in the form of a control program for the biosynthesis of the proteins.

Proteins consist of polypeptide chains built up from a maximum of about 20 amino acids [see *(1)*].



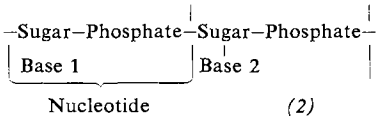
(1)

Amino acid residue (= Segment of the chain)

R^1, R^2, R^3 .... = side chains, by which the amino acid residues differ from one another. The peptide linkage has partial double-bond character, which prevents free rotation.

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Prof. Dr. G. Schwarz
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CH-4056 Basel, Klingelbergstrasse 80
(Switzerland)

Nucleic acids contain chains usually made up of at most four structural units, the nucleotides [see *(2)*].



(2)

Sugar = ribose in ribonucleic acid (RNA)
Sugar = deoxyribose in deoxyribonucleic acid (DNA)

The nucleotides differ essentially in their bases. In RNA these are cytosine (C), guanine (G), adenine (A), and uracil (U), while in DNA, U is replaced by thymine (T).

Biologically important chain molecules of this nature are referred to by the general term "biopolymers". The decisive difference between similar polymers lies in the sequence of the monomer units:

$$S_1S_2S_3 \ldots\ldots S_i \ldots\ldots S_N$$

where the N chain members are numbered from left to right and each S is a symbol for a monomer unit (*e.g.* C, G, A, or U in RNA chains).

Very simple sequences have been prepared synthetically, particularly polyamino acids, polypeptides with a periodically repeating sequence of a few amino acid residues, and analogous polynucleotides (*e.g.* poly-A). These synthetic biopolymers are useful as model substances, since the results of measurements are

easier to interpret than for the much more complicated natural biopolymers.

Under suitable conditions, most biopolymers have a specific steric structure (conformation), which is stabilized by noncovalent ("weak") interactions (such as van der Waals forces, hydrogen bonds, hydrophobic and electrostatic interactions) between the segments.

Native nucleic acids and synthetic polynucleotides frequently have relatively simple helical-linear conformations, the basic structure of which does not depend on the sequence of the segments. The best known is the double helix discovered by *Watson* and *Crick* (Fig. 1).

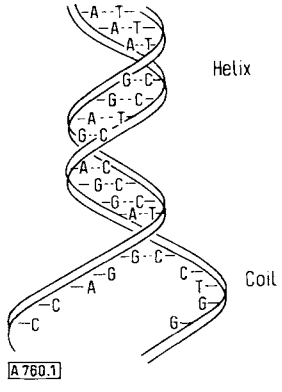


Fig. 1. Schematic representation of the DNA double helix after *Watson* and *Crick* [1]. The bands represent the sugar phosphate chains, which are joined in the helix *via* the bases A, C, G, T [see formula *(2)*] by hydrogen bonds (- -). A coil region is shown underneath.

Proteins generally have much more complicated, often globular arrangements of the polypeptide chains ("tertiary structure"), as might be expected from the great variety of possible sequences. A few basic structures ("secondary structures") are often found in limited regions of the protein; examples are the α-helix (Fig. 2), the pleated sheet (or β) structure, and the polyproline II helix (see Section 3.2). Since such structural types can be found in pure form in polyamino acids, these may be regarded as simple protein models.

The biological function of a biopolymer is usually confined to its structured (native) state. The enzymes are good examples of this. In their active sites, segments from different regions of the chains are brought close to one another by chain folding in such a way that they can cooperate in the catalysis of a metabolic reaction [3]. Even small changes in conformation generally lead to a large change in the enzymatic activity.

It has been found in a number of biological regulation phenomena that enzymes involved can assume conformations with different activities, between which reversible transitions occur. There is much to indicate that control processes of this nature are extremely

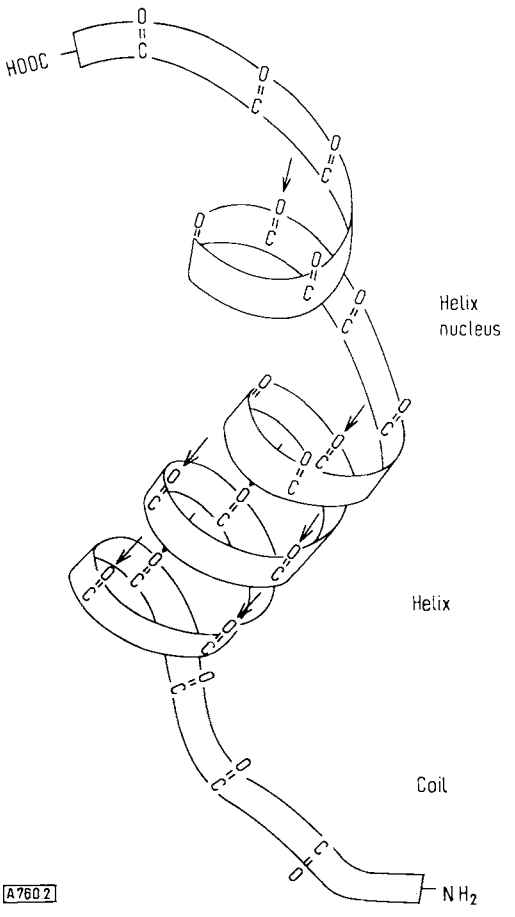


Fig. 2. Schematic representation of the α-helix after *Pauling* and *Corey* [2]. The band represents the polypeptide chain [see formula *(1)*], in which each amino acid residue is represented by its peptide CO group. In the helix, hydrogen bonds (arrows) connect the peptide NH group of each residue to the CO group of the third nearest residue. A helix nucleus (top) in a coil region has only one such hydrogen bond, but this fixes three residues in one turn of the helix.

important and widespread in molecular biology. An example is provided by the allosteric regulation process in enzymes consisting of several protein subunits ("protomers"). A regulating agent (substrate, activator, or inhibitor) becomes bound to an active site of the protein, as a result of which the activity of other sites in the same molecule are changed [4, 5].

This cooperative interaction is evidently due to induced conformational transitions of the protomers. Similar processes are postulated for the regulation of the function of repressors and biological membranes [6, 7]. There has been interesting speculation concerning its possible role in the short-term storage of information in the brain [8].

Nearly all biopolymers can change into a disordered (usually inactive) state of higher entropy. One example is the denaturation of proteins by changes in the

[1] *J. D. Watson* and *F. H. C. Crick*, Nature (London) *171*, 737, 964 (1953).

[2] *R. B. Corey* and *L. Pauling*, Proc. Roy. Soc. (London), Ser. B *141*, 10 (1953).

[3] *D. C. Philips*, Sci. American *215*, 78 (1966).

[4] *J. Monod*, *J. Wyman*, and *J. P. Changeux*, J. molecular Biol. *12*, 88 (1965).

[5] *M. Kirtley* and *D. E. Koshland*, J. biol. Chemistry *242*, 4192 (1967).

[6] *J. P. Changeux*, *J. Thiery*, *Y. Tung*, and *C. Kittel*, Proc. nat. Acad. Sci. USA *57*, 337 (1967).

[7] *G. Adam*, Z. Naturforsch. *23b*, 181 (1967).

[8] *A. Katchalsky* and *A. Oplatka*, Neuroscience Res. Progr. Bull. Suppl. *4*, 71 (1966).

temperature, the pH, or the solvent. In transitions of this type, the weak stabilizing interactions and the associated blockage of free rotation about chemical bonds are largely eliminated. In solution, the chains (like other filamentous molecules) take the form of a random coil. This will be referred to briefly as the coil state. The transition in the opposite direction (coil → specific conformation) is a decisive step in the biosynthesis of proteins[3,9,10]. On the other hand, a process of the type double helix ⇌ coil must be assumed in the duplication of DNA with its genetic information.

Conformational transitions often proceed cooperatively, *i.e.* the elementary processes in the individual segments are influenced by the state of other chain segments. There is usually a strong tendency to assume the state of the neighboring segment. Consequently, even relatively small variations in the external parameters (*e.g.* temperature, pH, solvent composition) can lead to practically complete conformational transition. This property is of fundamental importance to the physiological control functions mentioned above.

A second characteristic of cooperative reactions is the dependence of the transition on the chain length. The sharpness of the transition generally increases with the size of the molecule. This effect was first observed on investigation of linear synthetic model substances, since it is only here that the size of the molecule can be systematically varied. Transitions that have been fairly extensively investigated and that can be described theoretically are α-helix ⇌ coil for polyamino acids, helix I ⇌ helix II for polyproline, and double

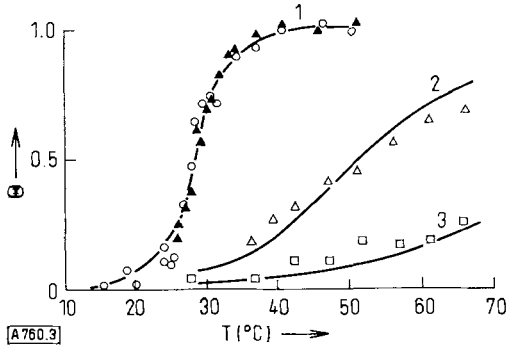


Fig. 3. Temperature-induced α-helix ⇌ coil transition of poly-γ-benzyl L-glutamate [R in formula *(1)* = $CH_2-CH_2-COO-CH_2C_6H_5$] in dichloroacetic acid/dichloroethane for various chain lengths, *N*. 1: $N = 1500$;, 2: $N = 46$; 3: $N = 26$. The degree of transition Θ was determined from the optical rotation α by means of the equation

$$\Theta = \frac{\text{Residues in the helix state}}{\text{Total number of residues}} = \frac{\alpha - \alpha_C}{\alpha_H - \alpha_C}$$

where α_H and α_C are the rotations of the pure helix form and of the pure coil form. The values indicated by circles were given by *Doty* and *Yang* [11], and all the other values by *Zimm*, *Doty*, and *Iso* [12]. The continuous curves were calculated [12, 13] (see Section 3.1).

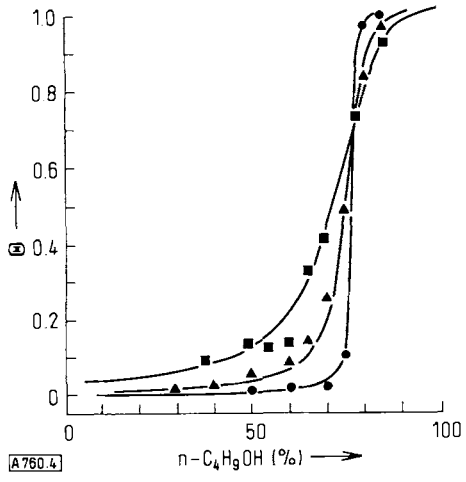


Fig. 4. Solvent-induced transition between two types of helix (I and II) of poly-L-proline [see formula *(3)*] having chain lengths $N = 12$ (●), $N = 30$ (▲), and $N = 132$ (■) [14]. The degree of transition Θ = number of residues in the I state/total number of residues was determined polarimetrically by a method similar to that used in the α-helix ⇌ coil transition (see caption of Fig. 3). The curves are calculated (see Section 3.2). Abscissa: *n*-butanol in trifluoroethanol, vol.-%.

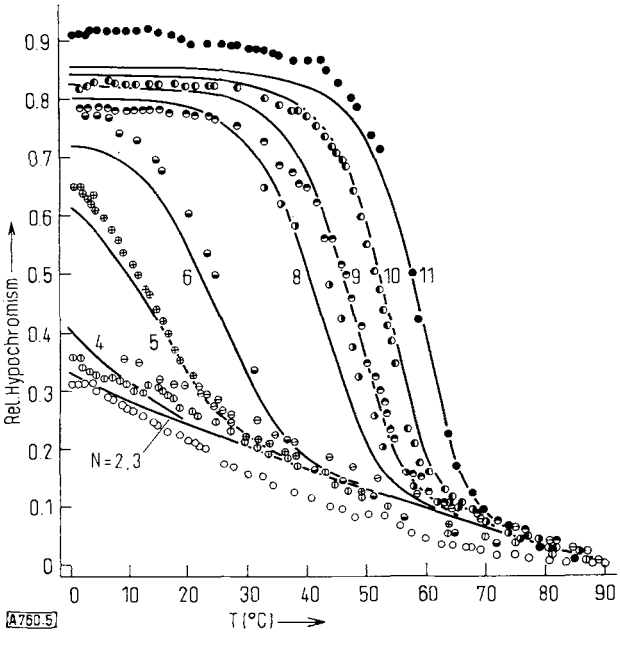


Fig. 5. Temperature-induced double helix ⇌ coil transition of polyadenylic acid [all bases = A in formula *(2)*] having various chain lengths *N* (after *Applequist* and *Damle* [15]). The hypochromism [16] (decrease in UV absorption on helix formation) used as the measured quantity does not give the degree of transition Θ directly, since it depends on the length of the helix section. This dependence was taken into account in the calculation of the curves shown [15].

○: $N = 2$; ⊖: $N = 3$; ⊙: $N = 4$; ⊕: $N = 5$; ◒: $N = 6$; ◑: $N = 8$; ◓: $N = 9$; ◐: $N = 10$; ●: $N = 11$.

helix ⇌ coil for polynucleotides (see Sections 3.1-3.3). At this stage we shall merely show a few typical transition curves (Figs. 3–5) based on optical measurements. The above-mentioned characteristics of cooperative transitions are clearly recognizable.

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2. Theoretical Principles[17]

The representation of the sequence of a biopolymer chain as a sequence of symbols for the segments can be extended to a formal description of the conformation. We make use of the fact that the conformation is determined by interactions between the monomer units. Thus the i-th segment S_i can conceivably have the states A_i, B_i, C_i, *etc.* Each sequence of possible states then represents a certain conformational state of the entire chain. In general, there will be a very large number of such structural forms, but only those with minimal free energies will be really stable.

These forms can in principle be predicted from theory if the energy interactions of the segments are known. However, such calculations are usually possible only with powerful computers. Very successful investigations of this nature have been possible for simpler structures[18–20]. Further developments in this field should one day make calculation of the conformation of a given sequence feasible.

The stability of a conformation naturally depends on the external conditions (*e.g.* temperature, pressure, solvent). Conformational transitions may therefore occur when these conditions are changed.

We have found that interactions occur between various segments within the macromolecule. Thus it will be readily understood that the free energy of a segment often depends not only on the external conditions and its own internal structure, but also on the states of other parts of the chain. Consequently, the thermodynamic (and kinetic) properties of the elementary processes of the change in state are influenced by the situation prevailing at that time in more or less distant segments. This is the same as saying that the conformational transitions proceed cooperatively. If the process were non-cooperative, the transitions of single segments could be dealt with individually, and the complete transition would not depend on the molecular weight and would not exhibit abnormal sharpness.

It is convenient in theoretical studies to consider the simplest possible linear biopolymers first. Chains built up from only one type of monomer unit (*i.e.* in which all the S_i are the same) are particularly suitable. This is the case for the transitions illustrated in Figures 3–5. Another fact that can be used here is that each segment has only two possible states; let these be denoted by A and B [*e.g.* in polyproline, A = *trans* configuration of the peptide linkage, B = *cis* configuration (see Section 3.2)]. One extreme form of the conformation will then be described as a pure sequence of A states (in our example, this corresponds to the polyproline II helix) and the other as a pure B sequence (polyproline I helix). There are, in principle, also many mixed conformations, *e.g.*

$$\underset{1\ 2\ 3\ 4}{A\,A\,B\,B\,.....\ B\,A\,B\,B\,....\ A\,B\,B}\qquad\qquad\underset{N}{} \qquad (1)$$

the total number being 2^N. With only 100 chain segments, therefore, we must expect about 10^{30} different states.

With cooperative interactions, the properties of the elementary process

$$A \rightleftharpoons B \qquad (2)$$

become more or less complicated. A particularly simple situation evidently arises if cooperative interactions occur only between immediately adjacent segments. This corresponds to the model of a linear lattice discussed by *Ising* in 1925 in connection with a theory of ferromagnetism[21]. This author was able to show that all the thermodynamic properties could be calculated relatively simply in this case. The two-dimensional and three-dimensional models that were of interest for his own purposes, however, led to extreme mathematical difficulties, and further work in this field was suspended for a long time.

With the growth of interest in cooperative transitions of biopolymers, the linear Ising model acquired fundamental importance for the theory of such processes[13,22–30]. The quantitative relationships can be represented particularly elegantly by the matrix method (introduced by *Kramers* and *Wannier*[31]). This method was first applied to a conformation transition by *Zimm* and *Bragg*[13], the particular case being the helix ⇌ coil transition of polypeptides (see Section 3.1). In its simplified form, the theory can be extensively generalized. It describes the essential properties of cooperative transitions by means of the fundamental thermodynamic parameters s and σ.

The parameter s is the equilibrium constant for the process

$$A\,A\,B \rightleftharpoons A\,B\,B \qquad (3)$$

(or for BAA ⇌ BBA), which obviously represents the growth of existing sequences of B or A states, since the reacting (middle) segment is immediately adjacent both to an A state and to a B state.

In

$$A\,A\,A \rightleftharpoons A\,B\,A \qquad (4)$$

on the other hand, a new B sequence is started or an existing one disappears. Let the equilibrium constant of this "nucleation process" (for B) be σs.

The parameter σ defined in this way is a measure of the cooperativity of the transition. If $\sigma < 1$, the segments tend to assume the same state as their neighbors, *i.e.* pairs of the type AA or BB are more probable than pairs AB or BA (positive cooperativity). If $\sigma = 1$, there is no cooperativity, since the equilibrium constants of equations (3) and (4) are equal (*i.e.* they do not depend on the states of the neighbors). If $\sigma > 1$, adjacent segments tend to assume different states. This negative cooperativity or anticooperativity has not yet been detected with certainty in biopolymers.

On grounds of microscopic reversibility, the nucleation rate of an A state in a B sequence is described by the same σ. The equilibrium constant for

$$B\,B\,B \rightleftharpoons B\,A\,B \qquad (5)$$

is $\sigma \times 1/s$. The difficulty of nucleation can be different for A and B states only at the chain ends. The terminal segments (with the numbers 1 and N) are in fact characterized in that they have only one neighbor. *Zimm* and *Bragg* made the simplifying assumption that the formation of nuclei of the α-helix at the ends of a polypeptide chain is also described by the parameter σ. This can be easily justified for helix ⇌ coil

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transitions (see Section 3). We shall introduce this assumption for B first, and we can then describe the equilibrium properties of the transition completely by means of s and σ.

To demonstrate this, let us calculate the equilibrium concentrations of each chain state for the case $N = 4$. If we start with the pure A state, then *e.g.* the pure B state can be reached in four steps by the following processes:

$$\mathrm{A\,A\,A\,A} \rightleftharpoons \mathrm{B\,A\,A\,A} \rightleftharpoons \mathrm{B\,B\,A\,A} \rightleftharpoons \mathrm{B\,B\,B\,A} \rightleftharpoons \mathrm{B\,B\,B\,B}$$

The first step here is associated with nucleation, and this is followed by three growth steps. The equilibrium concentrations are accordingly given by

$$\bar{c}_{\mathrm{B\,B\,B\,B}} = \sigma s \cdot s \cdot s s \cdot \bar{c}_{\mathrm{A\,A\,A\,A}} \tag{6}$$

For $\sigma s^4 \approx 1$, therefore, the two extreme forms would be present in roughly equal quantities. If, moreover, the cooperativity is so strong that

$$1/\sigma^{0,25} \gg 1$$

we find that the concentrations of all the intermediate forms are small in comparison with those of the extreme forms (*e.g.* for $\sigma = 10^{-4}$: $\bar{c}_{\mathrm{BBBA}} = 0.1\ \bar{c}_{\mathrm{BBBB}}$; $\bar{c}_{\mathrm{BBAA}} = 0.01\ \bar{c}_{\mathrm{BBBB}}$, and $\bar{c}_{\mathrm{BAAA}} = 0.001\ \bar{c}_{\mathrm{BBBB}}$). In this case the transition in a given chain proceeds practically to completion or not at all.

This "all-or-nothing" behavior is evidently to be expected whenever the chains are very short and the cooperativity is sufficiently strong. The quantitative condition is found to be

$$N\sigma^{1/N} \ll 1 \quad \text{or} \quad N(1 + \log N) \lesssim -\log \sigma \tag{7}$$

The degree of transition Θ, *i.e.* the fraction of B states formed, is then

$$\Theta = \sigma s^N / 1 + \sigma s^N \tag{8}$$

The double helix $\rightleftharpoons$ coil transition of oligonucleotides has been very satisfactorily described in this way [15, 32].

As with very short chains, relatively simple behavior is also found in the limiting case of very long chains. The degree of transition then becomes

$$\Theta = \frac{1}{2}\left(1 + \frac{s-1}{\sqrt{(s-1)^2 + 4\,\sigma\,s}}\right) \tag{9}$$

so that the transition no longer depends on the chain length. As can readily be seen, the midpoint of the transition ($\Theta = 1/2$) for any σ always corresponds to $s = 1$. However, the sharpness of the transition will increase as the value of the cooperativity parameter σ decreases. This leads *inter alia* to a characteristic increase in the apparent molar enthalpy of transition. Thus using the "apparent equilibrium constant"

$$K = \Theta/(1-\Theta)$$

which can generally be readily obtained by experiment, the temperature coefficient (disregarding the temperature dependence of σ, which is permissible at least when the cooperativity is strong) becomes

$$\frac{\mathrm{d} \ln K}{\mathrm{d}T} = \frac{1}{\Theta\,(1-\Theta)} \cdot \frac{\mathrm{d}\,\Theta}{\mathrm{d} \ln s} \cdot \frac{\mathrm{d} \ln s}{\mathrm{d}T} \tag{10a}$$

In particular, at the midpoint of the transition

$$\left(\frac{\mathrm{d} \ln K}{\mathrm{d}T}\right)_m = N_0 \frac{\Delta H_u}{RT^2} \tag{10b}$$

where ΔH_u is the molar enthalpy of transition for the elementary growth process (3) and

$$N_0 = 1/\sigma^{1/2} \tag{11}$$

is the cooperative length. The name refers to the fact that for $\Theta = 1/2$ and $N \to \infty$, the average length of unbroken A or B sequences is exactly $N_0 + 1$. We now see from eq. (10b) that the apparent molar enthalpy of transition (after *van't Hoff*) is greater by the factor N_0 than the value found from the elementary process.

$N_0 \cdot \Delta H_u$ in eq. (10b) is often referred to as the van't Hoff enthalpy $\Delta H_{\text{van't Hoff}}$, since its value is obtained from a "van't Hoff plot" ($\ln K$ against $1/T$). It follows from equations (10b) and (11) that

$$N_0 = \Delta H_{\text{van't Hoff}} / \Delta H_u \tag{12a}$$

or

$$\sigma = (\Delta H_u / \Delta H_{\text{van't Hoff}})^2 \tag{12b}$$

This behavior of apparently infinitely long chains is found when

$$N \gg N_0 \tag{13}$$

Chains of medium length with

$$N_0 \gtrsim N \gg -\log \sigma \tag{14}$$

can generally be described only by fairly complicated expressions. Typical features are the dependence on chain length and the fact that each chain practically contains only one to two nuclei (suppressed nucleation). The special end effects, which are disregarded in the simplified Zimm-Bragg model discussed so far, play a decisive role here and in the "all-or-nothing" range. It is found that whereas the dependence of helix $\rightleftharpoons$ coil transitions on the chain length is described very satisfactorily by the Zimm-Bragg model the intersecting transition curves of polyproline (Fig. 4) cannot be explained on this basis. It has been shown that this phenomenon can be explained only if nucleation parameters for *each* of the two states are considered [33]. It is difficult to believe that nucleation at the chain ends is hindered in only one of the two helix forms of polyproline. These considerations have led to a general theory of cooperative transitions of linear biopolymers, in which the interactions are still restricted to immediate neighbors, but where no other special assumptions are necessary [34, 35]. Four independent thermodynamic parameters are required in this theory.

From the detailed presentation of the general theory [35], we find that if we introduce the nucleation parameters σ'_A, σ'_B (at one end of the chain) and σ''_A, σ''_B (at the other end),

$$\sigma = \sigma'_A \sigma'_B = \sigma''_A \sigma''_B \tag{15}$$

σ agrees with the Zimm-Bragg σ value. It is convenient to define two end effect parameters

$$\beta' = \sigma'_B/\sigma'_A\,;\ \beta'' = \sigma''_B/\sigma''_A \tag{16a, b}$$

β' and β'' can be expressed (though less concisely) in terms of the free energies of the cooperative interactions, as follows:

$$RT \ln \beta' = -(G_{BA} - G_{AB}) + (G_{BB} - G_{AA}) - 2(G'_B - G'_A) \tag{17a}$$

$$RT \ln \beta'' = (G_{BA} - G_{AB}) + (G_{BB} - G_{AA}) - 2(G''_B - G''_A) \tag{17b}$$

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The terms G'_A, G'_B, G''_A, and G''_B denote any additional free energies of the end states that might be caused by the absence of the neighbor on one side, by the special chemical structure (end groups), and by special interactions with the solvent.

Similarly, σ can be expressed by

$$RT \ln \sigma = -(G_{BA} + G_{AB}) + (G_{AA} + G_{BB}) \quad (18)$$

Moreover,

$$RT \ln \sigma = RT \ln \sigma s - RT \ln s = -(\Delta G_K - \Delta G_W) \quad (19)$$

where ΔG_K and ΔG_W are the free energies of the nucleation step and of the growth step respectively.

Using the matrix method, the properties of the conformational equilibrium can now be calculated as a function of the chain length N, the Zimm-Bragg parameters s and σ, and the quantities β' and β''. The influence of β' and β'' decreases with increasing chain length. Finally, when $N \gg N_0$, the end effects can be completely ignored, so that irrespective of the particular β' and β'' values, the limiting case discussed in connection with the Zimm-Bragg model is realized. In general, therefore, the theory permits the representation of the transition curves in the form

$$\Theta = f(s, \sigma, \beta', \beta'', N) \quad (20)$$

where the four thermodynamic parameters must be regarded as a function of the variables of state. With stronger cooperativity and values of N that are not too small, however, the degree of transition Θ is influenced mainly by changes in s, since s, unlike σ, β', and β'', occurs in high powers (up to N) in eq. (20). Θ can then be regarded, to a first approximation, as a function of s alone (the other parameters being treated as constants). If the dependence of the latter on the experimental conditions (such as temperature, pressure, solvent) is known, the transition curves to be expected experimentally can be calculated from eq. (20). Since s is the equilibrium constant of the growth process, the required relations can often be deduced from known thermodynamic relations; for example, the temperature dependence can be given by the van't Hoff isochore

$$d \ln s / dT = \Delta H_u / RT^2 \quad (21)$$

as used earlier in eq. (10b). (For limitations see Section 3.2.)

The linear Ising model with interaction of nearest neighbors can in principle be extended *e.g.* to include cases where cooperative interactions extend beyond the nearest neighbors. However, this leads to much more complicated calculations, which are often not worth the trouble in any case, since if the cooperativity is strong and the chains are not too short, the actual interactions can be formally grouped together into interactions of nearest neighbors. For this reason, the theory discussed may be regarded as a useful basis, to a first approximation at least, for cooperative transitions of linear biopolymers that are of practical interest.

3. Experiments on Simple Linear Model Systems

Investigations on simple linear biopolymers are very important for an understanding of the principles of cooperative transitions. In these cases one can expect a theoretical description with few parameters and a molecular interpretation of the experimentally determined parameters to be possible.

A general comment is necessary concerning the number of these parameters. If the experimental transition data can be described to within the limits of error by a very small number of parameters (*e.g.* by s and σ), this does not necessarily mean that the theoretical model selected (in this example the Zimm-Bragg model) is strictly correct. It does, however, mean that additional parameters of a possibly more valid theory (*e.g.* β' and β'', or parameters that take long-range interactions and a complicated sequence into account) cannot be determined without further experiments. It is therefore also necessary in practice to apply the simplest possible theory that fits the main properties to the simplest possible systems.

For an understanding of the molecular causes of cooperativity, it has been found convenient to describe the experimental data by means of the theories discussed above, the parameters (*e.g.* σ) found by matching then being explained on the basis of the molecular facts of the case in question (*e.g.* σ by unfavorable interactions that arise in nucleation). A statistical thermodynamic treatment based directly on molecular data is less general and is also difficult, since the interatomic interactions in biopolymers and the polymer-solvent interactions are only approximately known.

3.1. The α-Helix ⇌ Coil Transition

Most of the investigations on this important transition have been carried out with poly-L-glutamic acid and its derivatives. A pioneering study was the theoretical description by *Zimm* and *Bragg*[13] of the temperature-induced rearrangement of poly-γ-benzyl L-glutamate [R in formula *(1)* = $CH_2-CH_2-COO-CH_2C_6H_5$] (Fig. 3). The transition is very sharp for long chains. The slope and position of the curves depend on the chain length.

For a quantitative description, *Zimm* and *Bragg* used their simple Ising model (see Section 2), which contains s and only one nucleation parameter σ. They defined an amino acid residue as being in the B state (helix) when its CO group is linked to the NH group of the third-nearest neighbor by a hydrogen bond of the type found in the α-helix (see Fig. 2). A residue is in the A state (coil) if its CO group is free. To fit the theoretical transition curves to the experimental values, it was assumed that s depends on the temperature exclusively in accordance with the van't Hoff isochore [eq. (21)]. The enthalpy of transition ΔH_u, which was unknown initially, was varied together with σ until the best fit was found for all the experimental values according to the criterion of least square deviations.

The values for the theoretical curves that describe the results well (see Fig. 3) are: $\sigma = 2 \times 10^{-4}$ and $\Delta H_u = 990$ cal/mole. The cooperative length N_0 is thus about 70 residues. The ΔH_u value has also been confirmed directly by calorimetric measurements. The most

reliable of the published results[36–39] is probably $\Delta H_u = 950 \pm 20$ cal/mole, which was obtained by a superior calorimetric method[36].

The surprising positive sign of ΔH_u (increase in the helix content with rising temperature) can be explained by the fact that the influence of the temperature on the stability of the α-helix is mainly indirect. In the solvent used (80 parts of dichloroacetic acid/20 parts of 1,2-dichloroethane), the dichloroacetic acid competes for the hydrogen bonds of the helix by adding to the free CO and/or NH groups of the residues in the coil state[40,41]. The temperature coefficient of this binding process determines the temperature dependence of the helix ⇌ coil transition[13,42]. This is supported by the fact that the transition can be induced by even a small increase in the dichloroacetic acid concentration.

If the calorimetric enthalpy of transition is known, σ values can be conveniently estimated by means of equations (10b) and (11) or (12) from the slope of a single transition curve. It is assumed in this method[38,43] that the Zimm-Bragg model is valid, that s depends in a simple manner on the temperature in accordance with the van't Hoff isochore, and that $N \gg N_0$. Whereas the last of these conditions can usually be satisfied by the synthesis of high molecular weight polyamino acids, the other assumptions need not be correct for every system (see Section 3.2).

For the molecular interpretation of σ, *Zimm* and *Bragg* assumed that the difficulty of nucleation is mainly due to entropy. In the growth step, *i.e.* in the addition of a residue to an existing helix section (see Fig. 2, bottom), the binding enthalpy ΔH_W of a NH···OC hydrogen bond is gained, and the energy $T\Delta S_W$ must be supplied. ΔS_W is essentially the entropy lost when an amino acid residue loses the free rotation about the HN–C_α and C_α–CO bonds [see formula *(1)*] on transition from the coil to the helix conformation. On formation of the first hydrogen bond corresponding to those in an α-helix (see Fig. 2, top), the same enthalpy is gained as in growth:

$$\Delta H_K = \Delta H_W \qquad (22)$$

(The subscripts refer to nucleation and growth.) However, the entropy loss ΔS_K is three times as large as for growth, since three residues are fixed in a helix conformation on nucleation. With eq. (22) it follows from eq. (19) that

$$\sigma = e^{-(\Delta S_K - \Delta S_W)/R} \qquad (23)$$

Since $\sigma \approx 10^{-4}$, $\Delta S_K - \Delta S_W \approx 18$ e. u., in agreement with the order of magnitude expected for the freezing-in of the degrees of freedom of two amino acid residues[13]. Though interactions other than hydrogen bonds (*e.g.* hydrophobic interactions of the side chains and binding of the solvent) and the change in entropy on solvation and desolvation are disregarded in this simplified picture, it undoubtedly shows the principal cause of the cooperativity of the α-helix ⇌ coil transition.

This picture also explains the validity of the simple Zimm-Bragg model with only one σ for the α-helix. The Zimm-Bragg theory may be regarded as a special case of the general theory with $\sigma = \sigma'_B = \sigma''_B$. According to eq. (15), therefore, $\sigma'_A = \sigma''_A = 1$. It is in fact to be expected that the formation of a helix (B) nucleus at the ends is at least as difficult as in the interior of the chain. The unfavorable entropy balance is the same in both cases, and a turn at the end of the helix lacks half of the stabilizing hydrogen bonds. In contrast, the formation of a coil (A) nucleus is much easier at the end than in the interior, since four hydrogen bonds have to be broken in the interior to form a coil nucleus, whereas only one hydrogen bond is broken at the end of the chain.

The validity of the simple entropy-based explanation of σ can be checked experimentally. Thus according to eq. (23), σ should be independent of the external conditions, whereas it must depend on the temperature whenever an interaction enthalpy is involved (as in poly-L-proline, see Section 3.2). It has unfortunately not yet been experimentally possible to separate the observed small dependences of σ on the temperature, the solvent concentration, and the polymer concentration from one another and from possible systematic errors in the determination of σ (see above and Section 3.2)[38,43]. A second conclusion from the simple entropy explanation is that σ should also be independent of the side chains of the polyamino acids forming the α-helix. Several interesting results have been obtained in this connection.

The solvent-induced helix ⇌ coil transition of another derivative of polyglutamic acid with uncharged side chains, *i.e.* poly-N^5-(3-hydroxypropyl)-L-glutamine [R in formula *(1)* = $(CH_2)_2$–CO–NH–$(CH_2)_3$–OH], in formic acid/water could be described by a σ value of 3×10^{-4}[44]. A similar σ value (1.5×10^{-4}) has also been found for poly-ε-benzoxycarbonyl-L-lysine [R = $(CH_2)_4$–NH–COO–$CH_2C_6H_5$][45]. The good agreement of the σ values indicates that the Zimm-Bragg hypothesis, according to which the cooperativity is independent of the side chains, is correct. The solvent evidently also has only a small effect on σ, since the polymers mentioned were examined in very different solvents.

On the other hand, a much lower cooperativity was found for polyglutamic acid [R = $(CH_2)_2$–COOH],

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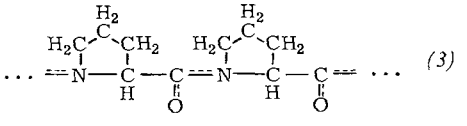
[45] *M. Cortijo, A. Roig*, and *F. G. Blanco*, Biopolymers *7*, 315 (1969).

which contains free and therefore ionizable COOH groups: $\sigma = 3\times10^{-3}$, cooperative length $N_0 \approx 16$ [46,47]. At low pH values when the COOH groups are undissociated, the helix is stable. However, it is broken up at higher pH values by electrostatic repulsion between the $COO^{\ominus}$ groups. The entropy of the resulting more disordered state is nevertheless undoubtedly lower than that of the uncharged coil, since repulsion between the side chains greatly restricts the mobility of the residues. Since the difference between ΔS_K and ΔS_W is thus smaller, a lower cooperativity is to be expected, in agreement with the entropy-based explanation of σ [eq. (23)].

A high cooperativity of non-entropic origin is observed in a completely different type of transition between two ordered helical conformations of the polyamino acid poly-L-proline.

3.2. The Helix I ⇌ Helix II Transition of Poly-L-proline

Poly-L-proline *(3)* can exist in two forms, I and II (see Fig. 6), the conformations of which are known from X-ray structure analyses [48,49]. Form I is a



(3)

shallow right-handed helix with all the peptide bonds in the *cis* configuration. The CO groups in this compact helix are almost parallel to the axis of the helix,

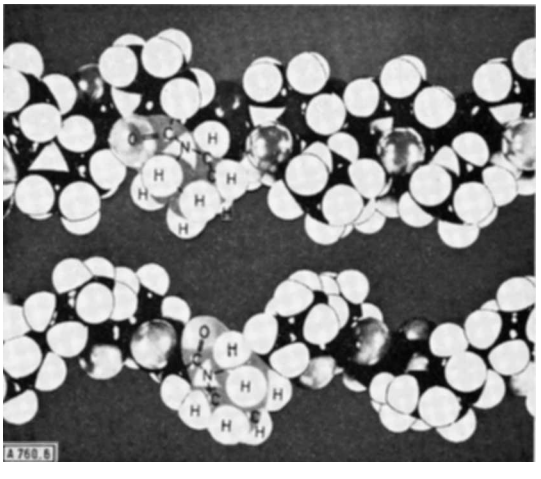


Fig. 6. Space-filling models of the I helix (top) and of the II helix (bottom) of poly-L-proline. The small white spheres and the large gray spheres are hydrogen and oxygen atoms respectively. The peptide nitrogen atoms appear as gray triangles. The carbon atoms are black [cf. *(3)*].

and are shielded to some extent by the proline rings. Form II is a steep left-handed helix with all the peptide linkages in the *trans* configuration. The CO groups are almost perpendicular to the axis, and are freely accessible to the solvent.

Both forms are sterically stabilized by the bulky rings. Intramolecular hydrogen bonds such as occur in the α-helix cannot occur here, owing to the absence of the peptide NH groups. Which of the two forms is more stable depends on the interactions with the solvent. Thus form I is more stable in *n*-butanol, and form II in benzyl alcohol or trifluoroethanol. It has been shown spectroscopically that all three alcohols form hydrogen bonds with the CO groups [50]. The relatively strong H-bond donors benzyl alcohol and trifluoroethanol prefer the open form II [51], and so displace the I ⇌ II equilibrium in favor of this form.

The reverse transition II → I can be induced by addition of *n*-butanol to benzyl alcohol or trifluoroethanol, and can easily be followed polarimetrically (Figs. 4 and 7). We again find the dependence of the transition on the chain length that characterizes cooperative transitions, but a new feature, which was not seen in the helix ⇌ coil transition, is an intersection of the curves (Fig. 4), which, as mentioned in Section 2, cannot be explained by the simple Zimm-Bragg model. There is no definite intersection in benzyl alcohol/*n*-butanol (Fig. 7), but the Zimm-Bragg theory does not lead to a satisfactory description even here.

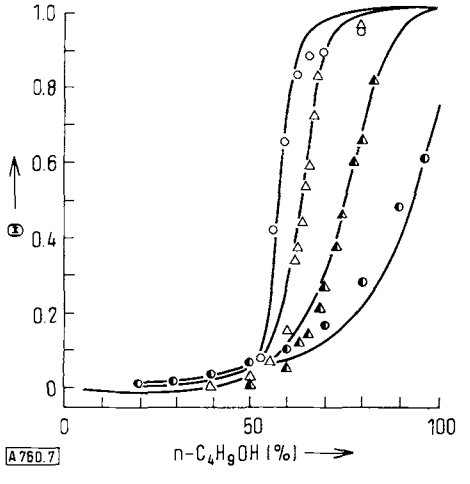


Fig. 7. Solvent-induced transition of poly-L-proline as in Fig. 4, but in benzyl alcohol/*n*-butanol (vol.-%). Experimental values for $N = 14$ (◐); $N = 33$ (▲), $N = 90$ (△), and $N = 217$ (○). The curves were calculated.

On the other hand, an attempt to describe the transition with the aid of the general equilibrium theory [35] (Section 2) was successful [14]. The I state of poly-L-proline was equated to the B state of the theory with no restriction of generality. To match the results, in contrast with the procedure described in Section 3.1, no definite function was given for the dependence of s on the composition of the solvent, but use was made

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of the facts that σ, β', and β'' should be equal in one solvent system and that there is one s value for each solvent composition q.

Theoretical transition curves that best describe all the experimental values for a solvent system on the basis of the least square deviation criterion can be found by an electronic computer with variation of σ, β', and β'', using a special program (*Gaushaus* [52]). This method of fitting has the advantage that the s function not only may be unknown, but is actually obtained from the experimental transition data (Fig. 8). The

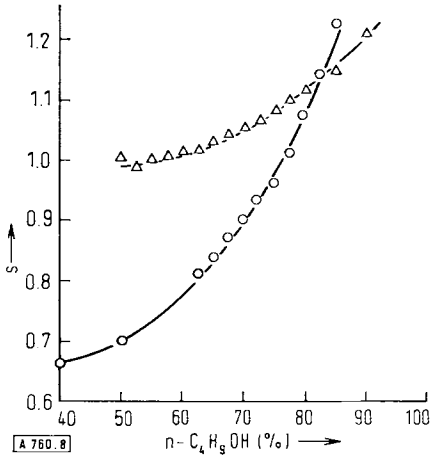


Fig. 8. Dependence of the equilibrium constant for the growth step of the I ⇌ II transition on the volume fraction of *n*-butanol in trifluoroethanol (○) and benzyl alcohol (△).

nucleation parameters determined by this method are unaffected by possible errors in the selection of an s function. The experimental results agree with theory to within the limits of error (see Figs. 4 and 7). The best values of σ, β', and β'' for the theoretical curves in Figures 4 and 7 are given in Table 1.

Table 1. Nucleation parameters for the helix I ⇌ helix II transition as found by fitting to the experimental values.

Solvent system	σ	β'	β''
Benzyl alcohol/ *n*-butanol	$(1.0 \pm 0.5)\ 10^{-5}$	0.05 ± 0.004	0.056 ± 0.004
Trifluoroethanol/ *n*-butanol	$(0.5 \pm 0.2)\ 10^{-5}$	$(9 \pm 4)\ 10^{-4}$	$(1.5 \pm 0.6)\ 10^{4}$

The very small values of σ point to a very high cooperativity. A nucleus is less probable by a factor of about 10^5 than an unbroken sequence having the same conformational states. The cooperative length is about 320. According to eq. (18), the unfavorable (positive) free energy that occurs in addition to the energy between the same states on nucleation is

$$\Delta G_\sigma = G_{I,II} + G_{II,I} - G_{I,I} - G_{II,II} \approx 6.5 \text{ kcal/mole} \qquad (24)$$

Since σ is the same for both solvent systems (Table 1), the explanation of ΔG_σ must be sought in the internal properties of the polyproline chain. It may be assumed that the entropy component in ΔG_σ is very small, since the helices I and II and molecules containing both forms are very rigid and do not differ greatly in their degrees of freedom. Thus unlike in the helix ⇌ coil transition, $\Delta G_\sigma = \Delta H_\sigma$ must be interpreted here as the enthalpy of the interaction between the residues. A large part of ΔH_σ is due to repulsion between CO groups, which occupy unfavorable positions in relation to one another at the boundary ··II-I·· (the N-terminal end of the chain being written on the left). The bulky model of the I nucleus in a sequence of II states (Fig. 9) shows, in addition to other contacts, a very



Fig. 9. Polyproline II helix interrupted at the very top of the drawing by a single *cis* linkage. The imino end is on the left. On the left-hand side of the nucleus, *i.e.* at the ·· II—I ·· boundary, electrostatic repulsion occurs between two CO groups indicated by crosses.

close proximity of two carbonyl oxygen atoms having a negative charge of about 0.4 e. Calculation of the electrostatic [14, 53] and van der Waals interactions [14] at the boundary leads to a ΔH_σ value that agrees well with the value calculated from σ by means of eq. (18).

The electrostatic interactions make the larger contribution [14], and have a considerable range. The apparent conflict between this fact and the success of the theory, which takes into account only interactions between nearest neighbors, is resolved as follows. Owing to the high cooperativity the length of the unbroken sequences of the same state in a chain is generally much greater than the range of the interactions. The latter can therefore be formally described as interactions between the nearest neighbors at a boundary between two sequences.

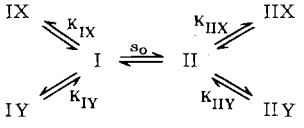
In contrast with the difficulty of nucleation in the interior of a chain (expressed by σ), the ratio of the difficulties of nucleation for the two forms at the chain ends (β' and β'') is strongly dependent on the solvent (Table 1). A possible explanation of this is *e.g.* that binding that depends on the conformation of the terminal residue occurs between the solvent and the amino or carboxyl end groups. Binding of this type and any other interaction of the solvent with the terminal residues influences β' and β'' *via* the terms G'_A, G'_B, G''_A, and G''_B in eq. (17). The difference between the interaction energies at the ··I-II·· and ··II-I·· boundaries, which is also involved here, as well as the loss of stabilization energy in the terminal

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residues as a result of the absence of neighbors, can be calculated from the molecular data for poly-L-proline [14,53,54].

However, since no detailed information about the influence of solvents is available, the β values cannot yet be calculated. On the other hand, the dependence of the s parameter on the composition of the solvent can be quantitatively described with the aid of the concept that the two forms are stabilized mainly by bonding of the solvent components X (benzyl alcohol



Scheme 1.

or trifluoroethanol) and Y (*n*-butanol) to the peptide CO groups of the proline residues. The complete binding system (Scheme 1) leads to the relation

$$s = s_0 \frac{1 + K_{IX}\, a_X + K_{IY}\, a_Y}{1 + K_{IIX}\, a_X + K_{IIY}\, a_Y} \qquad (25)$$

In this equation, s_0 is the equilibrium constant of the growth step of the free residues. This gives the ratio of I to II in the absence of interactions with the solvent, and has been estimated to be about 2 from calculations of the conformational energies of the I and II helices. K and a are the binding constants and the activities of the solvents. The dependence of the activities on the solvent composition and some of the binding constants have been determined experimentally. The experimental s functions can be satisfactorily described by eq. (25). Thus molecular interpretations have been found for all the theoretical parameters (σ, β', β'', and s) in the case of poly-L-proline [14].

It has already been mentioned that the use of a van't Hoff isochore for the temperature dependence of a transition can lead to errors in the determination of the nucleation parameters (see Section 3.1). Consideration of eq. (25) shows that for transitions involving binding processes (which also include the α-helix ⇌ coil transition), s_0 and all the binding constants may depend on the temperature, with the result that the dependence of s can no longer be represented by an equation of the type (21). Matching of the parameters without the use of assumptions is therefore also preferable in other cases.

The difference in the free energy that is required to convert poly-L-proline completely from one form into the other is also important. It can be seen from Figures 4 and 8 that for $N > 100$, a change of about 20 % in s is sufficient for about 95 % transition. This small change in the equilibrium constant corresponds to an energy change of about 0.1 kcal/mole. Thus this small energy difference is enough to stabilize one conformation or the other. In the case of poly-L-proline, it is supplied by the binding of the solvent. This strong dependence of the conformation on the free energy (over a small range of the external parameters) is a general property of cooperative systems. Consequently proteins and nucleic acids have a stable conformation even when the energy of their individual segments is only slightly more favorable than in the disordered state.

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3.3. The Double Helix-Coil Transition of Nucleic Acids

The DNA double helix (Fig. 1) is stabilized by hydrogen bonds between bases of different strands and by the stacking energy $\Delta G_{st.}$ between the bases of each strand [55]. $\Delta G_{st.}$, which is particularly important in aqueous solution, consists of a large hydrophobic component and special interactions between the aromatic systems of the bases [56]. The double helix ⇌ coil transition (Fig. 5), which can be induced *e.g.* by a temperature rise and can be readily detected spectroscopically by means of hypochromism in the UV, has a chain length dependence that is qualitatively similar to that of the α-helix ⇌ coil transition.

A system that has been extensively studied is that of polyadenylic acid (poly-A) [15,16], the double helix of which is basically the same as the Watson-Crick double helix [57]. The theoretical description of the transition was possible for $N < 11$ by transfer of the Zimm-Bragg model with only one nucleation parameter to the double helix. The nucleation step, with the equilibrium constant $\sigma \cdot s$, is bimolecular in this "zipper model" (see Fig. 10). Even better results are obtained by the "staggering zipper model", in which states with mutually staggered chains are also taken into account. The partition function was obtained for this model by combinatorial analysis, in which particularly unlikely states were omitted from the very beginning for simplicity. By fitting the theoretical curves to the experimental transition curves for $N = 2$ to 11 [15,16], a σ value of 2×10^{-3} l/mole was obtained, taking into account the dependence of the hypochromism on the chain length [15]. In this system we again find a new molecular cause of the cooperativity.

The initial coming together of two bases of different strands (nucleation) is more difficult by $\Delta G_{st.}$ than the growth step, since the stacking energy appears only when a base pair is added to an existing base pair (see Fig. 10). The contribution of the hydrogen bonds is the same for the nucleation and the growth steps, since the number of bonds formed is always the same. The entropy loss probably also differs by only a small amount of the order of RT ln 2, this difference being due to the bimolecularity of the nucleation. It must otherwise be assumed that the number of confor-

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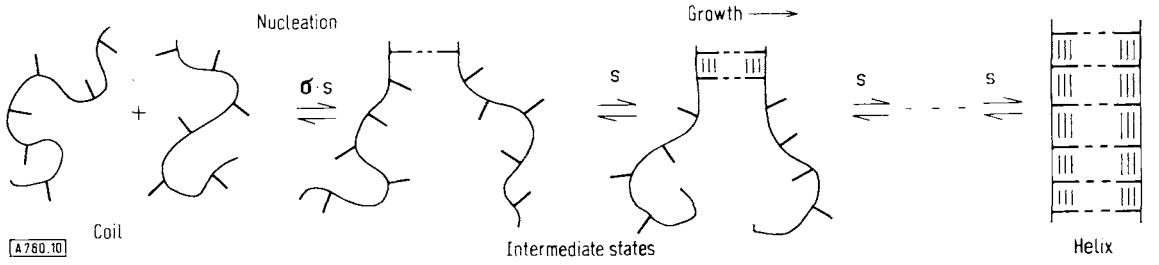


Fig. 10. Zipper model of the double helix ⇌ coil transition of nucleic acids having a short chain. —— = base; · · · = hydrogen bonds, ||| = stacking interactions.

mational degrees of freedom frozen in is similar in both elementary processes. Using these assumptions and eq. (19), a stacking energy of about − 4.5 kcal/mole can be estimated from the experimental σ value for the short-chain poly-A. Values of −5 to −7 kcal/mole were obtained from the transitions of high molecular weight polynucleotide systems[36] and of natural DNA[28].

At the large chain lengths of these last systems[28,36], as for multistrand helices in general[58,59], it is necessary to take into account a new type of statistical parameter that does not occur in single chains. If N becomes large, open rings of residues in the coil state inside closed helical regions can no longer be disregarded (Fig. 11). The difficulty of nucleation then depends essentially (apart from on the stacking energy) on the probability of meeting of the two ends of a ring

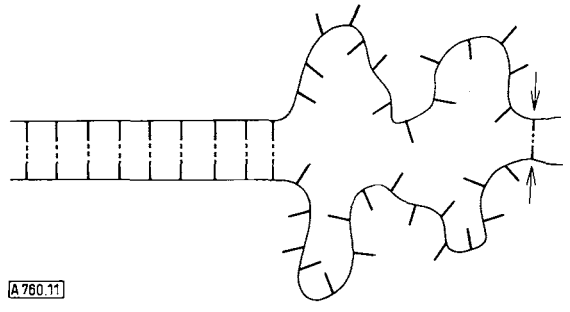


Fig. 11. Nucleation in a two-strand molecule having a long chain (see caption of Fig. 10 and text).

(arrows in the figure). This is inversely proportional to $(j+1)^{\alpha}$, where j is the number of segments in the ring (= number of unpaired residues in the two strands). The exponent α was found by computer simulation to be about 2[60]. If the probability of ring closure is taken into account, the theory predicts very sharp transition curves even at relatively small N, and true phase transitions of first and higher order occur for $\alpha \geq 2$[59–61].

Experimental evidence of phase transitions has actually been found for high molecular weight polynucleotides built up from chemically identical residues[61,62]. Natural DNA, which has extremely long chains, does not exhibit a phase transition, but gives a relatively flat melting profile. The reason for this lies in the inhomogeneity resulting from the sequence[63,64]. The double helix contains very stable as well as less stable base pairs. It must be expected in general that biopolymers in which different residues occur in rotation will give flatter melting curves than their conformational homologs built up from identical residues.

3.4. Outlook for Complicated Systems

An example of a more complicated system is the triple helix ⇌ coil transition of collagen[65]. Collagen is a relatively simple linear fibrous protein, in which three peptide chains are twisted into a three-stranded helix, for which simple model peptides with the same triple helix conformation have been synthesized. The dependence of the conformational transition on the chain length, which can never be determined in proteins, can be studied in these peptides[66,67]. The example of collagen is interesting, since here it is possible to explain the cooperativity in a real protein.

In general, a detailed understanding of the conformational transitions of proteins will be difficult even in cases where the steric structure in known. Since interactions occur in globular proteins in all directions between the residues, the linear Ising model can no longer be used, and the calculation of two-dimensional or three-dimensional models is possible only approximately and with a great deal of work.

A simplification results from the fact that most protein transitions appear to be "all-or-nothing" processes[68,69]. This conclusion was drawn in most cases from the observation that for each degree of transition, all the experimental quantities that are influenced by the transition consist additively of the

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[69] *C. Tanford*, Advances Protein Chemistry *23*, 121 (1968).

values for the two limiting structures (*e.g.* for the completely ordered and the completely coiled state). If intermediate states (*e.g.* semi-coiled molecules) were present, this additivity would not be expected for quantities that reflect complicated properties of the molecules (*e.g.* for the viscosity).

The all-or-nothing behavior of the large protein molecules points to a very high cooperativity. The transitions of the natural nucleic acids can be described better than those of proteins, since the nucleic acids usually have linear structures. Even here, however, their complicated and in most cases unknown sequence stands in the way of a quantitative understanding. On the other hand, the knowledge of the fundamental properties of simple cooperative transitions will suffice in most cases at least for a qualitative understanding of complicated systems.

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Pyramidal Inversion

By Arvi Rauk, Leland C. Allen, and Kurt Mislow [*]

Pyramidal inversion is discussed from the point of view of recent theoretical and experimental investigations in an attempt to provide a unified description of this process. Quantum mechanical studies of pyramidal molecules indicate that the origin of the inversion barrier may be dependent on the degree of angular constraint. Effects due to the electronegativity of substituents on the inversion center, to the presence of adjacent lone pairs, and to inclusion of d-type functions in the basis set are discussed. The utility and limitations of molecular orbital calculations, vibrational spectroscopy, microwave spectroscopy, direct kinetic measurements, and dynamic nuclear magnetic resonance (DNMR) spectroscopy as means for determining barriers to pyramidal inversion are discussed in context with a review of the highlights of experimental observations on the subject. Ambiguities that arise in the interpretation of barriers determined by DNMR are explored in detail. Factors that affect the magnitude of inversion barriers are discussed separately in four broad categories: steric effects; effects of conjugation (including $(p-d)_\pi$ conjugation) and hyperconjugation; effects of angular constraint; and effects of heteroatomic substitution. In the last category, critical reference is made to the question of electronegativity vs. lone pair-lone pair repulsions, the problem of rotation vs. inversion, and the role of d orbitals.

1. Introduction

A molecule that contains a tricoordinate atom whose stable position is not in the plane defined by the three atoms directly bonded to it, may, in principle, exist in two conceptually distinct conformations which are related by a transposition of the tricoordinate atom from one side of the plane to the other. We describe such a molecule as being *pyramidal* and, without specifying mechanism, define *pyramidal inversion* as any process that effects the interconversion of the two conformations. The conformers shall also be referred to as *invertomers*.

We shall restrict discussion exclusively to those molecules in which pyramidal inversion occurs without bond formation or breaking, and which remain in their electronic ground state throughout the process. Two competitive modes occur. Classically, a vibrational mode leads to inversion through a coplanar or near coplanar arrangement of groups about the inversion center; the observed rate of inversion depends on the relative populations of vibrational energy levels above and below the top of the potential barrier to inversion. Non-classically, inversion can occur by quantum mechanical tunneling: a particle in a potential well penetrates the walls of the well and therefore, if the wall is of finite thickness, has a finite probability of existing on the other side of the wall. The rate of tunneling depends in a complex way on the mass of the particle, the shape of the potential well, the height and shape of the barrier and the energy of the particle [1,2]. In practice, however, tunneling is an important consideration only when at least one of the ligands bound to the central atom is hydrogen or deuterium, when the invertomers are not diastereomers, and at tem-

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[1] *D. M. Dennison* and *G. E. Uhlenbeck*, Phys. Rev. *41*, 313 (1932).
[2] *R. S. Berry*, J. chem. Phys. *32*, 933 (1960).

peratures at which vibrational levels within 5 or 6 kcal/mole of the top of the potential barrier are substantially populated.

The distinction between classical and non-classical inversion modes is unimportant for the discussion of *barriers* to pyramidal inversion, so long as it is remembered that the interpretation of *rates* of inversion, from which the barriers are obtained, is dependent on the relative importance of the two modes. Of the various possible methods for determining the magnitudes of inversion barriers (Section 3) only microwave spectroscopy depends explicitly on the observation of the quantum mechanical tunneling phenomenon which causes a splitting of the vibrational energy levels. The amount of splitting, and therefore the rate of inversion due to tunneling, can be computed from an analysis of the vibrational spectrum. Other methods, which ultimately depend on transition state theory to yield a value of the barrier, are valid only when the absence of quantum mechanical tunneling can reasonably be assumed.

In this review we attempt to provide a merging of theory and experiment. In Section 2 is discussed information on the inversion process that can only be derived theoretically, and in Section 3, non-empirical methods are incorporated along with empirical methods as means of determining the magnitude of barriers to pyramidal inversion. In Section 4 we discuss factors which affect the magnitude of the inversion barrier. We intend this as a critical review, with an emphasis on what we regard as salient features of current studies in this area, and no attempt has been made at presenting an exhaustive catalog of the vast literature.

2. Theoretical Investigation of Pyramidal Inversion

The investigation of a wide variety of pyramidal molecules by nonempirical (*ab initio*) molecular orbital calculations has yielded information on the intimate details of the inversion process that are not available from experimental research, and has provided theoretical support for *ad hoc* principles derived empirically. In this section, a description of the origin of the inversion barrier will not be accompanied by an analysis of the inversion process in terms of changes in overlap or atomic populations, since the usual (Mulliken) definition of these quantities is too sensitive to choice of basis set.

2.1. Inversion in Hydrides

Ammonia is thus far the only molecule for which it has been shown that the inversion barrier is quantitatively calculable within the molecular orbital (Hartree-Fock) approximation [3]. Consequently, some statements regarding the origin of the barrier may be made with considerable confidence. Except as indicated, the following results, as derived from the ammonia calculations, are consistent with calculations on CH_3^- [4], SiH_3^- [5], PH_3 [5,6], and SH_3^+ [5], and therefore may be general for simple unstrained pyramidal molecules.

The stable conformation of a molecule is determined by a subtle balance of attractive and repulsive forces [7]. A partitioning of the total energy of the molecule, E_T, into a sum of attractive and repulsive components [8] permits a determination of the difference in these terms between planar and pyramidal forms of the molecule:

$$E_T = V_{attr} + V_{rep} = (V_{ne}) + (V_{nn} + V_{ee} + T) \qquad (a)$$

where V_{attr} $(= V_{ne})$ is the attractive potential between electrons and nuclei, and V_{rep} is the sum of internuclear repulsions (V_{nn}), interelectronic repulsions (V_{ee}), and the kinetic energy of the electrons (T). Ammonia is more stable in the planar form with respect to the attractive term; the bond length is shorter, the bond overlap population is greater, and the bond stretching force constant is greater in the planar form. On the other hand, the pyramidal form is more stable with regard to the sum of the repulsive terms [9]. Since the net change in the repulsive terms is greater than the net change in the attractive term, the molecule is pyramidal and the barrier is said to be repulsive dominant. The well-known heuristic argument of *Gillespie* and *Nyholm* [10], that lone pair-bond pair repulsion results in a pyramidal geometry, is strengthened by this result.

Pyramidal structures for molecules isoelectronic with ammonia and phosphine have long been predicted by *Walsh*'s rules [11], which are an example of the empirical rule of stereochemical control by the highest occupied molecular orbitals.

2.2. Role of d Orbitals

The much discussed question of the role of d orbitals, especially where second or higher row atoms are involved, is relevant to the phenomenon of pyramidal

[3] *A. Rauk, L. C. Allen,* and *E. Clementi,* J. chem. Phys. *52,* 4133 (1970).

[4] a) *R. E. Kari* and *I. G. Csizmadia,* J. chem. Phys. *50,* 1443 (1969); b) *R. E. Kari,* Ph. D. Thesis, University of Toronto, Toronto, Canada (1969).

[5] *A. Rauk, L. C. Allen,* and *K. Mislow,* unpublished work.

[6] *J.-M. Lehn* and *B. Munsch,* Chem. Commun. *1969,* 1327.

[7] For ammonia at its ground state equilibrium geometry, the attractive term of the total energy is 9.798484×10^4 kcal/mole while the sum of the repulsive terms is 6.269181×10^4 kcal/mole. Upon attaining a planar geometry, the attractive term increases by 164.41 kcal/mole and the sum of the repulsive terms increases by 169.48 kcl/mole. The difference in these changes, 5.07 kcal/mole, is the actual energy which is required to flatten the molecule.

[8] *L. C. Allen,* Chem. Phys. Letters *2,* 597 (1968).

[9] Both the interelectronic and the internuclear repulsions are greater in the planar form, overriding the much smaller variation in the opposite direction of the kinetic energy term.

[10] *R. J. Gillespie* and *R. S. Nyholm,* Progress in Stereochemistry *2,* 261 (1958).

[11] *A. D. Walsh,* J. chem. Soc. *1953,* 2260, 2296.

inversion, when such atoms become the inverting centers. Inclusion of d-type functions[12] into the basis set has been shown[3] to be almost entirely responsible for the magnitude of the barrier in ammonia. The d-type functions play the role of polarization functions, allowing more freedom of movement for the electrons, rather than of d orbitals as they are usually understood. Although the data for PH_3 are not as definitive, it is highly probable that d-type functions are utilized only as polarization functions in this second row hydride also, as shown by a recent calculation[6]. Incorporation of d-type functions brings about virtually complete agreement between calculated and experimentally determined equilibrium geometries of both NH_3 and PH_3. The inversion barrier calculated[6] for PH_3 increases from 30.9 kcal/mole to 37.2 kcal/mole when polarization functions (p-type functions on H and d-type functions on P) are added to the basis set. In a comparative study[5] of SiH_3^-, PH_3, and SH_3^+, the calculated inversion barriers were found to increase from 36.0, 30.9, and 17.6 kcal/mole, respectively, to 39.6, 40.4, and 30.0 kcal/mole, respectively, upon the addition of d-type polarization functions to the basis set.

2.3. The Effects of Angular Constraint, Electronegativity, and Adjacent Lone Electron Pairs

It has long been anticipated[13], on the basis of valence force field arguments, that severe angular constraint, as occurs in three-membered rings, should have the effect of increasing the magnitude of the barrier to pyramidal inversion. Subsequent experimental work has confirmed this expectation (Section 4.3). Independent non-empirical calculations[14] of the inversion barrier of aziridine *(1)*, R = H, have yielded values of 18.3[15] kcal/mole and 15.5[16] kcal/mole.



(1)

(2)

The barrier has not been determined experimentally but is expected to be in this range (see Section 4.3). A component analysis of the data of *Lehn et al.*[15] shows that the barrier in aziridine is attractive dominant, in contrast to the results for unstrained systems (see Section 2.1). In the strained molecule, the pyramidal form is stable with regard to nuclear-electronic attraction but unstable with regard to the sum of the repulsive terms. Energy lost through decreased nuclear-electronic attraction is not compensated for by decreased repulsive interactions in the planar form. Component analyses of model systems, derived from fixing the HNH angle of NH_2F and one of the HNH angles of NH_3 at 80° during inversion, have yielded the same results[17].

The inversion barrier in oxaziridine *(2)* was computed[14,15] to be 32.4 kcal/mole and a component analysis of the data shows that, as in aziridine, the barrier is attractive dominant. The endocyclic oxygen appears to increase the absolute value of the changes in both attractive and repulsive terms. In a real system it is not possible to dissociate the role of the oxygen as an electronegative substituent, which influences the inversion barrier through an inductive withdrawal of electrons, from its role as an atom with lone pair electrons which interact with the lone pair of the nitrogen to a different extent in the pyramidal than in the planar form. The effect of electronegativity and angular constraint on inversion barriers has been simulated[17] in a model system, NH_2H', by altering the nuclear charge of H′ to values greater than and less than unity, and by varying the HNH angle. LCAO–MO–SCF calculations in this model system[17] suggest that the increase in the magnitude of the inversion barrier with increased electron withdrawal by the substituent on nitrogen may be sufficient to account for a large portion of the observed effect of heteroatomic substituents. To assess the relative magnitudes of the effect of electronegativity and lone pair repulsion in actual molecules, similar calculations were performed[17] on NH_2F', in which the nuclear charge of F′ was varied to values greater than and less than nine. The calculations[17] show that electronegativity has a much smaller effect on the barrier than does angular constraint or the presence of adjacent lone pairs, and that the effects of both electronegativity and adjacent lone pairs increase as angle constriction increases. A component analysis on both models indicates that, regardless of the electronegativity of H′ or F′, the barrier is repulsive dominant where angular constraint is absent or small, but becomes attractive dominant when the HNH angle is constricted to values approaching the internal bond angles of three-membered rings. This result is in complete accord with the detailed calculations on aziridine and oxaziridine[15]. The generality of this phenomenon, which suggests a different physical origin for the inversion barrier in strained than in unstrained systems, requires further examination.

3. Methods for the Determination of Barriers to Pyramidal Inversion

Any meaningful discussion of pyramidal inversion requires a knowledge of the amount of energy that must be put into a molecule to cause it to undergo an

[12] For a discussion of s-, p-, and d-type functions, see Appendix 1 of *A. Rauk* and *I. G. Csizmadia*, Can. J. Chem. *46*, 1205 (1968).

[13] *J. F. Kincaid* and *F. C. Henriques, Jr.*, J. Amer. chem. Soc. *62*, 1474 (1940).

[14] d-Type polarization functions were not included in the basis set.

[15] *J.-M. Lehn, B. Munsch, Ph. Millie*, and *A. Veillard*, Theoret. chim. Acta *13*, 313 (1969).

[16] *D. T. Clark*, International Symposium, Quantum Aspects of Heteroatomic Compounds in Chemistry and Biochemistry, Jerusalem (1969).

[17] *A. Rauk, L. C. Allen*, and *K. Mislow*, in preparation.

inversion [18]. In the following subsections, brief descriptions are given of various methods that have been used to determine barriers to pyramidal inversion, with reference to the limitations of each method. A qualitative overview is required first to put these methods in the proper perspective. We consider on an equal footing such divers methods as rotation-vibration (microwave) and vibrational spectroscopy, dynamic nuclear magnetic resonance (DNMR) spectroscopy, kinetic methods, and molecular orbital (MO) calculations. There is seldom a decision to be made regarding the best method to use in determining the barrier for a particular system, since there is often little overlap in the range of applicability of the methods. The reliability of a method depends on the level of development of the theory supporting the method and the applicability of the theory to the problem at hand. For example, in MO theory, much of the formalism has been developed since the 1930's, but its practical application to even the simplest polyatomic systems has had to await the advent of large scale computers.

3.1. Molecular Orbital Methods for the Determination of Inversion Barriers

By these methods we mean theoretical methods that require no input of experimental data from the particular molecule whose inversion barrier is being determined, and which are based on the MO approach. Whereas in Section 2 we discussed information obtainable by nonempirical MO calculations regarding the *origin* of the inversion barrier, in this section we discuss the utility of MO calculations as means for deriving estimates of barrier *heights*. In principle, the MO methods have the widest applicability of any of the methods to be discussed. As indicated in Section 2.1, the nonempirical LCAO–MO–SCF method has yielded a quantitative value for the barrier of ammonia [3], and there is no reason to suppose that it cannot be extended to other inversion barriers. However, the inordinate amount of effort required to evaluate the properties of even the simplest invertible system precludes the investigation of most molecules of interest to the organic chemist. This difficulty can be partially surmounted in three ways:

a) Very high quality *ab initio* calculations may be performed on a simple model of the system of interest. The disadvantages of this approach, which arise because the numbers obtained for the model will not be strictly applicable to the actual system, are outweighed by the fact that a good deal of information can be obtained regarding the origin of the barrier and the effect on it of factors simulated by modifications to the model system, and by the reliability of the values so obtained.

b) Non-empirical calculations may be performed on actual systems if the basis sets are suitably chosen. Currently, a compromise must be reached with respect to size of systems to be studied, the size of the basis set (and hence the quality of the calculation); and the amount of computer time available. By this procedure, reasonably accurate barriers may be determined for systems involving, for example, three heavy atoms with their complement of hydrogen atoms.

c) For larger systems, recourse to semi-empirical schemes is necessary. Few reports of semi-empirical calculations of inversion barriers are on record [19].

The values of the barriers thus obtained are for the most part unreliable; however, *Dewar* and *Shanshal* [20] have recently shown that the reasonably sophisticated MINDO scheme can be parametrized to give qualitatively good inversion barriers for a variety of systems, including carbanions and radicals.

The calculated barrier is the difference in total energy of the pyramidal ground state (ideally at its calculated equilibrium geometry, but usually at the known experimental geometry) and the total energy of the planar transition state (ideally with calculated equilibrium bond lengths, but usually with the same bond length as in the pyramidal conformation) and refers to a molecule *in vacuo*, unperturbed by external forces. The number obtained is directly comparable to V_i which is determined by measurements in the gas phase by microwave or vibrational spectroscopy.

The chief advantage of the MO method is that barriers can be obtained for molecules which are too reactive or too unstable, or which have barriers that are too high or too low to be measured by empirical methods. In addition, many electronic properties of the molecule under study are obtained concurrently.

In approximate order of decreasing reliability, theoretical methods may be ranked as follows: LCAO–MO–SCF (Hartree-Fock) and LCAO–MO–SCF–CI, OCE–MO–SCF, two-electron semi-empirical schemes (MINDO, NDDO, CNDO/2), and one-electron semi-empirical schemes (EHMO).

3.2. Empirical Methods of Determining Inversion Barriers

The choice of the empirical method to be used in the determination of an inversion barrier hinges on the structure of the molecule and the magnitude of the barrier. Barriers in the range 0–5 kcal/mole are measurable by microwave spectroscopy, barriers in the range 10–20 kcal/mole by DNMR spectroscopy, barriers from 5–35 kcal/mole by infrared and Raman spectroscopy, and those in the range 20–40 by kinetic measurements. The ranges quoted are approximate and in some cases have been extended considerably by

[18] In the literature of this subject, the magnitude of the inversion barrier is generally expressed by $\Delta G^{\ddagger}$, $\Delta H^{\ddagger}$, E_a, or V_i, depending on the method of determination and the preference of the authors.

[19] See, for example, a) *K. Issleib* and *W. Gründler*, Theoret. chim. Acta *6*, 64 (1966); b) *M. Jaro*, *P. Knowlton*, *J. E. Bissey*, *H. Goldwhite*, and *W. R. Carper*, Mol. Phys. *13*, 165 (1967); c) *T. P. Lewis*, Tetrahedron *25*, 4117 (1969); d) *M. S. Gordon* and *H. Fischer*, J. Amer. chem. Soc. *90*, 2471 (1968); e) reference [20].

[20] *M. J. S. Dewar* and *M. Shanshal*, J. Amer. chem. Soc. *91*, 3654 (1969).

special techniques. Except for kinetic measurements, the interpretation of the observations always requires an intermediate level of interpretation to relate the observed quantity to a kinetic quantity. A brief discussion of each method is given below. Results are given in Section 4, which deals with factors that influence barrier heights.

3.2.1. Measurement of Inversion Barriers by Microwave Spectroscopy

The influence of inversion on the rotational spectrum of a pyramidal molecule has been treated in detail by *Townes* and *Schawlow* [21] so that only a brief qualitative description need be given here. Inversion is detectable in the rotation-vibration spectrum by a splitting, ΔE, of the vibrational energy levels due to quantum mechanical tunneling, the frequency of inversion by tunneling being given by $\Delta E/h$. In its ground vibrational state, NH_3 inverts about 2.4×10^{10} times a second. The frequency of inversion, and hence the splitting of the vibrational energy levels, increases as the vibrational quantum number increases. In order to derive a number for the inversion barrier, an assumption is made regarding the shape of the potential function (force field) along some normal coordinate that leads to inversion, and the force field is parametrized to reproduce the observed microwave spectrum.

Microwave spectroscopy has been used to determine the barriers to inversion of the simple amines, NH_3 [21,22], CH_3NH_2 [23], and $(CH_3)_2NH$ [24]. In the last case the barrier was calculated by the Wentzel-Kramers-Brillouin method which assumes a double minimum potential function for inversion described by a cosine barrier connected by the Kramers connection formulas to increasing and decreasing exponentials.

Swalen and *Ibers* [22] have reviewed various types of potential functions that have been utilized to describe the inversion of ammonia and these will not be repeated here. Their own form of the potential function

$$V(q) = 1/2\, aq^2 + 1/2\, bq^4 + ve^{-(cq)^2} \qquad \text{(b)}$$

where a, b, c, and v are potential constants and q is the normal coordinate of the motion, has yielded the currently accepted value of the inversion barrier of ammonia. The quartic term does not markedly improve the agreement with experiment. The same form of the potential was used for determining the barrier in methylamine [23].

For all practical purposes, the applicability of microwave spectroscopy as a means for determining inversion barriers is limited to primary or secondary amines of relatively simple structure with barriers below 5 kcal/mole.

3.2.2. Barriers from Vibrational Spectroscopy

Vibrational spectroscopy is similar to rotational or microwave spectroscopy (Section 3.2.1) in that an assumption must be made regarding the shape of the potential function along some vibrational mode which leads to inversion. *Kincaid* and *Henriques* [13] used a parabolic potential function of the form

$$V = kh^2/2 \qquad \text{(c)}$$

where

$$k = 4\pi^2 \nu^2 \mu \qquad \text{(d)}$$

and h is the height of the pyramid, ν is the frequency of the vibration which leads to inversion, and μ is an expression for the reduced mass of the system. For a symmetric top molecule, XY_3, in which the Y–Y distances are invariant, this is given by

$$\mu = 3M_xM_y/(3M_y + M_x) \qquad \text{(e)}$$

where M_x and M_y are the masses of groups or atoms X and Y. This simple potential function tends to overestimate the value of V_i since the barrier is peaked rather than rounded.

The Costain-Sutherland [25] model [equation (f)] of a valence force field has had much greater success in the determination of barriers in symmetric top molecules [26]. The potential has the form

$$V = \frac{3}{2}\,(k_l\,(l-l_e)^2 + k_\delta\,(\alpha-\alpha_e)^2) \qquad \text{(f)}$$

where l_e and α_e are the equilibrium X–Y bond length and equilibrium YXY bond angles, respectively, and the force constants, k_l and k_δ, depend on the symmetric stretching frequency, ν_1, and symmetric bending frequency, ν_2, respectively. By symmetry, $(l-l_e)$ is related to $(\alpha-\alpha_e)$ so that equation (f) may be reduced to

$$V = K\,(\alpha-\alpha_e)^2 \qquad \text{(g)}$$

and the barrier is given by

$$V_i = K\,(2\pi/3-\alpha_e)^2 \qquad \text{(h)}$$

Other types of double-well potential functions, specifically applied to the ammonia molecule, have also been used [22,27].

[21] *C. H. Townes* and *A. L. Schawlow*: Microwave Spectroscopy, McGraw Hill, New York 1955, pp. 62, 300.

[22] *J. D. Swalen* and *J. A. Ibers*, J. chem. Phys. *36*, 1914 (1962).

[23] *M. Tsuboi*, *A. Y. Hirakawa*, and *K. Tamagake*, J. mol. Spectry. *22*, 272 (1967).

[24] *J. E. Wollrab* and *V. W. Laurie*, J. chem. Phys. *48*, 5058 (1968).

[25] *C. C. Costain* and *G. B. B. M. Sutherland*, J. phys. Chem. *56*, 321 (1952).

[26] *R. E. Weston, Jr.*, J. Amer. chem. Soc. *76*, 2645 (1954); *G. W. Koeppl*, *D. S. Sagatys*, *G. S. Krishnamurthy*, and *S. I. Miller*, *ibid. 89*, 3396 (1967).

[27] *R. Moccia* and *L. Randaccio*, J. chem. Phys. *45*, 4303 (1966).

Vibrational spectroscopy, as a method for determining barriers to inversion, differs from microwave spectroscopy in that the parameters of the assumed force field are obtained by fitting as many vibrational levels as can be observed, rather than by fitting the splittings of the first and second vibrational levels. Vibrational spectroscopy is therefore applicable to molecules where the splitting of energy levels is immeasurably small, such as hydrides with large barriers to inversion, *e.g.*, PH_3 or AsH_3, or molecules in which three heavy atoms or groups are bonded to the inverting center. For molecules with high barriers, a large extrapolation is necessary to obtain a value for the barrier height, and the value so obtained is usually quite sensitive to the equilibrium geometry of the molecule.

3.2.3. Direct Kinetic Measurements of Inversion Barriers

Inversion, which is a unimolecular reaction, obeys first order kinetics[28],

$$\ln \frac{(P_t - P_\infty)}{(P_0 - P_\infty)} = kt \qquad \text{(i)}$$

where P_t is an observable directly related to the concentration of the invertomers, such as specific rotation or absorbances (NMR, IR, UV) due to invertomers, at time t. Application of this direct method for determining the rate constant for inversion is limited to compounds whose invertomers are diastereomers or enantiomers with distinguishable physical properties, which can be obtained as a nonequilibrium mixture, and which invert at a convenient rate in an accessible temperature range.

Inversion barriers can be estimated from the rate constants by the following expressions. We can write

$$\frac{d\ln k}{dT} = E_a/RT^2 \qquad \text{(j)}$$

or

$$k = Ae^{-E_a/RT} \qquad \text{(k)}$$

where k is the unimolecular rate constant for inversion at temperature T, E_a is the Arrhenius activation energy, and A is the frequency factor. If the rate constant at a certain temperature is known, then the free energy difference, $\Delta G^{\ddagger}$, between ground and transition states can be calculated from the Eyring equation, assuming a transmission coefficient of unity,

$$k = \left(\frac{kT}{h}\right) e^{-\Delta G^{\ddagger}/RT} \qquad \text{(l)}$$

In solution, the enthalpy of activation, $\Delta H^{\ddagger}$, is related to the Arrhenius activation energy by the relation

$$\Delta H^{\ddagger} = E_a - RT \qquad \text{(m)}$$

The entropy of activation, $\Delta S^{\ddagger}$, a measure of the relative degree of disorder in the transition state, is defined by

$$\Delta S^{\ddagger} = \frac{\Delta H^{\ddagger} - \Delta G^{\ddagger}}{T} \qquad \text{(n)}$$

For the thermal inversion process, where no dissociation occurs in the excited state, $\Delta S^{\ddagger}$ and log A values are expected to be, and are usually found to be, close to zero and 13, respectively[29].

3.2.4. Determination of Inversion Barriers by Dynamic Nuclear Magnetic Resonance (DNMR) Spectroscopy

The DNMR method for determination of inversion barriers differs from direct kinetic methods solely in the manner in which the rate constant is obtained. In contrast to the direct methods, which involve a measurement of the rate of conversion of one invertomer to another under necessarily nonequilibrium conditions, the DNMR method depends on the interpretation of observed spectral changes in terms of the rate of exchange of the two invertomers only under equilibrium conditions.

The theory and application of NMR spectroscopy to the measurement of intramolecular exchange processes has been reviewed elsewhere[31–34]. Two approaches are in common use: that employing the coalescence phenomenon, and total line shape analysis. For the former, as the simplest example of many, equation (o) gives the rate of exchange, k_c, at the coalescence temperature, T_c, provided that the two exchanging groups

$$k_c = \left(\pi/\sqrt{2}\right) \Delta\nu_{AB} \qquad \text{(o)}$$

are uncoupled, that the signals (A and B) are of equal intensity, and that the limiting chemical shift difference, $\Delta\nu_{AB}$, is much greater than the linewidth of the signals in the absence of exchange[35]. Where conditions are optimum, this approximate and rapid procedure yields substantially the same value of $\Delta G^{\ddagger}$ as does the more laborious complete line shape analysis which is otherwise necessary to give rates of exchange from which activation parameters can be calculated.

Numerous computer programs exist for performing a complete line shape analysis[36]. It is therefore a

[28] *A. A. Frost* and *R. G. Pearson*: Kinetics and Mechanism, 2nd. Edit., Wiley, New York 1961.

[29] For a remarkable exception to this statement, see *Jautelat* and *Roberts* [30], who found that for *(3)*, R = CH_3, log A and $\Delta S^{\ddagger}$ ranged from 16.33 to 21.67, and from 14 e.u. to 38 e.u., respectively, depending on solvent.

[30] *M. Jautelat* and *J. D. Roberts*, J. Amer. chem. Soc. *91*, 642 (1969).

[31] *J. W. Emsley, J. Feeney*, and *L. H. Sutcliffe*: High Resolution Nuclear Magnetic Resonance Spectroscopy. Pergamon Press, New York 1965, Vol. 1, Chapter 9.

[32] *G. Binsch* in *N. L. Allinger* and *E. L. Eliel*: Topics in Stereochemistry. Interscience, New York 1968, Vol. 3, p. 97.

[33] *C. S. Johnson, Jr.*, in *J. S. Waugh*: Advances in Magnetic Resonance. Academic Press, New York 1965, Vol. 1, p. 33.

[34] *J. D. Andose, J.-M. Lehn, K. Mislow*, and *J. Wagner*, in press.

[35] *A. Allerhand, H. S. Gutowsky, J. Jonas*, and *R. S. Meinzer*, J. Amer. chem. Soc. *88*, 3185 (1966).

[36] See, for example, *G. Binsch*, J. Amer. chem. Soc. *91*, 1304 (1969).

trivial matter to convert a temperature-dependent NMR spectrum to the appropriate activation parameters. However, the interpretation of the origin of the barrier requires careful assessment of such extraneous factors as specific solvent effects, solute-solute interactions (dimerization and higher association), the constitutional integrity of the molecule in solution, and competitive intramolecular conformational processes, all of which may impart a temperature dependence to the observed spectrum that is not at all relevant to the barrier under investigation. The effects of the first three factors can usually be disclosed by standard procedures such as variation of solvent, dilution experiments, and observation of reversibility of spectral changes, among others. The fourth effect is far more difficult to identify, especially if, as will concern us in Section 4.4, the competing processes are intramolecular inversion of configuration and hindered rotation about one or more bonds to the tricoordinate center.

The magnitude of the barrier is determined from an analysis of the observed temperature-dependent spectral changes due to the effective averaging of the environments of diastereotopic groups in the molecule. If, in principle, both inversion at the tricoordinate center and rotation about some or all of the bonds to the tricoordinate center must be rapid on the NMR time scale in order to average out nonequivalent environments, two major assumptions have to be made in order to assign the origin of the rate-determining process:

a) The intrinsic chemical shift difference is sufficiently large so that, even under conditions of rapid rotation but slow inversion, a chemical shift difference in the diastereotopic groups is still detectable.

b) In the potential surface for rotation-inversion, discrete transition states occur for rotation and inversion, rather than a single transition state for both rotation and inversion.

Given these assumptions, a decision may be made regarding the origin of the barrier by considering changes that occur in the magnitude of the barrier as a function of substituents. However, this now requires further, albeit reasonable, assumptions concerning the probable effect of the substituents on the barrier, namely that bulky groups [37], and groups which can delocalize the lone pair of electrons on the central atom [38], lead to a lower inversion barrier and a higher barrier to rotation.

Assumption (b) could be resolved by determining the potential surface for rotation-inversion by detailed quantum mechanical calculation on the system in question. The complete surfaces for the model compounds $^{-}CH_2SH$ [45], $^{-}CH_2S(O)H$ [46], and $^{-}CH_2S(O_2)H$ [47] have been calculated by the nonempirical LCAO–MO–SCF method using a minimal Gaussian basis set. In every case, a single transition state for rotation-inversion was found. However, although gross conformational features are reasonably well obtained by this procedure, it is not known whether a single transition state for rotation and inversion would be obtained from more accurate calculations. Assumption (b) could also be verified by the observation of two discrete barrier processes, *i.e.*, two discrete coalescence phenomena.

Failure to observe more than one coalescence phenomenon where competitive processes can in principle occur means that one of the following three circumstances may obtain. First, assumption (b) may be invalid, *i.e.*, there may only be a single transition state to inversion-rotation. Second, two or more transition states may exist, but $\Delta G_c^{\neq}$ for only one lies within the explored range of measurements. Third, two transition states may exist, and both barriers may be in the explored range of measurements, but assumption (a) may not be valid, *i.e.*, the chemical shift difference in diastereotopic groups under conditions of rapid rotation but slow inversion may be too small to be detected at any temperature (accidental degeneracy) and any observed coalescence phenomenon is ascribable to the rotational mode; conversely, under conditions of rapid inversion but slow rotation, accidental degeneracy may lead to a single coalescence phenomenon ascribable to the inversional mode. Unfortunately, there is no way of predicting the magnitude of the chemical shift difference between diastereotopic groups, and as to precedent, numerous cases are on record of accidental NMR equivalence of such groups. The point cannot be overemphasized that, unless two distinct coalescence phenomena are observed, and in the absence of compelling supporting evidence, the identity and magnitude of the inversion barrier cannot be regarded as *rigorously* established. In the case of the inversion-rotation dichotomy under discussion, we know of no report on record in which both barriers (*i.e.* coalescence phenomena) have been observed.

4. Factors That Affect the Magnitude of the Inversion Barrier

It will be convenient to group major factors that influence the magnitude of the inversion barrier into four broad categories: steric effects; effects of con-

[37] See, for example, references [39], [40], [41], and [42].

[38] See, for example, references [39], [43], and [44].

[39] *M. Raban, G. W. J. Kenney, Jr.*, and *F. B. Jones, Jr.*, J. Amer. chem. Soc. *91*, 6677 (1969).

[40] *M. Raban* and *G. W. J. Kenney, Jr.*, Tetrahedron Letters *1969*, 1295.

[41] *J.-M. Lehn* and *J. Wagner*, Chem. Commun. *1968*, 1298.

[42] *A. H. Cowley, M. J. S. Dewar*, and *W. R. Jackson*, J. Amer. chem. Soc. *90*, 4185 (1968).

[43] *J. R. Fletcher* and *I. O. Sutherland*, Chem. Commun. *1969*, 706.

[44] *M. J. S. Dewar* and *B. Jennings*, J. Amer. chem. Soc. *91*, 3655 (1969).

[45] *S. Wolfe, A. Rauk, L. M. Tel*, and *I. G. Csizmadia*, Chem. Commun. *1970*, 96. See also *A. Rauk*, Ph. D. Thesis, Queen's University, Kingston, Ontario, Canada (1968).

[46] *A. Rauk, S. Wolfe*, and *I. G. Csizmadia*, Can. J. Chem. *47*, 113 (1969).

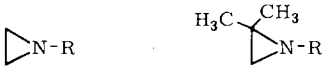
[47] *S. Wolfe, A. Rauk*, and *I. G. Csizmadia*, J. Amer. chem. Soc. *91*, 1567 (1969).

jugation or hyperconjugation; effects of angular constriction; and those due to heteroatomic substitution. The well-known increase of inversion barrier heights in a given group of the periodic table with increasing atomic numbers[26] (*e.g.*, $AsR_3 > PR_3 > NR_3$) will not be the subject of a detailed comparative analysis in the absence of a sound theoretical basis at this time. The less well defined effects of solvent on inversion barriers[48–51] and other special effects[52] will be considered outside the scope of this review.

4.1. Steric Effects on Inversion Barriers

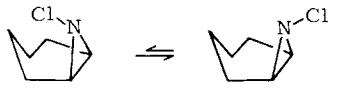
Steric size manifests itself as an electronic repulsion (due to the Pauli exclusion principle) between nonbonded groups. As the steric requirement of a substituent increases, the pyramidal ground state is destabilized relative to the less crowded transition state[53], with a resultant decrease in the barrier to inversion.

Steric acceleration of the rate of inversion in *N*-alkylaziridines has been confirmed by several studies[54–57]. For example, barriers of inversion of aziridines *(1)* decrease in the order of increasing steric requirement of R: $CH_3 < C_2H_5 < i\text{-}C_3H_7 \ll t\text{-}C_4H_9$[56,57]. Similarly, whereas simple *N*-haloaziridines are pyramidally

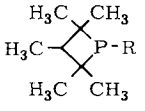


(1) *(3)*

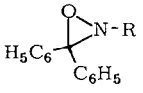
stable at room temperature[58–60], the relatively facile *cis* → *trans* conversion of *(4)* has been attributed to steric crowding in the *cis* conformation[61]. Steric arguments also explain the different inversion rates in the 1-methylphosphetane *(5)*, R = CH_3, which shows



(4)



(5)



(6)

approximately 5% stereomutation after heating for four days at 162 °C, and the 1-*t*-butyl derivative *(5)*, R = $t\text{-}C_4H_9$, in which inversion is readily followed in the temperature range 118 to 157 °C[62]. The difference in steric requirements of a methyl group and a *t*-butyl group is also reflected in the barriers to inversion of diphenyloxaziridines[63]: the activation energy for pyramidal inversion of the methyl derivative *(6)*, R = CH_3, is 6.4 kcal/mole larger than the inversion barrier of the *t*-butyl derivative *(6)*, R = $t\text{-}C_4H_9$, (E_a = 28.4 kcal/mole).

4.2. Conjugative and Hyperconjugative Effects on Inversion Barriers

For reasons of ease in visualization, conjugation and hyperconjugation are often discussed in terms of changes in hybridization of atomic s, p, and d orbitals, rather than in terms of the more physically reasonable canonical Hartree-Fock molecular orbitals. The LCAO procedure is only one of many ways of arriving at an expansion of the one-electron wavefunctions (MO's), and the correspondence between MO's and AO's becomes increasingly indistinct as one passes from the occupied MO's of lowest energy to the higher occupied (valence) MO's. In this context, the question of the participation of atomic d orbitals is irrelevant. Within the valence bond framework, however, it is often desirable to invoke participation of "unoccupied d orbitals" to rationalize the accommodation of extra electrons in the vicinity of a nucleus. Thus, in this section, our use of the term "$(p-d)_\pi$ conjugation" is consistent with the useful and generally accepted *ad hoc* valence bond description of electronic structure, and is not to be regarded as a commentary on the controversial question of the participation of d orbitals in bonding to second row atoms.

During inversion, the hybridization of the bonding orbitals at the inverting center may be qualitatively regarded as changing from sp^3 to sp^2, and that of the lone pair of electrons from sp^3 to p. Any factor which favors the rehybridization process, such as π delocalization of the lone pair, tends to flatten the pyramid and thus to lower the barrier to inversion. Adjacent unsaturated systems lead to significantly lower barriers

[48] *N. I. Bagdanskis* and *M. O. Bulanin*, Opt. Spectry. (USSR) *19*, 128 (1965).

[49] *F. G. Riddell*, *J.-M. Lehn*, and *J. Wagner*, Chem. Commun. *1968*, 1403.

[50] *D. E. Leyden* and *W. R. Morgan*, Chem. Commun. *1969*, 598.

[51] *M. Saunders* and *F. Yamada*, J. Amer. chem. Soc. *85*, 1882 (1963).

[52] For example, *G. W. Gribble*, *N. R. Easton*, and *J. T. Eaton*, Tetrahedron Letters *1970*, 1075.

[53] The transition state is closer to planarity than one or both of the ground states. It is not planar, however, when the invertomers are diastereomers, or when they are enantiomers in chiral media; *i.e.*, planarity obtains only in automerization reactions or in the interconversion of enantiomers under achiral conditions.

[54] *A. T. Bottini* and *J. D. Roberts*, J. Amer. chem. Soc. *80*, 5203 (1958).

[55] *F. A. L. Anet* and *J. M. Osyany*, J. Amer. chem. Soc. *89*, 352 (1967).

[56] *S. J. Brois*, J. Amer. chem. Soc. *89*, 4242 (1967).

[57] *S. J. Brois*, Trans. N. Y. Acad. Sci. *31*, 931 (1969).

[58] a) *S. J. Brois*, J. Amer. chem. Soc. *90*, 506 (1968); b) *S. J. Brois*, *ibid.* *90*, 508 (1968).

[59] *J.-M. Lehn* and *J. Wagner*, Chem. Commun. *1968*, 148.

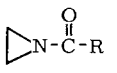
[60] *R. G. Kostyanovskii*, *I. I. Tchervin*, *A. A. Fomichov*, *Z. E. Samojlova*, *C. N. Makarov*, *Yu. V. Zeifman*, and *B. L. Dyatkin*, Tetrahedron Letters *1969*, 4021.

[61] *D. Felix* and *A. Eschenmoser*, Angew. Chem. *80*, 197 (1968); Angew. Chem. internat. Edit. *7*, 224 (1968).

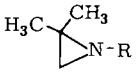
[62] *S. E. Cremer*, *R. J. Chorvat*, *C. H. Chang*, and *D. W. Davis*, Tetrahedron Letters *1968*, 5799; *S. E. Cremer*, personal communication.

[63] *F. Montanari*, *I. Moretti*, and *G. Torre*, Chem. Commun. *1968*, 1694.

to inversion at nitrogen and phosphorus. The near planarity of the amide bond is well known [64]. Although the geometry at nitrogen in *(7)*, R = *p*-BrC_6H_4, is pyramidal [66] by reason of angle strain, as will be discussed in Section 4.3, slow inversion has not been detected in a variety of *N*-acylaziridines [*(7)*,



(7)



(3)

R = C_6H_5, *p*-$CH_3OC_6H_4$, *p*-$(CH_3)_2NC_6H_4$, *p*-$NO_2C_6H_4$ [67]; R = CH_3 [55]], suggesting that $\Delta G_c^{\neq} <$ 6 kcal/mole [67]. For *(7)*, R = OCH_3, and *(7)*, R = $N(CH_3)_2$, barrier values of $\Delta G_c^{\neq}$ = 7.6 and 10.8 kcal/mole, respectively, were observed [55].

The free energy of activation for inversion of *(3)*, R = CH_3, is in the range 17.7–18.8 kcal/mole [30] or 20.5 kcal/mole [59]. By contrast, *N*-arylaziridines have barriers which are less by 5 to 10 kcal/mole (Table 1) [34]. This effect provides evidence that an

Table 1. Inversion barriers [34] for 1-aryl-2,2-dimethylaziridines. *(3)* R = aryl.

Aryl group	T_c (°C)	$\Delta G_c^{\neq}$ (kcal/mole) [a]
4-$CH_3OC_6H_4$	− 26	12.5
C_6H_5	− 49	11.2
4-ClC_6H_4	− 53	11.0
3-$CF_3C_6H_4$	− 59	10.7
4-$CF_3C_6H_4$	− 72	10.0
4-$NO_2C_6H_4$	−107	8.2

[a] Calculated from the Eyring equation.

adjacent aryl group lowers the barrier to inversion at nitrogen, presumably by a conjugative mechanism.

In phosphines, the effect of aryl substitution is not as pronounced as in amines; a recent study [68] has shown that the free energy change, $\Delta G_{130}^{\neq}$, is roughly proportional to the number of aryl substituents, each aryl group decreasing the value of $\Delta G^{\neq}$ by approximately 2–3 kcal/mole (Table 2).

Table 2. Inversion barriers [68] for $R_1R_2PCH_3$.

R_1	R_2	$\Delta G_{130}^{\neq}$ (kcal/mole) [a]
C_6H_{11}	*n*-C_3H_7	35.6
C_6H_5	*n*-C_3H_7	32.1
C_6H_5	CH_2=$CHCH_2$	32.8
C_6H_5	*t*-C_4H_9	32.7
C_6H_5	4-$CH_3OC_6H_4$	30.8
C_6H_5	4-$CH_3C_6H_4$	30.3
C_6H_5	4-$CF_3C_6H_4$	29.1
C_6H_5	β-$C_{10}H_7$	29.7

[a] In decalin.

[64] The geometry at the nitrogen in formamide is a very shallow pyramid with an inversion barrier of 1.06 kcal/mole [65]

[65] *C. C. Costain* and *J. M. Dowling*, J. chem. Phys. *32*, 158 (1960).

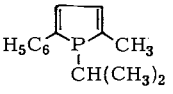
[66] *R. P. Shibaeva*, *L. O. Atovmyan*, and *R. G. Kostyanovskii*, Dokl. Akad. Nauk USSR *175*, 586 (1967).

[67] *G. R. Boggs* and *J. T. Gerig*, J. org. Chem. *34*, 1484 (1969).

[68] *R. D. Baechler* and *K. Mislow*, J. Amer. chem. Soc. *92*, 3090 (1970).

Comparison of the data in Tables 1 and 2 further reveals that the magnitudes of the barriers to inversion in arylphosphines are far less sensitive to *p*-substitution than are barriers in arylaziridines. The same insensitivity was observed in a study of inversion in arylsulfoxides [69]. The conclusion is inescapable that the rate of inversion at an element from the second row is less sensitive to conjugation than that at an element from the first row. We note that, as the electron-withdrawing power of the *p*-substituent increases, the inversion barrier decreases, and that a Hammett-type linear free energy relationship correlates the rates for inversion at nitrogen [34], phosphorus [68], and sulfur [69].

A striking example of the lowering of the inversion barrier due to $(2p-3p)_\pi$ conjugation occurs in the phosphole system. A barrier of $\Delta G_{25}^{\neq}$ = 16 kcal/mole has been found [70] for *(8)*, which represents a reduction of about 25 kcal/mole from barriers in the analogous saturated systems. Conjugation of the lone pair of



(8)

electrons on phosphorus with the ring $2p_\pi$ electrons is probably facilitated by achievement of the favorable $4n+2$ ($n = 1$) π electron configuration in the planar (transition state) conformation. An assumption of coplanar geometry at nitrogen has been made to fit the observed microwave spectrum of the analogous nitrogen heterocycle, pyrrole [71]. The barrier of 35.1 kcal/mole calculated for 2-azirene [16] exemplifies the converse, a raising of the barrier by antiaromatic behavior ($4n$ π electron configuration) in the transition state.

Delocalization of the lone pair electrons into empty d orbitals by $(p-d)_\pi$ conjugation when the inversion center is directly bonded to a second row atom has been postulated to explain lowering of inversion barriers in systems such as 1-sulfenylaziridines [41,72], diphosphines [73,74], diarsines [74,75], and thiolsulfinates [76] (see also Sections 3.2.4 and 4.4). The co-

[69] *D. R. Rayner*, *A. J. Gordon*, and *K. Mislow*, J. Amer. chem. Soc. *90*, 4854 (1968).

[70] *W. Egan*, *R. Tang*, *G. Zon*, and *K. Mislow*, J. Amer. chem. Soc. *92*, 1442 (1970).

[71] *L. Nygaard*, *J. T. Nielsen*, *J. Kirchheimer*, *G. Mattesen*, *J. Rastrup-Andersen*, and *G. O. Sorensen*, J. mol. Struct. *3*, 491 (1969).

[72] *F. A. L. Anet*, *R. D. Trepka*, and *D. J. Cram*, J. Amer. chem. Soc. *89*, 357 (1967).

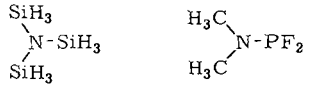
[73] a) *J. B. Lambert*, *G. F. Jackson*, *III*, and *D. C. Mueller*, J. Amer. chem. Soc. *92*, 3093 (1970); b) *J. B. Lambert* and *D. C. Mueller*, J. Amer. chem. Soc. *88*, 3669 (1966).

[74] *J. B. Lambert*, *G. F. Jackson*, *III*, and *D. C. Mueller*, J. Amer. chem. Soc. *90*, 6401 (1968).

[75] *J. B. Lambert* and *G. F. Jackson*, *III*, J. Amer. chem. Soc. *90*, 1350 (1968).

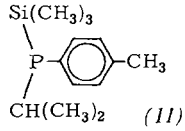
[76] *P. Koch* and *A. Fava*, J. Amer. chem. Soc. *90*, 3867 (1968). However, see *F. Wudl*, *R. Gruber*, and *A. Padwa*, Tetrahedron Letters *1969*, 2133.

planar structure at nitrogen in *(9)* [77] and *(10)* [78] may also be explained by $(p-d)_\pi$ conjugation involving the lone pair on nitrogen and the d orbitals of



(9) *(10)*

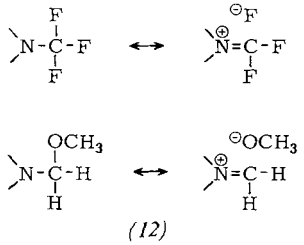
silicon and phosphorus, respectively. A striking example of the lowering of the inversion barrier due to $(3p-3d)_\pi$ conjugation is encountered in *(11)*, where



(11)

the inversion barrier is found [79] to be significantly lower than that of comparable non-silicon containing phosphines. Electronegativity effects undoubtedly contribute to the observed lowering of these barriers.

Electronegative groups *alpha* to the inversion center can also assist in π delocalization of the lone-pair electrons by hyperconjugation, as in *(12)*. Thus, trifluoromethyl-substituted aziridines [80] have substantially faster rates of inversion than alkyl-substituted aziridines, presumably because of C–F hyperconjugation. Similarly, in cyclic hydroxylamines [81] a



(12)

CH_2OCH_3 substituent on nitrogen has been found to lower the barrier relative to an *iso*-propyl substituent, presumably because of C–O hyperconjugation.

4.3. Effects of Angular Constraint

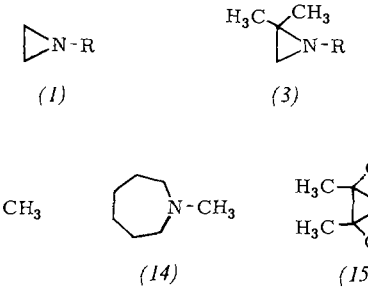
As a rule, simple amines undergo inversion at rates that are too fast to be measured by DNMR, and few measurements of barriers have been reported. Some of these are collected in Table 3. Values of the barrier lie in the range 4–8 kcal/mole.

Table 3. Inversion barriers in simple amines.

Amine	Barrier (kcal/mole)	Ref.
ammonia	V_i = 5.8 (mw) [a]	[22]
methylamine	V_i = 4.8 (mw)	[23]
dimethylamine	V_i = 4.4 (mw)	[24]
trimethylamine	V_i = 7.46 (vs) [b]	[26]
(13)	$\Delta G^{\ddagger}_{-100}$ = 8 (DNMR)	[82]
(14)	$\Delta G^{\ddagger}_{-125}$ = 7 (DNMR)	[82]

[a] Microwave spectroscopy. [b] Vibrational spectroscopy.

Early calculations led to the expectation [13,83] that severe angular constraint, as occurs in aziridines, should stabilize nitrogen pyramids at ordinary temperatures, and although the subsequently observed effect is not as dramatic as anticipated, angular constraint does lead to a substantial increase in the barrier to inversion. Thus, a lower limit of 11.6 kcal/mole has been estimated [84] for the inversion barrier of aziridine itself, and E_a = 10–12 kcal/mole has been measured [85] for *(15)*; the last value is also considered



(1) *(3)* *(13)* *(14)* *(15)*

a lower limit. *N*-Alkylaziridines apparently have considerably higher barriers, E_a = 19 kcal/mole [86] and $\Delta G_c^{\ddagger}$ = 17.7–20.5 kcal/mole [30,59] having been reported for *(1)*, R = CH_3, and *(3)*, R = CH_3, respectively.

The increased activation energy for inversion due to the angular constraint imposed by a three-membered ring is also apparent in cyclopropyl anions which are known to be capable of retaining configuration [87], and in cyclopropyl radicals which exist, at least transiently, as non-planar entities [88,89]. Inversion

[77] a) *E. A. V. Ebsworth, J. R. Hall, M. J. Mackillop, D. C. McKean, N. Sheppard,* and *L. A. Woodward,* Spectrochim. Acta *13*, 202 (1958); b) *K. Hedberg,* J. Amer. chem. Soc. *77*, 6491 (1955); c) For related systems, see *G. Glidewell, D. W. H. Rankin, A. G. Robiette,* and *G. M. Sheldrick,* J. mol. Struct. *4*, 215 (1969); *L. V. Vilkov* and *N. A. Tarasenko,* Chem. Commun. *1969*, 1176.

[78] *E. D. Morris, Jr.,* and *C. E. Nordman,* Inorg. Chem. *8*, 1673 (1969). For related systems, see *J. W. Cox* and *E. R. Corey,* Chem. Commun. *1967*, 123, and references cited therein.

[79] *R. D. Baechler* and *K. Mislow,* unpublished results.

[80] *A. L. Logothetis,* J. org. Chem. *29*, 3049 (1964).

[81] *D. L. Griffith* and *B. L. Olson,* Chem. Commun. *1968*, 1682.

[82] *J. B. Lambert* and *W. L. Oliver, Jr.,* J. Amer. chem. Soc. *91*, 7774 (1969).

[83] a) *R. Adams* and *T. L. Cairns,* J. Amer. chem. Soc. *61*, 2464 (1939); b) *P. Maitland,* Ann. Rept. chem. Soc. London *36*, 239 (1939); c) *J. Meisenheimer* and *L.-H. Chou,* Liebigs Ann. Chem. *539*, 70 (1939); d) *J. D. C. Mole* and *E. E. Turner,* Chem. and Ind. *17*, 582 (1939).

[84] *M. K. Kemp* and *W. H. Flygare,* J. Amer. chem. Soc. *90*, 6267 (1968).

[85] *T. J. Bardos, C. Szantay,* and *C. K. Navada,* J. Amer. chem. Soc. *87*, 5796 (1965).

[86] a) *J. P. Heeschen,* Ph. D. Thesis, University of Illinois, Urbana, Ill. (1959); b) *H. S. Gutowsky,* Ann. N. Y. Acad. Sci. *70*, 786 (1958).

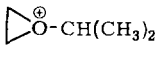
[87] a) *H. M. Walborsky, F. J. Impastato,* and *A. E. Young,* J. Amer. chem. Soc. *86*, 3283 (1964); b) *H. M. Walborsky* and *A. E. Young, ibid. 86*, 3288 (1964); c) *J. B. Pierce* and *H. M. Walborsky,* J. org. Chem. *33*, 1962 (1968).

[88] *J. Jacobus* and *D. Pensak,* Chem. Commun. *1969*, 400; b) see also *H. M. Walborsky, F. P. Johnson,* and *J. B. Pierce,* J. Amer. chem. Soc. *90*, 5222 (1968).

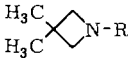
[89] a) *H. M. Walborsky* and *C.-J. Chen,* J. Amer. chem. Soc. *89*, 5499 (1967); b) *M. J. S. Dewar* and *J. M. Harris,* J. Amer. chem. Soc. *91*, 3652 (1969).

barriers of 20.85 kcal/mole [90] and 5.46 kcal/mole [4b] have been calculated for cyclopropyl and methyl anions, respectively. Theoretical [4b,91] studies of the methyl radical indicate that this species is planar, in agreement with experimental (ESR) data [92,93] on a variety of alkyl radicals, including the parent CH_3 [94].

Similarly, while theoretical [95] and experimental [96] evidence on H_3O^+ imply that unstrained oxonium ions are either planar or very shallow pyramids, an inversion barrier of 10 ± 2 kcal/mole has been reported [97] for *(16)*.



(16)



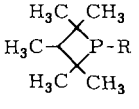
(17)

A rough estimate for the angle strain effect as a function of bond angle may be obtained by comparing the barriers in a series of cyclic tertiary amines, as given in Table 4. It is immediately apparent that, although the barrier for the azetidine derivative *(17)*, R = CH_3, may in part be lowered because of buttressing effects of the two methyl groups on C-3, the effect of angle strain on the barrier falls off rapidly as the CNC angle constriction is relaxed.

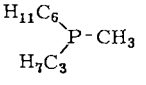
Table 4. Barrier height as a function of ring size.

Compound	Ring size	Barrier height (kcal/mole)	Ref.
(1), R = CH_3	3	19	[86]
(17), R = CH_3	4	8.8	[59]
(13)	5	8.0	[82]
(14)	7	7.0	[82]
(5), R = CH_3	4	*ca.* 40	[62]
(18)	—	35.6	[68]

An indication that angle constraint is an important factor in stabilizing phosphorus pyramids is also seen from the last two entries in Table 4. The pyramid in the four-membered ring phosphorus system *(5)* is more stable than that in the acyclic phosphorus compounds *(18)*, even though buttressing effects in *(5)*,

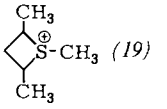


(5)



(18)

R = CH_3, would tend in the direction of lowering the barrier. Similarly, racemization of unstrained sulfonium salts is conveniently followed [98,99] in the temperature range 50–70 °C, but isomers of *(19)* have been reported [100] not to undergo pyramidal inversion up to the temperature of decomposition, 80 °C.



(19)

4.4. Effects of Heteroatomic Substitution

The following attributes of heteroatoms adjacent to an inverting center have been invoked to explain the observed effects on the inversion barrier:

1. The inductive (electronegativity) effect of the substituent.
2. The effect of lone pair-lone pair interactions.
3. Use of substituent d orbitals for delocalization of the lone pair of electrons of the inverting center.
4. Delocalization of the lone pair of electrons of the substituent into d orbitals of the inverting center.

Both increasing electron withdrawal from the inverting center by a non-conjugative mechanism [101] (Section 2.3) as well as the presence of non-bonded electron pairs on the substituent [72,102] are expected to lead to increased inversion barriers. In no instance has it been possible to assess convincingly from empirical studies the relative importance of lone pair-lone pair repulsions and electronegativity of the heteroatom to the increased barrier height, although theoretical studies (Section 2.5) indicate that the former effect may be dominant in halides. The question of torsional angular dependence of the inversion barrier (in the case of axially non-symmetric heteroatomic substituents) remains unanswered. The effects due to use of d orbitals have been mentioned in Section 4.2 and are further discussed below.

A lively controversy exists with regard to the interpretation of the origin of barriers observed by DNMR (Section 3.2.4) in heteroatomically substituted pyramidal molecules. Due to the possible existence of substantial torsional barriers about some heteroatom-heteroatom bonds, an ambiguity arises in assigning the origin of the observed rate process to either rotation or inversion whenever the bond to the substituent containing the heteroatom is not axially symmetric.

The following discussion on heteroatomic effects is subdivided into two parts, the first dealing with in-

[90] *D. T. Clark* and *D. R. Armstrong*, Chem. Commun. *1969*, 850.

[91] *Ph. Millie* and *G. Berthier*, Internat. J. quant. Chem. *2S*, 67 (1968).

[92] *M. C. R. Symons*, Nature *222*, 1123 (1969).

[93] *R. W. Fessenden* and *R. H. Schuler*, J. chem. Phys. *39*, 2147 (1963).

[94] *R. W. Fessenden*, J. phys. Chem. *71*, 74 (1967).

[95] *J. W. Moskowitz* and *M. C. Harrison*, J. chem. Phys. *43*, 3550 (1965).

[96] *R. Savoie* and *P. A. Giguère*, J. chem. Phys. *41*, 2698 (1964), and references therein.

[97] *J. B. Lambert* and *D. H. Johnson*, J. Amer. chem. Soc. *90*, 1349 (1968).

[98] a) *D. Darwish* and *G. Tourigny*, J. Amer. chem. Soc. *88*, 4303 (1966); b) *D. Darwish*, *S. H. Hui*, and *R. Tomilson*, *ibid.* *90*, 5631 (1968).

[99] *R. Scartazzini* and *K. Mislow*, Tetrahedron Letters *1967*, 2719.

[100] *B. M. Trost*, *W. L. Schinski*, and *I. B. Mantz*, J. Amer. chem. Soc. *91*, 4320 (1969).

[101] *H. A. Bent*, Chem. Reviews *61*, 275 (1961).

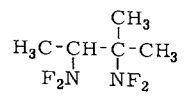
[102] *D. L. Griffith* and *J. D. Roberts*, J. Amer. chem. Soc. *87*, 4089 (1965).

version at tricoordinate, first row atoms in which the main quantum number of the inverting atom is 2, the second dealing with inversion at second or higher row atoms (main quantum number greater than 2).

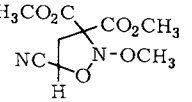
4.4.1. Inversion at First Row Atoms

Heteroatomic substitution slows inversion at nitrogen, as has been shown for five- or six-membered ring hydroxylamines [49,81,103] and hydrazines [104–109]. The effects on the barrier of heteroatomic substitution and angular constraint are compounded in *N*-haloaziridines [58–61], *N*-aminoaziridines [110,111], diaziridines [112], and oxaziridines [63,113–115]. In some cases invertomers have been separated [58b,61,63,103,112,114,115].

Multiple heteroatomic substitution leads to a marked increase in inversion barriers, even in unstrained systems. The powerful effect of fluorine on the stability of the pyramidal structure is seen in NF_3 and CF_3: a value of 42 kcal/mole [26], estimated from vibrational frequencies, for the inversion barrier of NF_3 has recently been revised [116] upward to 56–59 kcal/mole, and a barrier of 27.4 kcal/mole has been calculated [117] for inversion of CF_3 radical, which is known to be pyramidal from ESR data [118], in contrast to the unsubstituted methyl radical which is planar (Section 4.3). In addition, a recent study [119a] of some alkyldifluoroamines has yielded a lower limit of 18.0 kcal/mole for the barrier to inversion ($\Delta G^{\ddagger}$) at the nitrogen atom attached to the tertiary carbon atom in *(20)*, and barriers (E_a) in the range 29–30 kcal/mole have been found [103] for the interconversion of invertomers



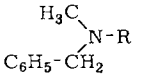
(20)



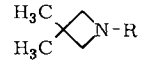
(21)

of *(21)*. The observed [119b] pyramidal stability of $-CFClBr$ in aqueous solution is a further example of this effect

In principle $(p-d)_\pi$ delocalization of the nitrogen lone pair is possible in *N*-haloaziridines and this effect was originally proposed to rationalize the apparent rapid inversion in *N*-chloroaziridines [120] (since shown to be slow [58,59,61]) and in *(22)*, R = Cl [102]. However, the low barrier (11.9 kcal/mole) of *(17)*, R = Cl [59], as measured by DNMR, is in sharp contrast to

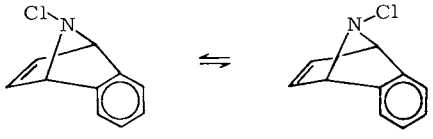


(22)



(17)

the high inversion barrier ($\Delta G^{\ddagger}$ = 23.5 kcal/mole) [121] of *(23)*, as measured by direct kinetics, even though the internal bond angles at nitrogen are similar in the two compounds. Relatively high rates of inversion



(23)

have been reported [72] for aziridines *(1)* with sulfur and phosphorus centered groups attached to nitrogen, and are in the order [72]: $R = P(O)(C_6H_5)_2 \gg S(O_2)C_6H_5 > S[2,4\text{-}(NO_2)_2\text{-}C_6H_3] > SC_6H_5 > S(O)C_6H_5$. Once again, $(p-d)_\pi$ delocalization could here be invoked; unfortunately, in no case where a coalescence temperature was observed can slow rotation about the N–S or N–P bond be ruled out as the rate determining step, for reasons discussed below.

Barrier phenomena (10–20 kcal/mole) have been observed in *acyclic* hydroxylamines [40,102], hydrazines [43,44,122], sulfonamides [123,124], sulfinamides [125], sulfenamides [39,124,125,126], and aminophosphines [42,127,128]. The interpretation of the ori-

[103] *K. Müller* and *A. Eschenmoser*, Helv. chim. Acta *52*, 1823 (1969).

[104] *E. L. Allred, C. L. Anderson, R. L. Miller*, and *A. L. Johnson*, Tetrahedron Letters *1967*, 525.

[105] *J. E. Anderson* and *J.-M. Lehn*, Bull. Soc. chim. France *1966*, 2402.

[106] *J. E. Anderson* and *J.-M. Lehn*, J. Amer. chem. Soc. *89*, 81 (1967).

[107] *J. P. Kintzinger, J.-M. Lehn*, and *J. Wagner*, Chem. Commun. *1967*, 206.

[108] *J. E. Anderson* and *J. D. Roberts*, J. Amer. chem. Soc. *90*, 4186 (1968).

[109] *R. A. Y. Jones, A. R. Katritsky*, and *A. C. Richards*, Chem. Commun. *1969*, 708.

[110] *S. J. Brois*, Tetrahedron Letters *1968*, 5997.

[111] *R. S. Atkinson*, Chem. Commun. *1968*, 676.

[112] *A. Mannschreck* and *W. Seitz*, Angew. Chem. *81*, 224 (1969); Angew. Chem. internat. Edit. *8*, 212 (1969).

[113] *W. D. Emmons*, J. Amer. chem. Soc. *79*, 5739 (1957).

[114] *D. R. Boyd*, Tetrahedron Letters *1968*, 4561; *D. R. Boyd* and *R. Graham*, J. chem. Soc. (C) *1969*, 2648; *D. R. Boyd, R. Spratt*, and *D. M. Jerina*, J. chem. Soc. (C) *1969*, 2650.

[115] *A. Mannschreck, J. Linss*, and *W. Seitz*, Liebigs Ann. Chem. *727*, 224 (1969).

[116] See Table 1, footnote (f) of reference [19d].

[117] By LCAO–MO–SCF (Hartree-Fock) calculations using a fairly limited 5s2p Gaussian basis set for C and F; *K. Morokuma, L. Pedersen*, and *M. Karplus*, J. chem. Phys. *48*, 4801 (1968).

[118] *R. W. Fessenden* and *R. H. Schuler*, J. chem. Phys. *43*, 2704 (1965).

[119] a) *S. K. Brauman* and *M. E. Hill*, J. chem. Soc. (B) *1969*, 1091; b) *M. K. Hargreaves* and *B. Modarai*, Chem. Commun. *1969*, 16.

[120] *V. F. Bystrov, R. G. Kostyanovskii, O. A. Panshin, A. U. Stepanyants*, and *O. A. Iuzhakova*, Opt. Spectry. (USSR) *19*, 122 (1965).

[121] *V. Rautenstrauch*, Chem. Commun. *1969*, 1122.

[122] *J. E. Anderson, D. L. Griffith*, and *J. D. Roberts*, J. Amer. chem. Soc. *91*, 6371 (1969).

[123] *M. Raban, G. W. J. Kenney, Jr., J. M. Moldowan*, and *F. B. Jones, Jr.*, J. Amer. chem. Soc. *90*, 2985 (1968).

[124] *M. Raban* and *F. B. Jones, Jr.*, J. Amer. chem. Soc. *91*, 2180 (1969).

[125] *M. Raban*, Chem. Commun. *1967*, 1017.

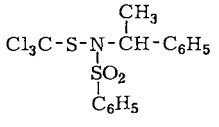
[126] *M. Raban, F. B. Jones, Jr.*, and *G. W. J. Kenney, Jr.*, Tetrahedron Letters *1968*, 5055.

[127] *H. Goldwhite* and *D. G. Rowsell*, Chem. Commun. *1969*, 713.

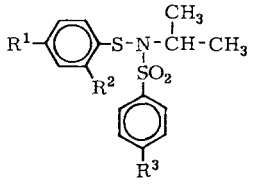
[128] *M. P. Simonnin, J. J. Basselier*, and *C. Charrier*, Bull. Soc. chim. France *1967*, 3544.

gin of the barrier in these molecules is ambiguous, as discussed in Section 3.2.4. Most of the barriers observed in acyclic molecules have been attributed to hindered rotation.

Assuming the validity of assumption (a) of Section 3.2.4, the values of $\Delta G^{\ddagger}$ obtained set upper limits on the barriers to pyramidal inversion in these compounds. However, in none of these systems has there been experimental verification of the validity of this assumption, and it follows that there is as et no unambiguous DNMR estimate of a barrier to inversion in acyclic heteroatom-substituted nitrogen compounds. The conformational interconversion of diastereomers of *(24)*, $\Delta G_c^{\ddagger}$ = 17.2 kcal/mole at 68 °C, ascribed to nitrogen inversion [123], may alternatively be a manifestation of rotational diastereoisomerism, as in *(25)* [124,126].

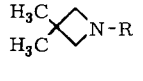


(24)

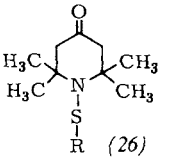


(25)

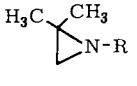
A similar ambiguity in interpretation exists for cyclic amines with an exocyclic heteroatomic substituent without axial symmetry. The stereomutations of sulfenamides *(17)*, R = $SCCl_3$ or SC_6H_5, and *(26)*, R = CCl_3, C_6H_5, or CH_3, were attributed [41] to rotation about the N–S bond. The observed steric effects in *(3)*, R = $SCCl_3$, $\Delta G_c^{\ddagger}$ = 9.1; *(3)*, R = S-*t*-C_4H_9, $\Delta G_c^{\ddagger}$ = 12.2; *(3)*, R = SC_6H_5, $\Delta G_c^{\ddagger}$ = 12.2; and *(3)*, R = S–CH_3, $\Delta G_c^{\ddagger}$ = 13.3 kcal/mole [41], are in the direction expected for an inversion process but small enough to render this interpretation uncertain. Similarly, low barriers observed [72] in the aziridines *(1)*, R = $P(O)(C_6H_5)_2$, $S(O_2)C_6H_5$, 2,4-$(NO_2)_2C_6H_3S$, SC_6H_5, $S(O)C_6H_5$, may be ascribed to rotational



(17)



(26)



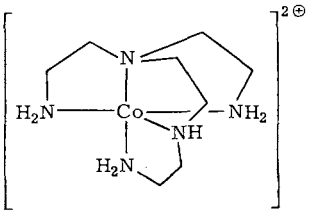
(3)



(1)

motions, with inversion being an invisible (by DNMR) process, possibly of much higher energy, in consonance with the high barriers found for 1-haloaziridines. In the single case *(1)*, R = $S(O)C_6H_5$, where chemical shifts due to diastereotopic protons were observed at room temperature, the magnetic nonequivalence was assumed [72] to be due to the asymmetric sulfoxide grouping.

Hydrogen exchange at nitrogen coordinated to transition metals has been found to proceed with a high degree of stereospecificity. For example, in *(27)*, hydrogen exchange occurs at a rate that is 2.3×10^6



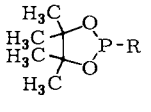
(27)

times faster than the rate of racemization [129]. Since nitrogen is the only center of asymmetry in the complex, the nitrogen pyramid formed after abstraction of the proton is remarkably stable to inversion. Similar, though less dramatic, results have been obtained in complexes of other transition metals [130,131].

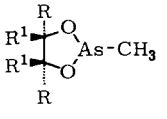
4.4.2. Inversion at Second or Higher Row Atoms

Tricoordinate sulfur compounds such as sulfoxides [69,132], sulfinate esters [133], sulfinamides [134], sulfilimines [135], and sulfites [136] possess stable sulfur pyramids at ordinary temperatures. A study [69,132] of pyramidal inversion in sulfoxides yielded barriers ($\Delta H^{\ddagger}$) in the range 35–42 kcal/mole. Similarily, it has been assumed in studies involving these compounds that aminophosphines and chlorophosphines do not invert at phosphorus [42,127,128].

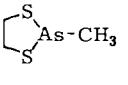
In view of the pyramidal stability of the majority of compounds containing tricoordinate second or higher row atoms, numerous reports in recent years of surprisingly labile P, As, and S pyramids must therefore be critically examined. Although no inversion was



(28)



(29)



(30)

[129] *D. A. Buckingham, P. A. Marzilli,* and *A. M. Sargeson,* Inorg. Chem. *8*, 1595 (1969).

[130] *D. A. Buckingham, L. G. Marzilli,* and *A. M. Sargeson,* J. Amer. chem. Soc. *91*, 5227 (1969), and references therein.

[131] *J. B. Goddard* and *F. Basolo,* Inorg. Chem. *8*, 2223 (1969).

[132] *D. R. Rayner, E. G. Miller, P. Bickart, A. J. Gordon,* and *K. Mislow,* J. Amer. chem. Soc. *88*, 3138 (1966).

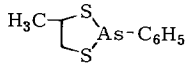
[133] For example: *K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons,* and *A. L. Ternay, Jr.*, J. Amer. chem. Soc. *87*, 1958 (1965).

[134] For example: *A. Nudelman* and *D. J. Cram,* J. Amer. chem. Soc. *90*, 3869 (1968).

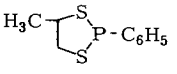
[135] For example: a) *J. Day* and *D. J. Cram,* J. Amer. chem. Soc. *87*, 4398 (1965); b) *D. R. Rayner, D. M. v. Schriltz, J. Day,* and *D. J. Cram, ibid. 90*, 2721 (1968).

[136] For example: a) *J. G. Pritchard* and *P. C. Lauterbur,* J. Amer. chem. Soc. *83*, 2105 (1961); b) *P. C. Lauterbur, J. G. Pritchard,* and *R. L. Vollmer,* J. chem. Soc. *1963*, 5307

observed [137] in *(28)*, R = OCH_3, $N(CH_3)_2$, OC_6H_5, C_6H_5, up to 150 °C, the structurally similar compounds *(29)*, R = R′ = H and R = R′ = CH_3, and *(30)* showed [138] chemical shift equivalence of the *cis* and *trans* groups at the 3 and 4 ring positions. However, accidental equivalence is more reasonable than the proffered [138] explanation of rapid inversion or coplanar geometry at arsenic, since invertomers of *(31)* (up to 110 °C) and *(32)* (at room temperature) can be

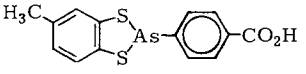


(31)

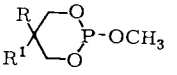


(32)

distinguished in the NMR spectrum [139], and since *(33)* has been resolved [140]. The ready equilibration [141,142] of isomers of *(34)*, R = *t*-C_4H_9, R′ = H; R = CH_3, R′ = CH_2Cl, may be ascribed to traces of methanol in the system [143].

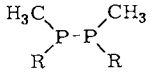


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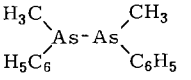


(34)

Barriers ($\Delta G^{\ddagger}_{150}$) of 22.5 to 24 kcal/mole have been measured [73,74] for a series of diphosphines *(35)*, R = *p*-$CH_3C_6H_5$, *p*-$CF_3C_6H_5$, C_6H_5, and $CH_2C_6H_5$, and a barrier (E_a) of 27 ± 1 kcal/mole for the diarsine *(36)* [74,75], all by DNMR. The spectral changes are

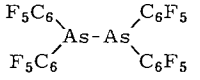


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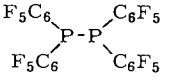


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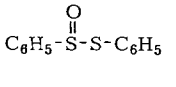
consistent with inversion at phosphorus and arsenic on the assumption that rotational barriers in these compounds are low. The separation of isomers of the diarsine *(37)* by sublimation *in vacuo* at 140 °C and 230 °C [144] suggests that a substantial barrier to inversion *and* rotation exists for this compound. In principle, the *gauche* isomer should display two sets of



(37)



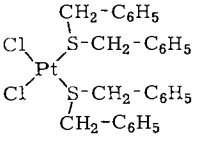
(38)



(39)

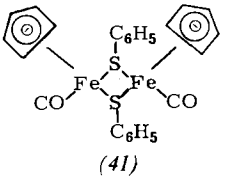
pentafluorophenyl resonances, but this was not observed. The analogous diphosphine *(38)* showed only a single set of ^{19}F resonances, implying one stable isomer. The postulate [73,74,75] that $(3p-3d)_\pi$ or $(4p-4d)_\pi$ resonance is operative in lowering the barrier to inversion in the diphosphines and diarsines is strongly supported by the thermal racemization [76] of the analogous compound *(39)*, but not by the pyramidal stability of *(37)* [144].

Transition metal complexes where some of the ligands are organosulfides constitute another class of heteroatom-substituted tricoordinate centers that are capable of inversion of configuration. An activation energy of 18.0 kcal/mole was found [145] for the *cis*-bis(dibenzyl sulfide)platinum(II) complex *(40)* by NMR. Because of the low activation energy inversion was postulated [145] to proceed through a "partially dissociated transition state" in which both lone pairs of the sulfide are equally delocalized into the metal orbitals. The *trans*-complex *(40)* was found to invert more rapidly



(40)

than the *cis*-complex. A substantially higher activation energy barrier of 30.7–31.8 kcal/mole was measured [146] for inversion at sulfur in *(41)*.



(41)

The effect (magnitude and direction) on the inversion barrier of the fourth attribute of heteroatomic substituents mentioned at the beginning of this section, *i.e.*, delocalization of the lone pair(s) of electrons of the substituent into d orbitals of the inverting center, is uncertain. Although $(2p-3d)_\pi$ conjugation apparently contributes to the stabilization of carbanions adjacent to phosphorus and sulfur [147], no racemization of sulfoxides is observed [148,149] during base-catalyzed hydrogen exchange at attached carbon atoms, nor is racemization observed upon generation of the lithiated phosphine *(42)* [150]. The barrier to

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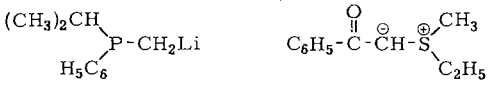
[147] For example, see *D. J. Cram*: Fundamentals of Carbanion Chemistry. Academic Press, New York 1965, p. 71.

[148] *D. J. Cram* and *S. H. Pine*, J. Amer. chem. Soc. *85*, 1096 (1963).

[149] *Y.-H. Khim*, *W. Tagaki*, *M. Kise*, *N. Furukawa*, and *S. Oae*, Bull. chem. Soc. Japan *39*, 2556 (1966).

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pyramidal inversion in the sulfonium ylide *(43)*, $\Delta H^{\ddagger}$ = 23.3 kcal/mole [151], is somewhat lower than that for sulfonium salts ($\Delta H^{\ddagger}$ = 25–29 kcal/



(42) *(43)*

mole) [98,99], and much lower than barriers found in sulfoxides ($\Delta H^{\ddagger}$ = 35–42 kcal/mole) [69]. Although substantial $(2p-3d)_{\pi}$ bonding is postulated to occur in sulfoxides [152], and, by extension, in sulfilimines, it is not clear at present whether the pyramidal stability of these compounds should be attributed to the effect of the π bonding, rather than to the effect of the electronegativity of the oxygen and nitrogen substituent or to lone pair-lone pair interactions.

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New Forms of Carbon

By Otto Vohler, Peter-Ludwig Reiser, Renato Martina, and Dieter Overhoff [*]

A number of novel carbon materials whose unique properties fit them for many uses have recently been developed. Pyrolytic graphites are excellent conductors of heat and electricity parallel to the surface, whereas they are semiconductors perpendicular to the surface. A similar anisotropy is found in graphite foils, which are impermeable, but also very flexible. Glasslike carbon, which is also impermeable, is, however, completely isotropic. Carbon foams and felts are extremely light and exhibit very good thermal insulation up to high temperatures. In addition to very high strength, carbon fibers have values of Young's modulus greater than that of any other fibers or wires. Carbon fiber/resin composites are therefore more rigid than any other known materials; their specific Young's modulus is five times that of steel.

1. Introduction

Up to the end of the 19th century, graphitic carbon was known practically only in the form of mined natural graphite. Though synthetic carbons had been prepared by heating mixtures of anthracite, coke, charcoal from wood and sugar, and retort carbons with carbonaceous binders such as sugar syrup, tar, and pitch, and the partial conversion of these synthetic carbons into synthetic graphite had repeatedly been observed, *e.g.* in an electric arc, the economic production of synthetic or artificial graphite was made possible only by the graphitizing process patented by *Acheson* [1] in 1896.

In this process, the material to be graphitized forms the thermally and electrically insulated heating core of an electric resistance furnace, as shown diagrammatically in Figure 1. The charge is heated to about 3000 °C by direct passage of current, *via* a resistor pack of granular coke. The graphitization that occurs at this temperature leads to extensive ordering within the crystallites of the coke grains and of the binder coke [2].

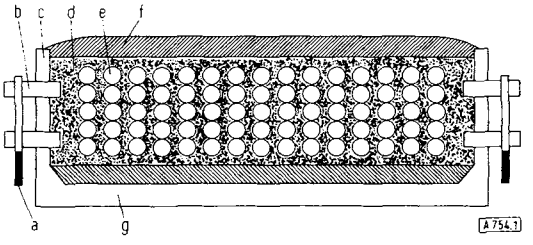


Fig. 1. Acheson graphitizing furnace, schematic.
a) Current connection, b) current supply electrodes, c) port, d) resistor pack of granular coke, e) artificial carbon to be graphitized, f) insulating layer, g) furnace bed.

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[1] *E. G. Acheson*, US-Pat. 568323 (1895).

[2] *E. Dönges* and *O. Vohler* in *K. Winnacker* and *L. Küchler*: Chemische Technologie. Vol. I, 3rd. Edit., Hanser, München 1969.

As a result of its unique combination of chemical, electrical, mechanical, and high-temperature properties[3], artificial graphite has since become widely used in research and industry, *e.g.* as electrodes in arc furnaces for the production of electric steel, in carbide, reduction, and resistance furnaces, as anode material in aqueous and fused salt electrolysis, as casting molds and lining material, in the production of chemical equipment, as fuel element and moderator material in nuclear reactors, in rockets, and for small components, particularly in electrical engineering (cf. [2]).

In recent years, often as a result of extreme requirements for spacecraft, a series of novel carbons have been developed, not by additional treatment or transformation of classical artificial graphite, but by fundamentally different processes; examples are pyrolytic graphite by pyrolysis of gaseous carbon compounds, flexible graphite by explosive decomposition and subsequent compaction of graphite intercalation compounds, glasslike carbon and carbon foams by controlled carbonization of synthetic resins, and carbon fiber materials by crosslinkage and carbonization of suitable organic fibers.

These new carbon materials have unique properties, as a result of which they have found many uses. Some examples of extreme fields of application are electrical heating and thermal insulation, gaskets and porous filters, flexible parts and composites that are more rigid than any other material known.

2. Graphite Single Crystals

Some of these new carbons posses the typical graphite structure only in small regions, and their X-ray reflections are often considerably broadened because of the small crystallite size; in some cases, in fact, only two-dimensional order can be detected. It is nevertheless convenient to derive their properties from the crystal structure of graphite.

Graphite crystallizes mainly in a hexagonal layer lattice of space group D_{6h}^4 (Fig. 2). Each carbon atom within the layers is bonded to three neighboring atoms by very strong, covalent sp^2 bonds with a C–C distance of 1.415 Å. On the other hand, the π bonding between the layers is very weak; the distance between two neighboring *a,b* planes is 3.3539 Å.

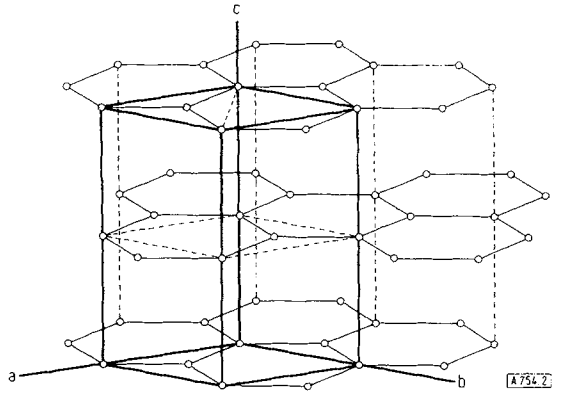


Fig. 2. Crystal lattice of graphite (hexagonal modification).

Because of this pronounced layer lattice, the properties of the graphite single crystal are strongly dependent on direction (Table 1); examples are the Young's modulus, the specific electrical resistance and the thermal conductivity, which is directly related to the nature and strength of the chemical bonding. Parallel to the *a,b* planes, the conductivity of the graphite single crystal is comparable with that of good metallic conductors such as aluminum or copper; perpendicular to the layers, on the other hand, it is a semiconductor. This anisotropy is particularly marked in the thermal expansion [3].

Table 1. Properties of graphite single crystals.

	parallel to *a,b* planes	perpendicular to *a,b* planes
Density (g/cm³)	2.266	
Young's modulus (kg/cm²)	$\approx 1 \times 10^7$	$\approx 3.5 \times 10^5$
Electrical resistance (ohm mm²/m)	≈0.5	$\approx 1 \times 10^4$
Thermal conductivity (kcal m⁻¹ h⁻¹ deg⁻¹)	>350	7
Coefficient of thermal expansion (20–200 °C) (deg⁻¹)	-1.5×10^{-6}	$+28.6 \times 10^{-6}$

This strong dependence on direction is found only for particularly well-formed natural graphite flakes, and is much less pronounced in the properties of the porous artifical graphite objects made by the classical methods for the production of synthetic carbon from solid fillers and pitch-like binders. In these artifacts, the anisotropy of the single crystal is greatly weakened by the various orientations of the crystallites, by microcracks and pores within the grains, and by the porous structure of the shaped article. However, the anisotropy is very pronounced in some new types of carbon, such as pyrolytic graphite, graphite foils, and the high-tensile or high-modulus carbon fibers.

3. Pyrolytic Carbon and Graphite

The formation of carbon by pyrolytic decomposition of gaseous or vaporized carbon compounds is not new; retort carbons were obtained in this way even before *Acheson* described his graphitizing process. It was only in the last decade, however, that suitable equipment has been developed for the production of pyrocarbon as coating and in the form of a compact, self-supporting body under controlled conditions, and hence with properties that could be varied as desired.

Pyrocarbon coatings and compacts are produced from gaseous or vaporized carbon compounds, which are decomposed pyrolytically on hot graphite supports (800–2800 °C) [4–6]. Examples of suitable carbon compounds are methane, ethane, propane, acetylene, benzene, and carbon tetrachloride.

[3] *W. N. Reynolds*: Physical Properties of Graphite. Elsevier, Amsterdam 1968.

[4] *R. J. Diefendorf*, J. Chim. physique *57*, 815 (1960).

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3.1. Pyrocarbon Coatings

The structure and properties of the pyrocarbon layers obtained depend mainly on the temperature, pressure, residence time, and nature of the carbonaceous gas. The variability of pyrographite is extremely wide, and ranges from almost isotropic, *via* granular, to the highly anisotropic laminar structures.

These pyrocarbon structures have been examined in particular detail in connection with deposition in the fluidized bed reactor [7]. This deposition has gained considerable technological importance for the coating of fuel particles for nuclear reactors.

Multiple layers are used having various mechanical properties and irradiation behavior and exhibiting good fission product retention.

Another important application is the production of pyrocarbon coatings on artificial graphite bodies (see Fig. 3), the deposition then no longer taking place in a fluidized bed, but on fixed graphite objects. The pyrocarbon coating gives the artificial graphite a very smooth surface; it becomes substantially impermeable and its resistance to oxidation and erosion is greatly enhanced.

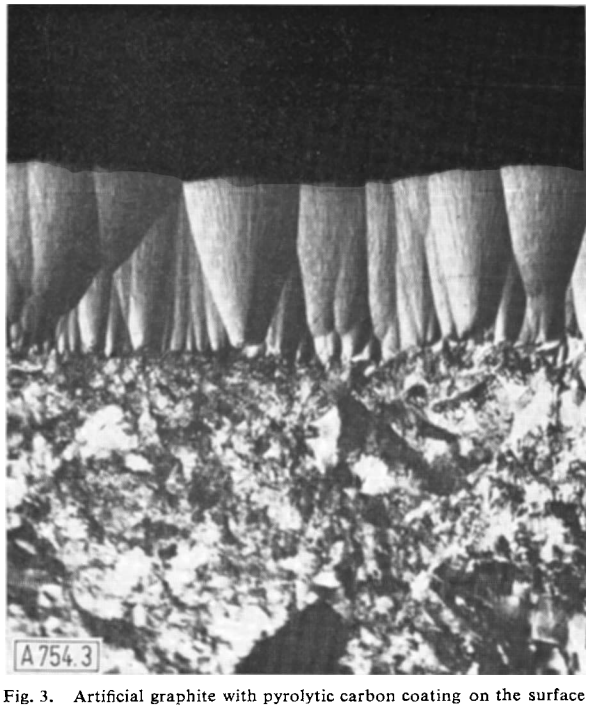


Fig. 3. Artificial graphite with pyrolytic carbon coating on the surface (magnification 1000 ×).

If the coating is applied only to the outer surface of the shaped body, it provides only incomplete protection against slow selective oxidation, such as occurs *e.g.* in graphite components in nuclear reactors. If the protective surface layer is damaged, the oxidizing gas can pass through the pores of the graphite body and so destroy the material. To prevent this, it is necessary to deposit the pyrocarbon within the pores (see Fig. 4). This is possible at slow deposition rates (low temperature, low partial pressure) [8]. Even after the surface of articles coated in this way has been attacked, the protective action of the pyrocarbon in the pores persists.



Fig. 4. Artificial graphite with pyrolytic carbon coating within the pores (magnification 1000 ×).

Graphites coated with pyrocarbon are used in particular where severe erosion and oxidation are likely to occur, *e.g.* as sleeves in CO_2-cooled nuclear reactors. They are also used for special purposes, such as vaporization dishes in the vapor-deposition of metals or as graphite molds for the sealing of terminals in tube bases. Owing to their high purity, graphites coated with pyrocarbons are being increasingly used in semiconductor technology as mold materials and as plates for epitaxy. Since blood has only a small tendency to clot in the presence of pyrocarbon layers, this could offer a new application in medicine, *e.g.* for artificial heart valves [9].

3.2. Compact Pyrolytic Graphite

Compact pyrolytic graphite bodies are produced at a constant temperature and a constant pressure at the lowest possible deposition rate. Crystalline order is obtained only within the layer planes; the material is turbostratic. Growth and ordering processes that lead also to extensive crystalline order in the *c* direction can be induced by additional heat treatment at temperatures up to 3000 °C.

The growth rate, density, and microstructure depend mainly on the deposition temperature [10]. Whereas pyrolytic carbons having a density of only 1.35 g/cm³ are obtained at 1600 °C, the bulk density of pyrographite deposited at about 2100 °C is between 2.20 and 2.23 g/cm³.

[7] *J. C. Bokros* and *R. J. Price*, Carbon *3*, 503 (1966).
[8] *O. Vohler*, *P.-L. Reiser*, and *E. Sperk*, Carbon *6*, 397 (1968).
[9] *J. C. Bokros*, 9th Carbon Conference, Paper CP-inv., Boston 1969.
[10] *J. C. Bokros* and *R. J. Price*, Carbon *6*, 213 (1968).

Because of the good alignment of the layer planes, pyrolytic graphite bodies, like single crystals, are strongly anisotropic. Thus the ratio of anisotropy for the specific electrical resistance (perpendicular/parallel) is 1400; the parallel/perpendicular ratio for the thermal conductivity is about 440. As in the single crystal, the thermal expansion is negative parallel to the surface and strongly positive in the perpendicular direction (cf. Table 2).

Table 2. Properties of pyrolytic graphite.

	parallel to surface	perpendicular to surface
Bulk density (g/cm³)	2.20	
Young's modulus (kg/cm²)	2.5×10^5	—
Flexural strength (kg/cm²)	1×10^3	—
Compressive strength (kg/cm²)	1×10^3	4×10^3
Electrical resistance (ohm mm²/m)	5	7×10^3
Thermal conductivity (kcal m^{-1} h^{-1} deg^{-1})	350	0.8
Coefficient of thermal expansion (20–200 °C) (deg^{-1})	-0.8×10^{-6}	$+25 \times 10^{-6}$

A crystallographically almost ideal graphite has been obtained by uniaxial hot compression of pyrolytic graphite followed by annealing at a very high temperature and low pressure [11]. The ratio of anisotropy for the electrical resistance of this material at 300 °K was 4000, and increased to 90000 on cooling to 4.2 °K.

Owing to the high degree of alignment and the resulting strong anisotropy, pyrolytic graphite bodies can be produced only in limited thickness. The maximum thickness attainable for slab materials at present is about 10 mm. In the case of tubes it is proportional to the radius of curvature, *i.e.* maximum wall thickness/radius of curvature = 0.05. Bodies with sharp edges or thick walls can be produced by further machining or by combining thinner pyrographite plates.

The marked anisotropy of pyrolytic graphite and its increased resistance to erosion and oxidation, together with the high emission coefficient and high sublimation point of carbon, offer great advantages *e.g.* when used as rocket nozzles, as reentry cones of space vehicles, for the nose cones and wing leading edges of space gliders, or as protective shields. Owing to the excellent conductivity parallel to the *a,b* planes of the graphite crystal, the heat is well distributed over the surface, and both the radiation and the ablation take place over the entire surface. At the same time, underlying structural material is thermally protected by the insulating effect in the *c* direction. Compact pyrolytic graphite plates are often used when a very uniform distribution of heat over a surface is desired. Pyrolytic graphite is also used to advantage in electronic tubes [12].

Pyrographite alloys, *e.g.* with B, Si, Hf, and Co, are obtained when a vaporized organic compound of the alloying component is added to the gaseous carbon compound. A particularly well-known example is the pyrographite-boron alloy, which is characterized by higher elasticity, lower oxidizability, and greater insulation perpendicular to the layer planes and by an increase in the strength of the pyrographite, which is high even in the unalloyed state.

4. Carbon Foils and Membranes

It is well known that foreign atoms can be inserted between the layers of well-ordered graphite crystals to give intercalation compounds, such as potassium graphite, graphite hydrogen sulfate, and graphite oxide [13–16]. In graphite oxide, oxygen and hydroxyl groups are located between the carbon layers. *Luzi* found as early as about 1890 that graphite oxide can be thermally expanded to more than 100 times its original volume. A more recent process for the economical production of flexible graphite foils is based on the compression of this expanded material [17].

The starting material is generally coarsely crystalline, very pure natural graphite. The graphite is oxidized with fuming nitric acid or with a sulfuric acid/nitric acid mixture, and then hydrolyzed. If the graphite oxide, after drying, is heated in a fraction of a second to about 1000 °C, it decomposes explosively. The gases liberated expand the graphite lattice normal to the

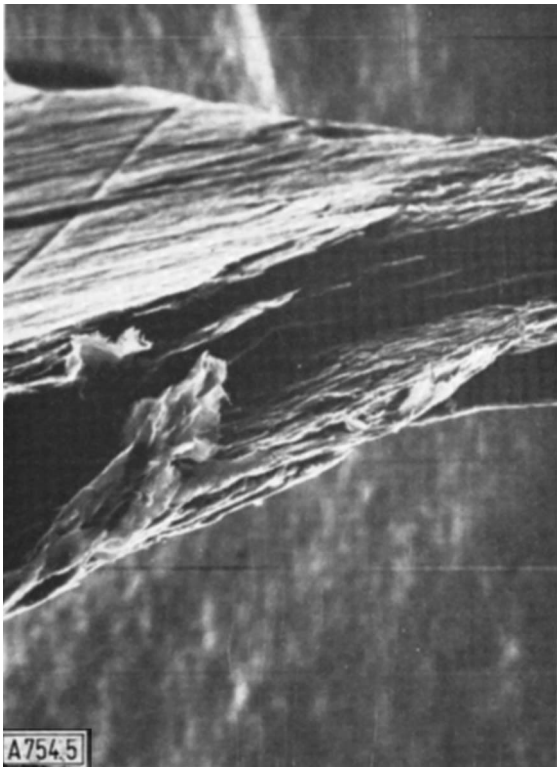


Fig. 5. Electron-scan micrograph of a carbon foil (magnification 125 ×). The micrograph was prepared in the Labor für Raster-Elektronen-Mikroskopie Dr. *H. Klingele*, München.

[11] *I. L. Spean, A. R. Ubbelohde*, and *D. A. Young*, Second Conference on Industrial Carbon and Graphite, London 1965, p. 123, Society of Chemical Industry, London 1966.

[12] *J. M. Osepchuk* and *J. E. Simpson*, 9th Carbon Conference Paper CA-18, Boston 1969.

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[14] *U. Hofmann* and *A. Frenzel*, Ber. dtsch. chem. Ges. *63*, 1251 (1930).

[15] *U. Hofmann* and *E. König*, Z. anorg. allg. Chem. *234*, 311 (1937).

[16] *H. Thiele*, Z. anorg. allg. Chem. *206*, 407 (1932).

[17] *J. H. Shane, R. J. J. Russel*, and *R. A. Bochman*, French Pat. 1395964 (1963), High Temperature Materials.

layer planes by a factor of more than 100. The separated carbon layers of the graphite lattice are then firmly bonded together by mechanical pressure; the resulting products are gas-tight, flexible, strongly anisotropic carbon foils having a density of about 1.1 g/cm³. An electron scan micrograph (Fig. 5) shows the pronounced layer structure of this material.

These foils are produced without binders; they consist of pure carbon, and can therefore be used up to temperatures above 3000 °C in inert and reducing atmospheres or under vacuum. The strong dependence of the properties on direction is again remarkable. The ratio of anisotropy for the specific electrical resistance is even higher than in pyrolytic graphite (cf. Table 3). The electrical conductivity parallel to the surface is comparable with that of well-ordered artificial graphite. Special emphasis must be placed on the impermeability of these foils to gases and liquids up to very high temperatures. Graphite foils are also much more resistant to oxidation than artificial graphites. Their surface is very smooth and resistant to abrasion.

Table 3. Properties of carbon foils.

	parallel to surface	perpendicular to surface
Bulk density (g/cm³)	0.9–1.1	
Electrical resistance (ohm mm²/m)	8	4×10^4
Thermal conductivity (kcal m⁻¹ h⁻¹ deg⁻¹)	150	3
Permeability (air) (cm²/s)	—	$<10^{-6}$

The flexible graphite is produced in the form of foils in thickness of 0.1 to 0.3 mm. These films are used directly or made into laminates several mm thick, the individual layers of which may be bonded together by carbonizable resin binders. Dense molded bodies can also be produced without binders. They are then equivalent to the foils in their resistance to corrosion and heat and in their thermal and electrical properties. Owing to their greater thickness, however, they no longer posses high flexibility.

Graphite foils and laminates have proved excellently suited for use in several fields:

a) as corrosion-resistant seals (gaskets and packings) for very low to very high temperatures: high thermal conductivity and hence good heat dissipation, self-lubricating, impermeable with and without cooling, long life, no maintenance, corrosion-resistant;

b) for the lining of press molds and casting molds: smooth surface, low friction, dense, abrasion-resistant;

c) as radiation shields in high-temperature furnaces: high reflection factor and good thermal conductivity parallel to the surface, combined with poor thermal conductivity normal to the surface;

d) in electrochemistry and electrical engineering, *e.g.* as a surface heater: high anisotropy of electrical and thermal conductivity;

e) as linings for chemical equipment: very flexible, corrosion-resistant, impermeable to gases and liquids;

f) as films for bursting disks: impermeable to gases and liquids, corrosion-resistant, heat-resistant.

Expanded graphite can also be made into porous foams (density 0.05–0.1 g/cm³) by compression under a lower pressure and without a binder. These foams may then be compressed further during use.

Self-adhesive or plastic-coated graphite foils are already on the market.

Carbon membranes only a few μm thick have now also been developed. Though thin enough to be translucent, these membranes are nevertheless impermeable to gases and liquids.

The membranes are again prepared from graphite oxide, which is made into a thixotropic gel in aqueous suspension. This gel is deposited on well-polished surfaces. Very careful drying gives a membrane of graphite oxide, which is reduced in a stream of hydrogen above 500 °C [18]. The resulting carbon membrane, which has a highly imperfect graphite crystal lattice, is graphitized above 2500 °C; during this process, the density increases to 1.8–2.2 g/cm³. Carbon membranes of this nature are used *e.g.* as dialysis membranes for the desalination of sea water.

5. Glasslike Carbon

The coking of coal-tar pitch or residues from the distillation of petroleum yields cokes that change into more or less well-ordered graphite on subsequent graphitizing treatment above 2500 °C. Three-dimensionally crosslinked synthetic resins, on the other hand, decompose without passing through a liquid phase; they therefore give poorly graphitizing carbons. The crystallites remain small even after heating at about 2800 °C (*e.g.* $L_a \approx 70$ Å, $L_c \approx 30$ Å) [19]. The distance between the layers is 3.44 Å, as compared with 3.354 Å in a well-ordered graphite.

The carbon obtained is very hard, and resembles glass in its impermeability and breaking behavior; it is therefore known as glasslike carbon.

The structure of this carbon contains small regions of graphite-like layers, which are joined by numerous crosslinks. The large proportion of crosslinking C atoms is the reason for the non-graphitizability of glasslike carbon and for its isotropy.

The density of glasslike carbon is very low (about 1.5 g/cm³). Its impermeability to gases is nevertheless excellent; the permeability as found mass-spectrometrically with helium is about 10^{-11} cm²/s, and is thus of the same order of magnitude as that of silicate glasses [20].

Table 4. Properties of glasslike carbon.

Bulk density (g/cm³)	1.45–1.50
Pore volume (vol.-%)	<1
Young's modulus (kg/cm²)	2.6×10^5
Flexural strength (kg/cm²)	700
Electrical resistance (ohm mm²/m)	50
Thermal conductivity (kcal m⁻¹ h⁻¹ deg⁻¹)	3
Coefficient of thermal expansion (deg⁻¹)	3×10^{-6}
Permeability (air) (cm²/s)	10^{-11}

[18] *J. Maire, H. Colas*, and *P. Maillard*, Carbon *6*, 555 (1968).
[19] *F. C. Cowlard* and *J. C. Lewis*, J. Materials Sci. *2*, 507 (1967).
[20] *S. Yamada* and *H. Sato*, Nature (London) *193*, 261 (1962).

Glasslike carbon is much stronger and stiffer than conventional carbons and graphites (Table 4). Its electrical and thermal conductivity are comparable with those of hard carbons.

Owing to the small number of accessible pores and its high impermeability, glasslike carbon is very corrosion-resistant. However, it is attacked by alkali metals with formation of intercalation compounds, as well as by carbide-forming metals [19].

To prepare glasslike carbon, partially precondensed phenolic or furan resins are mixed with catalysts, poured into molds with very smooth surfaces, and cured. The material is then removed from the molds and carbonized in accordance with a strictly defined heating schedule. The resulting shrinkage is pronounced, but quite definite and isotropic, so that moldings can be produced with a dimensional accuracy of $\pm 0.5\,\%$. Owing to its hardness, glasslike carbon can only be worked with diamond tools or by an ultrasonic technique. It is therefore preferable to work the cured resin before carbonizing, taking the amount of further shrinkage into account [21].

Glasslike carbon is produced as plates, tubes, crucibles, boats, *etc.* with wall thicknesses of about 3 mm. It has found a number of applications, particularly in laboratory work. The similarity of its coefficient of expansion to that of many borosilicate glasses makes it possible to bond the two materials permanently. Since glasslike carbon is not wetted by most molten metals, it can be used in metallurgy for melting crucibles, and also for pipes for passing corrosive gases into molten metals and as vaporization dishes for the evaporation of metals. Glasslike carbon has a high resistance to erosion, and is therefore also being tested as a rocket nozzle lining [22].

6. Highly Porous Carbon, Carbon Foam

Carbons in which up to 75 % of their volume is occupied by open pores of very uniform structure can be produced from microcrystalline cellulose without binders [23, 24].

These homoporous carbons are used mainly as electrode materials for the direct conversion of chemical into electrical energy in electrochemical fuel cells. Owing to the uniformity of their pores, such electrodes can accept very high loads.

Carbons with much greater pore volumes (carbon foams) are obtained by carbonizing foamed synthetic resins. The starting materials are open-pored rigid synthetic resin foams. There are two basic types:

a) A skeleton of a foam that gives only a low carbon yield on pyrolysis *e.g.* a foam based on polyurethane, which has been impregnated with a carbon-supplying synthetic resin, *e.g.* a phenolic resin [25].

b) A foam made from a synthetic resin that itself gives a relatively high coke yield, *e.g.* a phenolic resin foam [26, 27].

The carbon foams obtained by carbonization are extremely light, having densities of only about 0.05 g/cm³. The percentage decreases in volume and in weight are the same, so that the carbon foams have the same bulk density as the synthetic resin foam used. Carbon foam is composed of very thin carbon cell walls (cf. Fig. 6); it can be used up to temperatures higher than

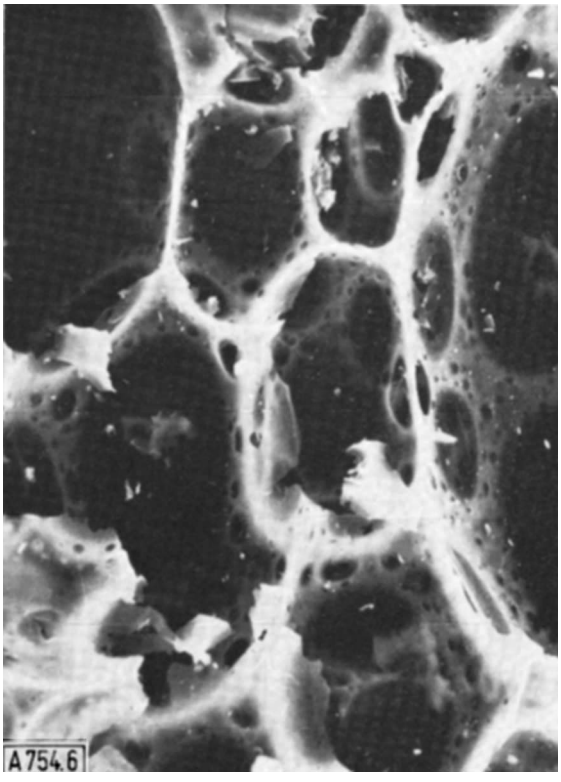


Fig. 6. Electron-scan micrograph of carbon foam (magnification 250 ×). The micrograph was prepared in the Labor für Raster-Elektronen-Mikroskopie Dr. *H. Klingele*, München.

3000 °C in an inert gas or under vacuum. Its thermal insulating qualities are outstanding (cf. Table 5); the thermal resistance of foamed synthetic resins is only slightly better (thermal conductivity about 0.03 kcal $m^{-1}\,h^{-1}\,°C^{-1}$). However, synthetic resin foams can only be used below their decomposition temperatures, *i.e.* below 180 °C.

Table 5. Properties of carbon foam.

Bulk density (g/cm³)	0.055–0.065
Pore volume (total (vol.-%))	97
Pore volume (open (vol.-%))	95
Young's modulus (kg/cm²)	1200
Compressive strength (kg/cm²)	4.8
Electrical resistance (ohm mm²/m)	5500
Thermal conductivity (kcal $m^{-1}\,h^{-1}\,deg^{-1}$)	0.04
Coefficient of thermal expansion (20–200 °C) (deg^{-1})	2.1×10^{-6}
(20–1000 °C) (deg^{-1})	2.5×10^{-6}
Permeability (cm²/s)	$\approx 10^{2}$

[21] French Pat. 1475809 (1966), Carbone Lorraine.

[22] Chem. Engng. *76*, No. 27, p. 38 (1969).

[23] *O. Vohler* and *R. Martina*, Allg. prakt. Chemie *17*, 500 (1966).

[24] *O. Vohler, R. Martina, M. Schmid*, and *F. Königsheim*, German Pat. 1254520 (1964), SIGRI.

[25] French Pat. 1388818 (1963), Carbone Lorraine.

[26] *W. D. Ford*, US-Pat. 3121050 (1960), Union Carbide Corporation.

[27] *B. R. Atkins*, Brit. Pat. 1016449 (1963), Nobrac Carbon.

The thermal resistance of carbon foam is superior to that of refractory bricks by a factor of thirty, whereas its density is lower by a factor of about twenty. For the same weight of material, therefore, the thermal resistance is six hundred times as high.

The compressive strength of the highly porous carbon foam is relatively low. It can be increased merely by variation of the starting material or of the foaming; however, the thermal conductivity increases at the same time. The compressive strength can be increased to 1000–2500 kg/cm² by impregnation *e.g.* with pyrolytic carbon; this is accompanied by an increase in the thermal conductivity by a factor of about ten (approx. 0.35 kcal m^{-1} h^{-1} $°C^{-1}$) [28].

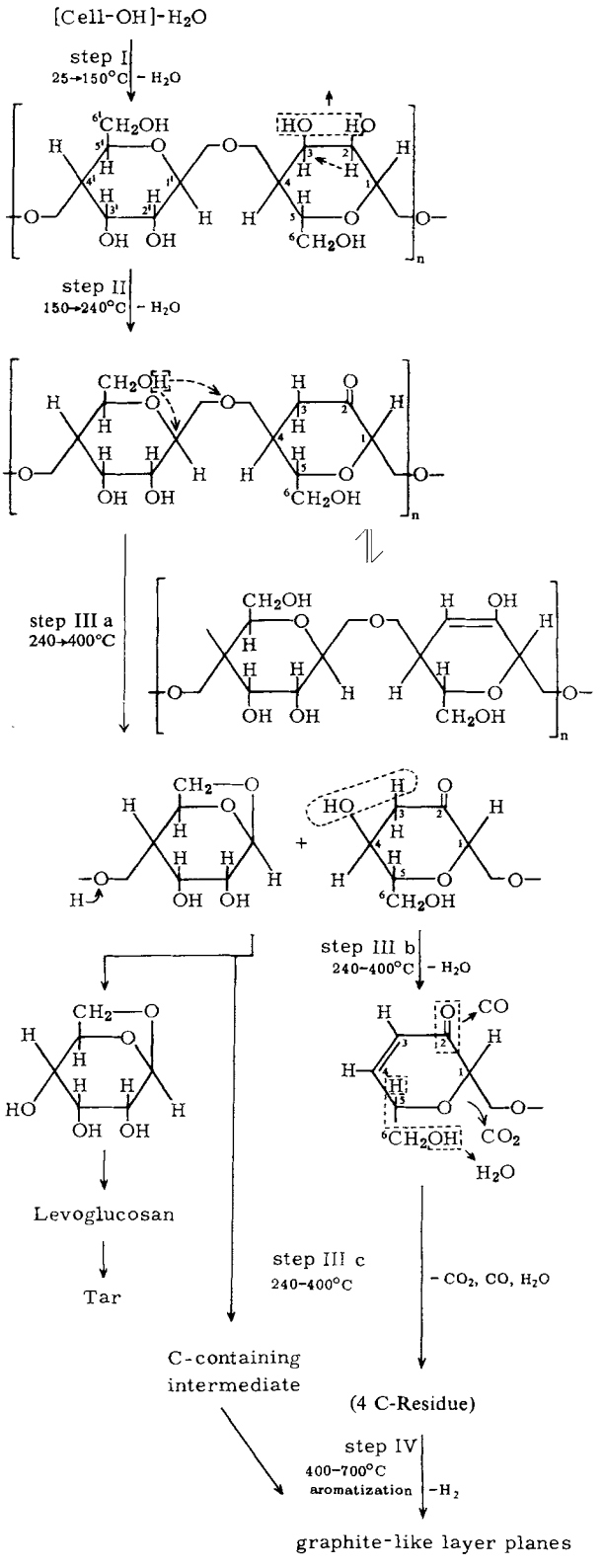
The most important application of carbon foam is insulation, in particular up to high and very high temperatures. It is also used as a filter for corrosive agents, for frits for the uniform distribution of gases in reaction mixtures, and as a support material for catalysts. Fire-resistant sandwich materials represent another application.

7. Carbon Fiber Materials

Edison (1880) was the first to carbonize cellulose filaments for the newly developed carbon filament lamp. The mechanical strength of these first carbon filaments was very low, and they were not very flexible. It was not until 1959 that flexible carbon fibers and fabrics, which were then available only on a laboratory scale, were first described in the technical literature [29, 30]. The starting material was again cellulose, now in the form of rayon.

In 1961, *Shindo* investigated the thermal degradation of polyacrylonitrile fibers and found that this material (particularly after preoxidation) leads to extremely strong carbon fibers with good carbon yields [31]. These investigations formed the main basis of the development of high-tensile and high-modulus carbon fibers at Farnborough [32].

The thermal degradation of other starting materials, *e.g.* animal fibers [33], polyvinyl acetate [34], polyvinyl alcohol [35], pyrolysis products of polyvinyl chloride [36], copolymers of vinyl chloride, vinyl esters, and vinyl alcohol [37], furfuryl alcohol condensates, and more recently phenol-formaldehyde condensates, has also been studied.



Scheme 1. Thermal degradation of cellulose [38, 39].

Step I: desorption of physically adsorbed H_2O. Step II: removal of chemically bound H_2O. Step III: depolymerization and chain cleavage with dehydration, decarbonylation, and decarboxylation. Step IV: dehydrogenation, demethanation.

In general, materials are suitable for the production of carbon fibers only if they satisfy the following basic requirements:

1. The fibrous form should be retained on pyrolysis, *i.e.* the material must not melt when heated, or it must

[28] *B. Lersmacher*, DGLR Yearly Conference Bremen 1969, Paper No. 57.

[29] Metal Progr. *75*, 115 (1959).

[30] *J. A. Mock*, Mat. Design Engng. *49*, 149 (1959).

[31] *A. Shindo*: Studies on Graphite Fiber. Rep. Government Ind. Res. Inst., Osaka, No. 317 (1961).

[32] *W. Watt, L. N. Phillips*, and *W. Johnson*, Engineer *815*, 221 (1966).

[33] *E. Sperk, O. Vohler, F. Jeitner*, and *V. Gierth*, German Pat. 1255629 (1963), SIGRI.

[34] *A. Shindo*: Highly Crystallite-oriented Carbon Fibers from Polymeric Fibers. ACS Polymer Preprints Vol. 9, No. 2, 1327 (1968).

[35] *A. Shindo*, Symp. on Carbon, Tokyo 1964.

[36] *S. Otani*, Carbon *3*, 31 (1965).

[37] Brit. Pat. 1177739 (1967), Wacker.

be capable of being pyrolytically decomposed below its melting point.

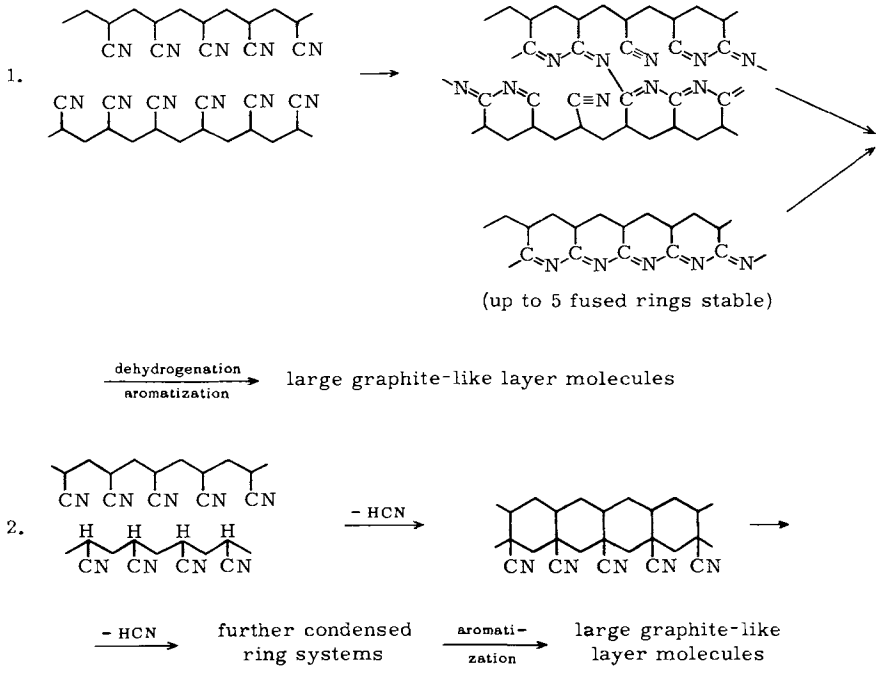
2. The carbon skeleton should be capable of being readily changed into a two-dimensional graphite structure.

3. The pyrolysis should take place without appreciable evaporation of carbon-containing volatile components.

These requirements are satisfied by cellulose and crosslinkable polymers such as polyacrylonitrile. According to *Tang* and *Bacon*, cellulose is decomposed as shown in Scheme 1 [38, 39].

The dehydration is assisted by treatment with phosphates, borates, vanadates, *etc.* Each cellulose unit ultimately contributes an average of four C atoms, which aromatize to form graphite layers.

When polyacrylonitrile is used as the starting material, it is treated with oxygen at 200 to 300 °C before thermal degradation. This leads to crosslinking and cyclization, with the result that a structure consisting of condensed dihydropyridine rings is formed. Above 350 °C, the nitrogen is removed as ammonia or hydrogen cyanide. Above 600 °C, further crosslinking takes place, with dehydrogenation, to give large graphite-like layer molecules. Reactions verified by IR spectroscopy are shown in Scheme 2.



Scheme 2. Thermal decomposition of polyacrylonitrile [40].

Because of their fibrous structure, the carbon fiber materials combine the characteristics of carbon (low vapor pressure up to very high temperatures, high sublimation point, chemical stability) with typical textile properties such as flexibility, elasticity, and lightness.

[38] *M. M. Tang* and *R. Bacon*, Carbon *2*, 211 (1964).

[39] *R. Bacon* and *M. M. Tang*, Carbon *2*, 221 (1964).

[40] *E. Bähr*: Hochtemperaturbeständige Kunststoffe. Hanser, München 1969.

When textiles made of organic fibers are subjected to suitable heat treatment, the organic substances are ultimately converted entirely into carbon, while the textile form is retained. Carbon felts, wools, and fabrics can be made in this way [41]. Carbon fabrics are also made in special cases by weaving continous carbon fibers (see Section 7.2).

The starting materials are generally textiles made from cellulose fibers, though materials made from completely synthetic fibers, such as polyacrylonitrile, are used in some cases. However, only needled felts, which are relatively spongy, can be produced from these fibers. Suitable starting materials for the production of denser carbon felts are pressed felts of animal fibers, particularly sheeps' wool. As can be seen in Figure 7, the surface structure of the wool fibers with flat scale-like cells is retained even after carbonization.

The heat treatment of the textiles generally takes place in three steps:

First step (up to about 300 °C): precarbonizing.

Second step (up to about 1000 °C): carbonizing.

Third step (up to above 2500 °C): graphitizing.

In the first step the fiber material is decomposed into products that are already black. Crosslinking agents must be used in some cases to prevent softening or even melting before chemical degradation. In the case of polyacrylonitrile, for instance, atmospheric oxygen is used, while a special method has been developed for animal fibers [33]. The thermal decomposition may also be carried out in high-boiling liquids [42,43] or in at-

[41] *O. Vohler* and *E. Sperk*, Ber. dtsch. keram. Ges. *43*, 199 (1966).

[42] *G. R. Hogg jr.* and *J. L. Allison*, DAS 1234608 (1963), Great Lakes Carbon.

[43] *M. T. Cory*, DOS 1469250 (1963), Basic Carbon.

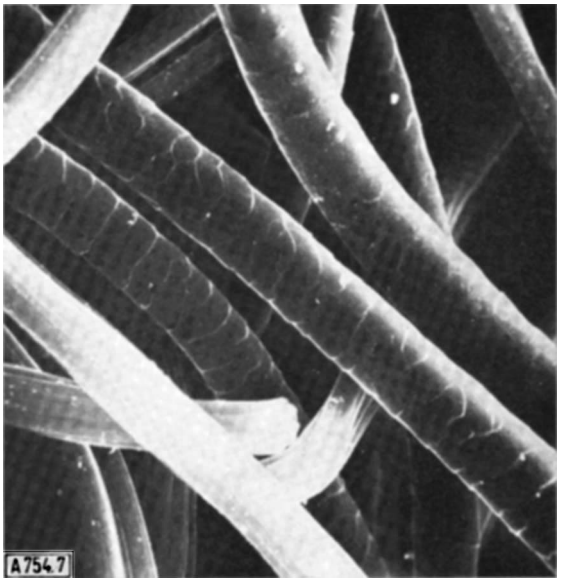


Fig. 7. Electron-scan micrograph of carbon felt based on sheeps' wool (magnification 1250 ×). The micrograph was prepared in the Labor für Raster-Elektronen-Mikroskopie Dr. *H. Klingele*, München.

mospheres containing halogen or nitric oxide [44,45]. In the second step the precarbonized material is degraded to elementary carbon in the absence of air.

These carbon felts, wools, and fabrics can be used in this form for most purposes. For special applications the materials are heated in a third step to above 2500 °C (graphitization). The resulting products are known as graphite felts, wools, and fabrics, though there is crystallographically no pronounced graphitic structure.

Owing to the wide range of starting materials, it is possible to obtain products with various combinations of properties, as is shown by Table 6 for carbon and graphite felts.

Table 6. Properties of carbon and graphite felts.

	SIGRATHERM FA 5 G		SIGRATHERM F I/3		SIGRATHERM FD 400	
	Carbon	graphite	carbon	graphite	carbon	graphite
Weight per unit area (g/m²)	200	180	330	280	350	320
Bulk density (g/cm³)	0.05	0.05	0.20	0.17	0.08	0.08
Thermal conductivity (20 °C) (kcal m^{-1} h^{-1} deg^{-1})	0.05	0.10	0.08	0.15	0.05	0.30
Square resistance (ohm)	3.5	1.5	2	0.2	0.5	0.1
Tensile strength (kg/cm²)	0.5	0.3	4	1.5	1	0.5
Breaking strain (%)	25	20	15	5	10	5

The bulk density of these felts ranges from 0.05 to 0.20 g/cm³. The felts with the higher bulk densities, while having practically the same thermal insulating powers, are more stiff, and can therefore be used *e.g.* as self-supporting insulating shields. The insulating power of these carbon felts is illustrated in Figure 8.

Carbon and graphite felts are thus used mainly for thermal insulation up to very high temperatures both in resistance and in induction furnaces. They are cheaper and more effective than metal shields. Their insulating properties are superior to those of carbon black. Since the bulk density is

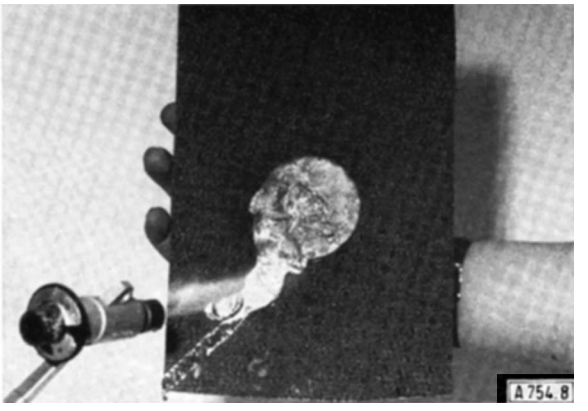


Fig. 8. Insulating power of carbon felt (melting of aluminum on a hand insulated with carbon felt).

only a fraction of that of carbon powder, suitably insulated furnaces can be heated and cooled more rapidly. Felt shields are also reasonably strong, and their strength increases with rising temperature. Since they can be cut with scissors or knives and stitched together with carbon yarn, insulators of any desired shape can be produced quickly and easily. Furthermore the material is so uniform that no hot spots occur, and uniform temperatures are obtained inside the furnace.

Their chemical corrosion resistance also offers other advantages, *e.g.* for use as a filter material for corrosive substances (gases, solutions, molten metals), as a support material for catalysts, as corrosion-resistant linings in chemical equipment, and (also in metalized form [46]) as "fiber-porous" electrodes in accumulators and fuel cells.

The electrical properties of the carbon and graphite felts provide unique and new methods of resistance heating (more flexible than the finest metal conductors, very good heat dissipation by black body radiation, high power densities, low heat capacity, fast heating and cooling).

Owing to their low neutron absorption cross section, carbon felts and wools are also used in nuclear engineering [47].

Carbon and graphite wools prepared from artificial cotton or similar starting materials are particularly suitable for use as packing materials for high-temperature insulation. Carbon and graphite fabrics are used basically for the same purposes as the felts, but not as insulating materials.

All carbon fiber materials have the disadvantage of restricted application in air above 300 °C, owing to their ease of oxidation. Their high-temperature properties are fully utilizable up to temperatures above 3000 °C only in inert or reducing atmospheres. The resistance to corrosion and erosion can however be increased by pyrolytic graphite, carbide, or silicide coatings.

[44] *C. L. Gutzeit*, DAS 1272801 (1965), Hitco.

[45] *R. O. Moyer jr.*, *D. R. Ecker*, and *W. J. Spry jr.*, US-Pat. 3333926 (1963), Union Carbide Corp.

[46] *P. Faber*, DAS 1299056 (1966), Rheinisch-Westfälische Elektrizitätswerke.

[47] *K. Schoen*, DAS 1242766 (1965), AVR GmbH.

7.2. Carbon Fibers

Carbon felt, wadding, wool, *etc.* generally do not possess high mechanical strength; the graphite single crystal, however, owing to its strong covalent bonds in the *a,b* direction, has an extremely high Young's modulus (about 1×10^7 kg/cm²) and a tensile strength of about 1×10^6 kg/cm².

In the production of continuous carbon fibers, the *a,b* planes can be extensively oriented parallel to the fiber axis if *e.g.* carbonized rayon filaments are stretched at about 2500 °C[48]. Stretching by a factor of 50% increases the Young's modulus *e.g.* from 1×10^6 to 4×10^6 kg/cm². The tensile strength simultaneously increases from 100 to 300 kg/mm².

With polyacrylonitrile fibers as the starting materials, stretching is carried out between 200 and 300 °C[32]. Carbon fibers from polyacrylonitrile attain their maximum strength after heat treatment at 1500 °C (cf. Table 7: high-tensile). As the treatment temperature is further raised, the Young's modulus rapidly increases; the high-modulus fibers of Table 7 were heated at 2500 °C. Additional high-temperature stretching above 2500 °C results in a further increase in the Young's modulus and tensile strength.

Table 7. Mechanical properties of carbon fibers, carbon fiber reinforced plastics, and other materials.

	Tensile strength (kg/cm²)	Young's modulus (10^3 kg/cm²)	Tension length (km)	Specific Young's modulus (km) [a]
Fibers and wires				
Graphite (high modulus)	21000	4200	110	22000
Graphite (high tensile)	30000	2300	170	13000
Boron (on tungsten)	30000	3800	115	14500
Asbestos	60000	1900	240	7600
Glass	28000	700	110	2800
Steel	42000	2100	53	2650
Titanium	20000	1200	44	2600
Aluminum	1700	700	6	2600
Other materials				
Graphite fiber/ resin composite (V_f = 0.5) [b]	8400	2100	54	13600
Glass fiber/ resin composite (V_f = 0.5) [b]	9000	500	50	2800
Steel	14000	2100	18	2650

[a] Specific Young's modulus Σ Young's modulus/density.
[b] V_f = bulk factor (based on the volume fraction).

The tensile strength of high-tensile carbon fibers is exceeded only by those of asbestos fibers, steel wires, and of graphite whiskers.

The great advantage of carbon fibers over metals becomes all the more impressive when one considers the specific strengths and specific Young's moduli, *i.e.* those based on unit weight. The specific tensile strength corresponds to the tension length, *i.e.* the minimum length of a fiber or wire for which it breaks under its own weight. The high-tensile carbon fibers have a tension length of 170 km. As can be seen in Table 7, metal fibers have tension lengths of only a fraction of this value.

The decisive advantage of carbon fibers, however, lies in their extremely high stiffness, which is expressed by Young's modulus. Young's modulus of highly stretched carbon fibers is inferior only to that of graphite whiskers. The specific Young's modulus of high-modulus carbon fiber is eight times that of a metal wire.

The carbon fibers are produced in ropes containing 2000 to 1000 individual filaments. In the individual filaments, which have a diameter of about 8 μm, the two-dimensionally ordered graphite layer planes are aligned parallel to the fiber axis. As in textile fibers, large crystalline zones are combined to form supermolecular structures; under the electron microscope they exhibit a fibrillar structure in the form of strip-shaped zones arranged substantially parallel to the fiber axis.

Carbon fibers are used mainly for the production of high-tensile and high-modulus composite materials, which are discussed in Section 7.4.

7.3. Carbon Whiskers

Young's moduli and tensile strengths even higher than those of the carbon fibers described in the last section can be attained in carbon whiskers. These are hair-like crystals of carbon, a few centimeters long, whose diameter (about 0.5–5 μm) is appreciably smaller than that of carbon fibers. Since the strength of fibers in general increases rapidly with decreasing diameter, these carbon whiskers have the highest strength reached so far. *i.e.* a tensile strength of up to 2000 kg/mm² and Young's modulus of up to 7×10^6 kg/cm².

Graphite whiskers were first obtained in the mid-1950's by *Bacon* and *Bowman*[49]. They were prepared from graphite vapor by a high-energy electrical discharge. The methods used nowadays, however, make use of gaseous carbon compounds. Under very strictly limited deposition conditions, the pyrocarbon (cf. Section 3) formed on pyrolysis can be made to grow in the form of whiskers. This leads first to very thin primary whiskers having a diameter of about 0.01 μm[50], which then thicken as a result of secondary deposition of pyrolytic carbon. The main difficulties in the production of whiskers lie in the suppression of this secondary growth. Several methods have been used for this purpose, such as the addition of catalysts to the pyrolyzing gas[51,52]. The deposition of the

[48] *G. E. Cranch* and *J. S. Shinko*, DOS 1469492 (1963), Union Carbide Corp.

[49] *R. Bacon* and *J. C. Bowman*, Bull. Amer. physic. Soc. Ser. II, *2*, 131 (1957).

[50] See ref. [5], p. 832.

[51] *H. F. Kauffman*, *D. J. Griffiths*, and *J. S. Mackay*, US-Pat. 2796331 (1954), Pittsburgh Coke and Chemical Comp.

[52] *R. J. Diefendorf*, US-Pat. 3107180 (1961), General Electric Comp.

whiskers in steep temperature and concentration gradients has proved very favorable [53].

All these methods are being used only on a laboratory scale at present. Owing to their outstanding strength properties, carbon whiskers will undoubtedly be used in future for materials subject to extreme loads, though they will always be much more expensive than carbon fibers.

7.4. Carbon Fiber Reinforced Materials

All the common metals have roughly equal stiffness for equal weights; they have roughly equal specific Young's moduli. This is an inherent property of metals, and cannot be fundamentally altered by alloying or the like.

Because of the low defect concentration, wires, fibers, and above all whiskers always have higher tensile strength and Young's modulus than compact materials. In the development of new materials with extremely high specific stiffness, therefore, one starts with thin fibers or wires, which are combined with matrix substances to produce composite materials. The strength of these composites is roughly proportional to the volume fraction of the fibers that are arranged parallel to the direction of the stress.

Graphite whiskers are ten times as strong as carbon fibers. However, it is very difficult to embed them in a matrix material. Moreover, they do not differ so much from carbon fibers in their Young's modulus.

On the other hand, continuous carbon fibers, like glass fibers, can be easily embedded in a synthetic resin matrix in volume fractions of more than 50%, *e.g.* by the filament winding method. The matrix materials are generally epoxy resins, though polyester and phenolic resins are also used. Figure 9 shows an electron-scan micrograph of the point of fracture of a carbon fiber/synthetic resin composite. The good adhesion of the synthetic resin matrix to the surface of the fibers is obvious.

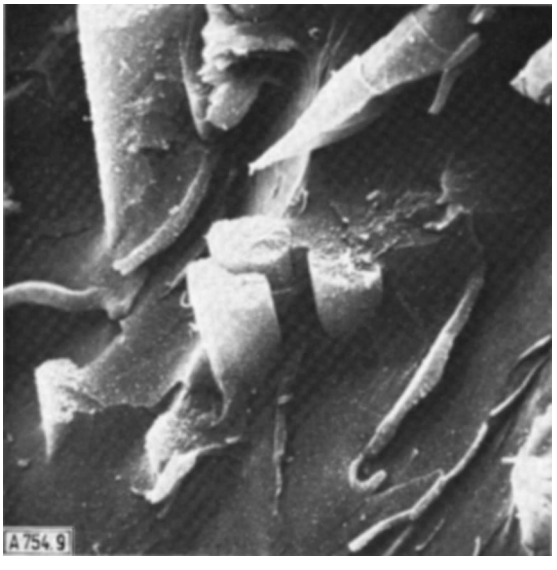


Fig. 9. Electron-scan micrograph of the fracture point of a carbon fiber-synthetic resin composite (magnification 1250 ×). The micrograph was prepared in the Labor für Raster-Elektronen-Mikroskopie Dr. *H. Klingele*, München.

As can be seen from Table 7, a composite of this type with a bulk factor of 0.5, *i.e.* consisting of 50 vol.-% of fibers and 50 vol.-% of synthetic resin, is as stiff as a steel body having the same dimensions; the specific Young's modulus, on the other hand, is five times that of steel. This means that a component made of carbon fiber reinforced plastic suffers only one fifth of the deformation under load exhibited by a comparable steel component.

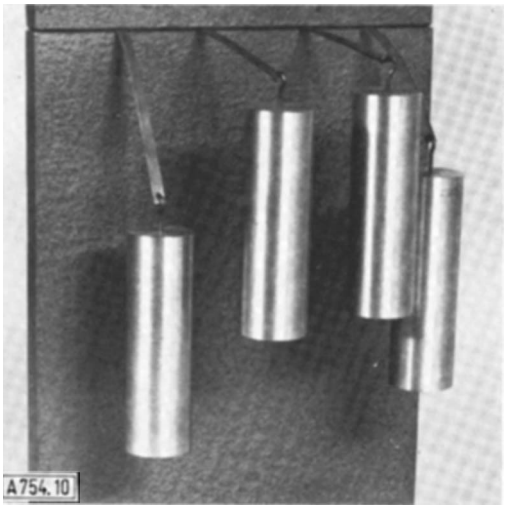


Fig. 10. Rigidity of materials, from left to right: aluminum, carbon fiber reinforced plastic, steel, glass fiber reinforced plastic.

The high rigidity of the carbon fiber reinforced plastics is illustrated by Figure 10. Strips of aluminum, glass fiber reinforced plastic, steel, and carbon fiber reinforced plastic having the same dimensions were loaded with equal weights. Bending is clearly least for the carbon fiber reinforced plastic and the steel. However, the steel strip is five times as heavy as the carbon fiber product.

Carbon fiber systems are unaffected by moisture. Their good electrical and thermal conductivity is also particularly advantageous.

These systems will be used in particular where high strength and high rigidity are required in conjunction with low weight, *i.e.* in rapidly rotating components and in aircraft and automobile construction. Examples are turbine blades in the Rolls-Royce RB 211 engine, heavy-duty jet housings, edges of aircraft wings, and floors of aircraft (in combination with honeycomb structures). There are also possible applications outside of aviation and space technology, *e.g.* for large centrifuges, spinning and weaving machines, sports cars, mountaineering equipment, and sailboat masts.

The application temperature of carbon fiber reinforced plastics is limited by the thermal stability of the plastic. Important advantages will result from the use of synthetic resins with high thermal stabilities, such as polyimides and polyimidazoles. The highest tem-

[53] *E. Fitzer* and *H. G. Schlesinger*, DAS 1269933 (1966), SIGRI.

peratures at which the composites may be used will be further raised by the use of glasses or metals as matrix materials [54, 55]. Carbon fiber reinforced carbons are stable up to 3000 °C in inert or reducing atmospheres. However, their production is still in the experimental stage.

The further development of these new fiber-reinforced high-temperature materials will open up wide fields of application for carbon fibers.

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Translated by Express Translation in Service, London

[54] *D. H. Bowen, R. A. J. Sambell, K. A. D. Lambe*, and *N. J. Mattingley*, DOS 1925009 (1968), U.K.A.E.A.

[55] *A. A. Baker* and *R. J. Bache*, Brit. Pat. 1177301 (1968) Rolls Royce.

Electroplating of Plastics in Theory and Practice

By Kurt Heymann, Wolfgang Riedel, and Günter Woldt [*]

Electroplated plastics combine many advantages of plastics and of metals; they have the low weight and ease of shaping of plastics, together with the luster, hardness, and electrical conductivity of metals. An important part of any process for the electroplating of plastics is a pretreatment to ensure good adhesion of the metal film. Etch activation in the straight-through method requires only six steps for pretreatment.

1. Introduction

The rapid growth of the consumption of plastics in the last 20 years is primarily due to the ease with which they can be shaped to obtain useful objects. This was greatly appreciated by industrial users, who required versatility of types and shapes with no great increase in production costs, such as arises *e.g.* in the processing of metals.

For this reason the users accepted disadvantages in color matching, the attraction of dust by static electricity, and the relatively soft surface of injection molded thermoplastics.

These "made-to-measure materials" offer considerable scope for the work of the chemist. The polymers can be suited to a wide range of uses by modification of the nature of the monomers, the polymerization conditions, and pigmentation, and because of the possibility of reinforcement with glass fibers. Nevertheless, plastics have to compete with the traditional metal.

It seemed natural, therefore, to seek a good combination of plastic and metal, *i.e.* a genuine composite of plastic and metal.

An important factor here is undeniably the wish to give a plastic surface a metallic luster for decorative reasons, since large sections of the market like the glitter of metals. It is in fact impossible to tell by appearance whether a chromium-plated object is made of metal or plastic; the difference can be felt only by touch. Electroplated plastic feels warm and is much lighter. Because of its lightness, it is easier to transport and handle, and this is a further argument in favor of metalized plastics.

Plastics can be shaped more easily, more cheaply, and in greater variety than metals. To obtain shiny surfaces, the mold into which the plastic is injected is polished instead of each individual article. Without knowing the market, one might think that the electroplating of plastics is a passing fashion. However, this practice has many technical advantages, apart from its decorative value.

Many plastics are damaged by ultraviolet radiation. This damage is prevented by a film of metal. The flammability of plastics is also reduced by metalization.

Use is often made in the electrical industry of chassis having complicated shapes. To produce a metal chassis of this kind, several individual parts have to be fitted together and welded. It has been found in

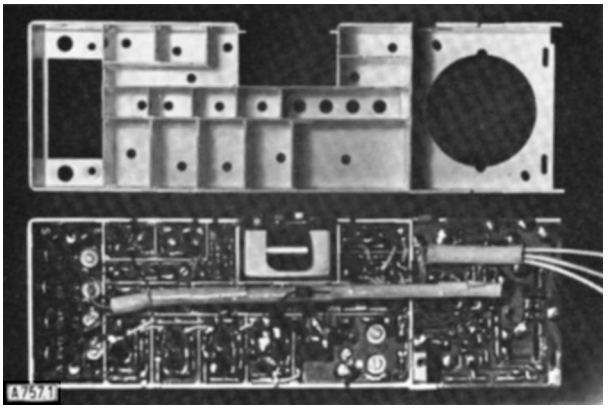


Fig. 1. Chassis of ABS plastic (Bosch Elektronik GmbH, Berlin).

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1 Berlin 65, Postfach 59 (Germany)

practice that the same result can be achieved by injection molding of the chassis in one operation, followed by electroplating (Fig. 1). The metal deposit is electrically conductive. Contacts can be made as before if soldering is carried out quickly and without too much heat.

In other cases a metal deposit is desirable to prevent static build-up. Other uses are discussed in Section 4.

As long as there have been plastics, there have been efforts to electroplate them[1]. Plastics, like other nonconductors, clearly require petreatment to make them electrically conductive for the plating operation. The surface must first be made wettable and active, and then covered with a thin film of metal in electroless baths. Though promising methods were known[1,2], all efforts remained unsuccessful for years, since an adhesive bond could not be produced between the plastic and the electrochemically applied metal film. Conducting lacquers seemed for a time to offer a suitable bonding substance, but this plan failed because the conducting lacquer rounded the contours of the surfaces, and the metal pigments could not be uniformly exposed and built up by electrodeposition.

Around 1964, it was found by the work of *Narcus*[3], *Saubestre*[4], and investigators at Marbon Chemical[5,6] that ABS plastics (acrylonitrile-butadiene-styrene graft polymers) are excellently suited for electroplating. On this basis and with steady improvement of the pretreatment methods, the electroplating of plastics was developed in only five years into an industrially recognized process[7].

2. The Plating Processes

The sequences of operations involved in the electroplating of plastics are summarized in Table 1. For the first step of the pretreatment, *i.e.* etching, the ABS objects are mounted on jigs and immersed in chromosulfuric acid at 65 °C. This makes the surface of the plastic hydrophilic, and the butadiene units are oxidatively degraded. Cavities are formed at these points, and these later provide mechanical anchorage for the metal coating[8,9]. To make the plastic conductive, metal is deposited on it by electroless plating. However, deposition of metal on objects immersed in a copper or nickel reduction bath is possible only if electrons can be transferred from the reducing agent to the metal ions to be reduced *via* the solid phase. For this to happen, the solid phase must be a good electronic conductor and allow fast electron exchange. This condition is satisfied by many metals; however, noble metals are preferred since they can be deposited particularly readily in the cavities in the plastic by reduction of their ions. It is also possible to apply colloidal noble metals to the surface of the plastic.

Table 1. Sequence of operations in various methods for the electroplating of ABS and zinc die castings.

	ABS Conventional process	ABS Staight-through process	ABS Etch activation (straight-through process)	Zinc die castings Standard process
1.	Etching	Etching	Etching + activation	Mechanical polishing
2.	Rinsing	Rinsing	Rinsing	Cleaning in tetrachloroethylene
3.	Decontamination	Decontamination	Decontamination	Degreasing
4.	Rinsing	Rinsing	Rinsing	Rinsing
5.	Activation Sn^{2+}	Activation Pd^{2+}	Acceleration	Pickling
6.	Rinsing	Rinsing	Chem. deposition of Ni	Rinsing
7.	Activation Ag^{+} or Pd^{2+}	Reduction	Rinsing	Electroplating
8.	Rinsing	Rinsing	Electroplating	
9.	Chem. deposition of Cu or Ni	Chem. deposition of Cu or Ni		
10.	Rinsing	Rinsing		
11.	Pickling	Pickling		
12.	Electroplating	Electroplating		

The production of the noble metal particles that catalyze the chemical deposition of metal is known in the plating industry as "activation of the plastic", or as "nucleation". This can be achieved by the following methods:

a) Immersion in stannous chloride solution and then, after rinsing with water, in silver nitrate, palladium(II) chloride, or gold(III) chloride solution.

b) Immersion in a solution of a palladium salt and then in hydrazine hydrate or sodium tetrahydroborate solution.

c) Immersion in a colloidal palladium solution.

d) Etch activation in chromosulfuric acid containing noble metal.

Method (a) was chemically dependable, but required too many workers for its execution. While the parts are being rinsed with water after activation with stannous chloride solution, hydrolysis leads to the formation of gel-like oxide chloride, which remains adsorbed not only on the ABS but also on the insulated jig. The result is that noble metal nuclei, and later copper or nickel, are deposited on the insulation of the jig. To confine the electrodeposition of metal to the ABS plastic, the parts are then transferred to different in-

[1] *S. Wein*: Metallizing Non-Conductors. Finishing Publ., Inc., Westwood, USA, 1945.

[2] *S. Wein*: Metal Finishing *58/60*, 69 (1948).

[3] *H. Narcus*: Metalloberfläche *17*, 284 (1963).

[4] *E. B. Saubestre, C. J. Durney, J. Hajdu*, and *E. Bastenbeck*, Plating *52*, 982 (1965).

[5] *J. B. McNamara*, Metal Progr. *86*, 112 (1964).

[6] *C. R. Holt* and *B. J. Jensen*, Plastverarbeiter *2*, 72 (1965).

[7] *K. Heymann* and *G. Woldt*, Galvanotechnik *61*, 221 (1970).

[8] *K. Heymann, W. Riedel*, and *G. Woldt* in *H. Wiegand*: Metallische Überzüge auf Kunststoffen. Hanser Verlag, München, 1966, p. 48.

[9] *K. Wiebusch, H. Hendus*, and *E. Zahn* in *H. Wiegand*: Metallische Überzüge auf Kunststoffen. Hanser Verlag, München 1966, p. 9.

sulated jigs that have not been in contact with the pretreatment baths. The efforts to overcome this disadvantage and to ensure selective deposition of the metal on the ABS led first to the introduction of activation methods (b) and (c).

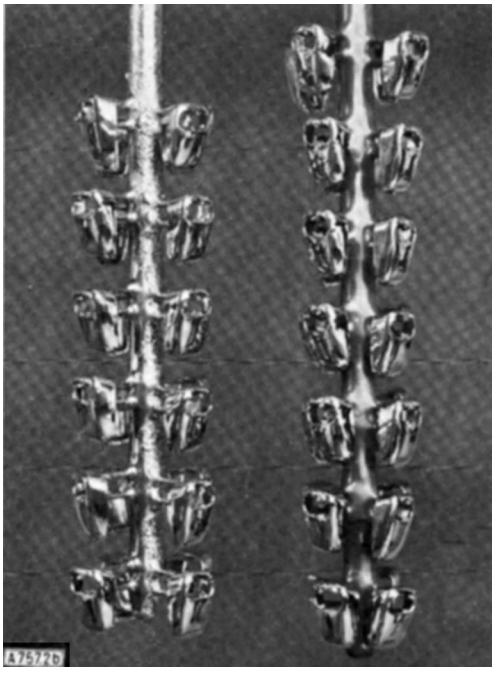


Fig. 2. Jigs with ABS components. Left: conventional process (deposition of metal on jig). Right: straight-through process (metal deposited on ABS only).

Processes involving no change of jig are known as "straight-through" processes, since the jig passes continuously through the plants from etching to plating with the object (Fig. 2).

Further rationalization of the pretreatment has recently been achieved by etch activation [7]. In this case some steps are no longer necessary, as can be seen in Table 1, so that the electroplating of plastics is now as simple as the electroplating of metals. Noble metals are added to the etching solution, and are carried into the plastic by the chromosulfuric acid.

It can be verified by experiments with radioactive isotopes that the noble metal is very firmly fixed to the plastic under these conditions, and is not washed out again. In these experiments, the noble metal compound was first activated by neutrons in a nuclear reactor, and then added to the etching solution. Several ABS samples were etched in the resulting activated etching acid for 4, 8, or 12 minutes at 65 °C, and were then vigorously rinsed for 1 or 10 minutes with introduction of air. After the samples had been dried, the radioactivity was monitored with a Geiger-Müller counter. Despite the vigorous rinsing, the activity of the samples decreased by only about 10%. This small decrease is of no importance to the subsequent chemical deposition of metal [7].

The next step after activation is the chemical deposition of metal from copper or nickel reduction baths. The principal components of these baths are the metal salts together with complexing agents and reducing agents. The reductions for copper-formaldehyde and nickel-hypophosphite solutions can be represented by the following simplified equations:

$$Cu^{2+} + HCOH + 3\,OH^- \rightarrow Cu^0 + HCOO^- + 2\,H_2O$$

$$Ni^{2+} + H_2PO_2^- + H_2O \rightarrow Ni^0 + H_2PO_3^- + 2\,H^+$$

Unlike the deposition of silver, which takes place spontaneously in silver salt-formaldehyde solutions, the deposition of copper and of nickel is strongly inhibited and occurs only in the presence of catalytically active nuclei.

The carry-over of small quantities of noble metal activator into a metalization bath was at first a great danger to practical operation, since these activators caused decomposition of the metalization bath. It was only with the development of efficient stabilizers, which prevent the spontaneous precipitation of copper or nickel (compounds of sulfur, selenium, and some heavy metals, as well as cyanides and oxygen, are suitable for use as stabilizers), that this danger was eliminated and the chemical deposition of metals became economical [10].

Once the plastic objects have been made conductive by the deposition of metal, the metal film can be built up by electrodeposition. The first step is the electrodeposition of copper from a sulfuric acid electrolyte. Any metal capable of being electrodeposited can then be applied. Electrolytes having a smoothing effect are preferred, since the deposition of the metal then proceeds in such a way that any depressions already present in the surface are preferentially filled up (Fig. 3).



Fig. 3. Smoothing of a rough base material by electroplating with copper.

A copper base about 20 µm thick ensures that the composite withstands thermal shocks between +80 and −40 °C despite the difference in the expansion coefficients of the plastic and of the metal.

The thermal shock test devised by the "Electroplated Plastics" work group of the German Standards Committee for quality control [11] specifies the following conditions:

105 min +80 °C
15 min room temperature
105 min −40 or −30 or −20 °C, as required
15 min room temperature

This cycle is repeated three times. The metal must not blister or crack. If the plastics processor and the electroplater have followed the correct procedures for injection molding and electroplating, the production parts will pass the test. If on the other hand highly strained plastics articles are electroplated without following the rule that the copper film should be twice as thick as the nickel-chrome film deposited on it, the quality standard will generally not be satisfied.

[10] *G. Woldt*, Jahrbuch der Oberflächentechnik *25*, 178 (1969).
[11] Galvanotechnik *58*, 669 (1967).

3. Theory of Adhesion

ABS plastics are thermoplastics prepared from acrylonitrile, butadiene, and styrene either by copolymerization or by graft polymerization. Chemically speaking, they are ternary materials, but they consist morphologically of two phases, *i.e.* the finely dispersed, soft butadiene rubber phase and the relatively rigid styrene-acrylonitrile copolymer phase [12]. Figure 4 shows a transmission electron micrograph of an ABS graft polymer [13]. The polybutadiene phase, which is in the form of globular particles, is visible as a result of material contrast. Depending on the type of plastic, the rubber particles have diameters of 10^{-5} to 10^{-4} cm.

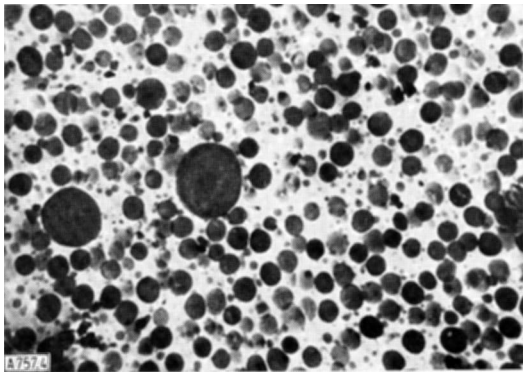


Fig. 4. Electron micrograph of ABS graft polymer (after [13], magnification 3700 ×).

During the etching of ABS plastics, the double bonds of the polybutadiene are oxidized, and this phase is selectively dissolved out of the ABS plastic. Figure 5 shows an ABS film that has been cast from solution, etched, and activated with silver nuclei [8]. The preparation of a film of this type from a solution naturally leads to relatively good homogenization of the macromolecular components. The etching has produced spherical holes wherever the polybutadiene component was present in the film.

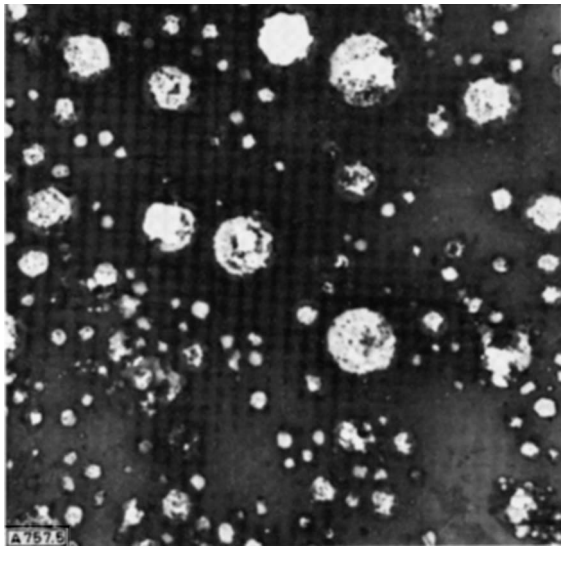


Fig. 5. Electron micrograph of cast, etched, and activated ABS plastic after *Wiesenberger* (from [8], magnification 6000 ×).

The activation and the chemical deposition of metal take place preferentially on the inside walls of the holes, as is shown by Figure 6, which was taken after a copper-plating time of 45 s. After 1.5 min, all the cavities have already been filled with copper.

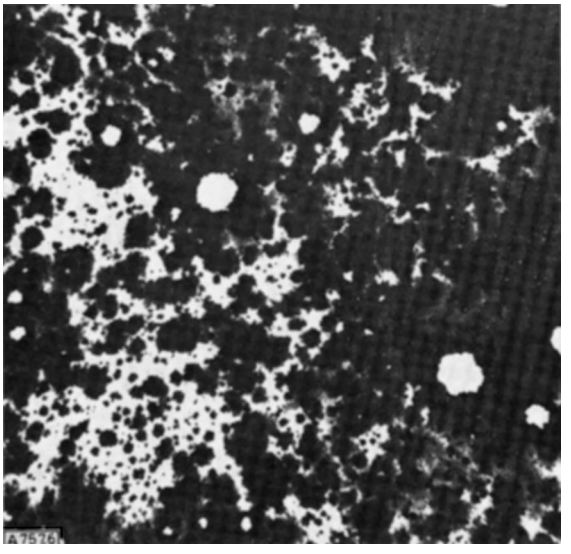


Fig. 6. Electron micrograph of an ABS film with incipient deposition of copper (after [8], magnification 6000 ×).

The chemical attack of the etching solution on the ABS graft polymer thus leads to dissolution of the elastomer out of the surface of the plastic, as was clearly recognizable. The resulting spherical cavities are more or less completely filled with metal during the chemical metalization. The good adhesion of the metal to the ABS plastic could thus be explained by mechanical anchoring of the metal in the ABS matrix polymer [8, 14]. Figure 7 shows a model of mechanical anchoring ("snap fastener theory" [17]).

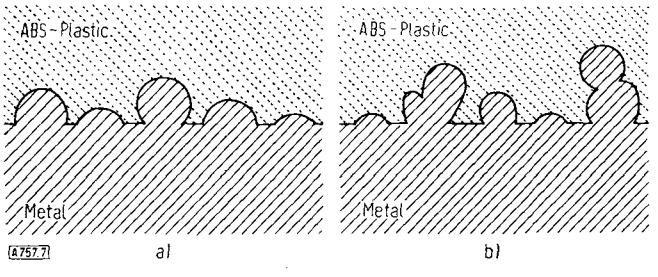


Fig. 7. Schematic diagram of the adhesion of metal to ABS plastic. a) Ideal model, b) real structure.

To check whether this hypothesis could explain adhesions of about 200 kg/cm² in a tensile test and peel strengths of about 4 kg/inch, an attempt was made to estimate the adhesion [8, 15].

[12] *K. Kato*, Kolloid-Z., Z. Polymere *220*, 24 (1967).

[13] *E. Zahn* and *K. Wiebusch*, Kunststoffe *56*, 773 (1966).

[14] *K. Heymann*, *W. Riedel*, *R. Blaschke*, and *G. Pfefferkorn*, Kunststoffe *58*, 309 (1968).

[15] *W. Riedel*, Galvanotechnik *57*, 579 (1966).

The force required to pull a metal sphere of radius r out of the matrix polymer AS when the center of the sphere is situated at a distance a under the surface ($a < r$) is:

$$K_L \approx 2\pi (r - \sqrt{r^2 - a^2}) S$$

S = tensile strength of the AS matrix.

For random variation of the depth a with $0 \leqslant a \leqslant r$, the force required to separate the bonded surfaces over an area of 1 cm² in the tensile test is:

$$K_S \approx \frac{2\pi r S}{e^2} \times \frac{1}{e} \int_0^{e/2} (r - \sqrt{r^2 - a^2})\, da \approx \frac{2\pi r^3}{e^3} \left(1 - \frac{\pi}{4}\right) \times S$$

If the butadiene spheres form a three-dimensional trivial lattice with a lattice constant e, then

$$e^3 = \frac{400\pi r^3}{3B}$$

B = volume fraction of butadiene in the ABS copolymer (%).

Thus the adhesion in the tensile test is

$$K_S \approx 3.22 \times 10^{-3} SB$$

Taking into account a number of second order factors such as the compressibility of the metal, the polydispersity and the shape factor of the holes, and the microroughness, we obtain K_S values of the order of 150 kg/cm² with $S \approx 750$ kg/cm² and $B \approx 25\%$. This almost agrees with the adhesions found experimentally [8, 16].

In practice, the adhesion is usually taken to be not the tensile strength but the peel strength in accordance with DIN 40802. The peel strength is defined as the force required to pull the coating away from a strip of plastic 1 inch wide with a pull parallel to the normal to the surface.

The peel strength P consists of two components, one taking the deformation of the metal into account (P_V), and the other the force needed to overcome the adhesion (P_H) [15]:

$$P = P_V + P_H = \frac{E\bar{a}\, b\, h^3}{4\, y^3} + \frac{K_L\, y\, b}{e^2}$$

E = elasticity modulus of the metal, $\bar{a}$ = average "immersion depth" of the snap fasteners, b = width of the metal film (2.5 cm), h = thickness of the metal film, y = contact length.

The unknown contact length y, *i.e.* the length of the zone in which stresses are acting to break the contact, can be eliminated by optimization:

$$y(h) = \left(\frac{3E\bar{a}\, h^3 d^2}{4 K_L}\right)^{1/4}$$

The peel strength is therefore:

$$P = 1.76 \left(\frac{E\bar{a}\, h^3 b^4 K_L^3}{4 d^6}\right)^{1/4}$$

$E = 1.3 \times 10^6$ kg/cm², $\bar{a} = 0.2 \times 10^{-4}$ cm, $K_L = 1.65 \times 10^{-6}$ kg, $d = 1.26 \times 10^{-4}$ cm, h (in cm) gives

$$P = 222 \times h^{3/4}$$

Thus the peel strength of a copper coating is theoretically strongly dependent on the thickness of the metal film. Figure 8 shows the measured and estimated dependence of the peel strength on the thickness of the copper coating. For a film thickness of 40 μm, one can expect a peel value of 3.5 ± 1.5 kg/inch if adhesion is assumed to be due to mechanical anchoring in accordance with the snap fastener theory. Good agreement is found between the experimental and the estimated values. It can thus be concluded that the bonding between the plastic and the metal may be of a mechanical-physical nature. There is therefore no need to postulate the existence of chemical, dipole, or van der Waals forces between the materials in contact, as was done by *Saubestre et al.* [4] and by *Logie* and *Rantell* [18].

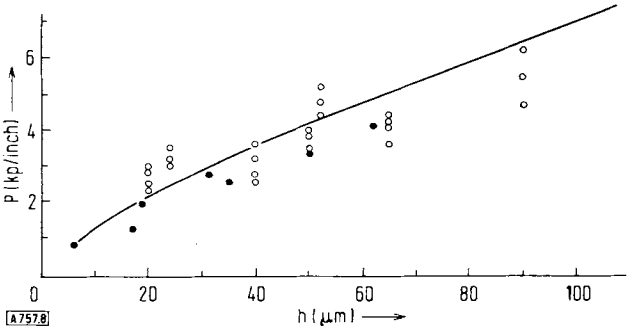


Fig. 8. Dependence of the peel strength P on the thickness h of the copper film (after [15]; — calculated. ● our experimental values, ○ *Saubestre*'s values).

The surfaces of bulk-injected or extruded ABS articles after etching naturally differ in morphology from the surfaces of cast ABS films. Figures 9–11 show electron-scan micrographs of an ABS plastic after etching for 2 min, 8 min, and 32 min, respectively. The morphological similarity of the specimen exhibiting optimum etching (Fig. 10) to that of Figure 5 is unmistakable.

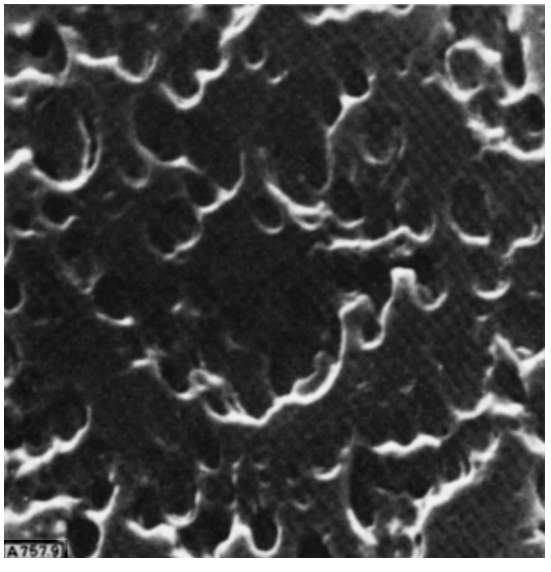


Fig. 9. Electron-scan micrograph of ABS plastic after etching for 2 min (magnification 6000 ×).

[16] *N. F. Murphy* and *E. F. Swansey*, Plating *56*, 371 (1969).
[17] *K. Heymann*, Galvanotechnik *56*, 413 (1965).
[18] *G. R. Logie* and *A. Rantell*, Trans. Inst. Metal Finishing *46*, 91 (1968).

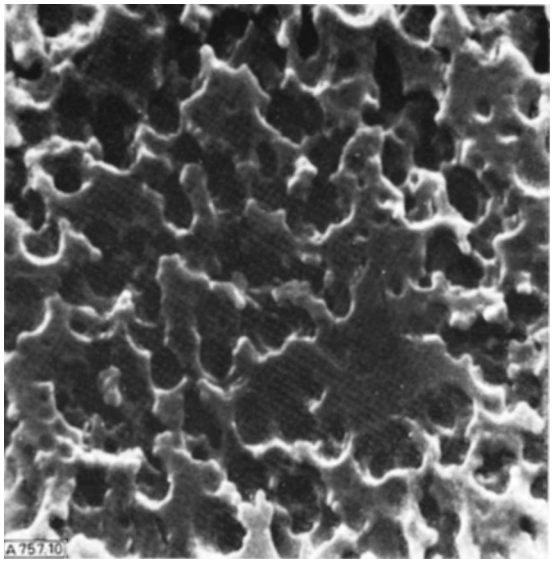


Fig. 10. Electron-scan micrograph of ABS plastic after etching for 8 min (magnification 6000 ×).

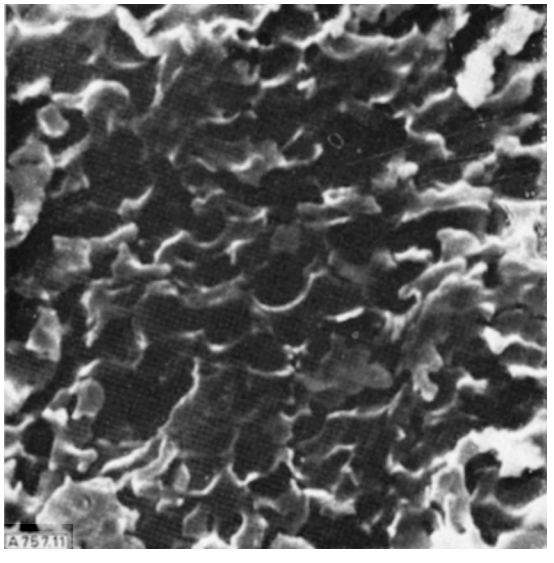


Fig. 11. Electron-scan micrograph of ABS plastic after etching for 32 min (magnification 6000 ×).

Figure 12 shows a cross section through the ABS-metal composite after *Zahn* and *Wiebusch*[13], in which the mechanical anchorage of the metal film in the plastic is visible.

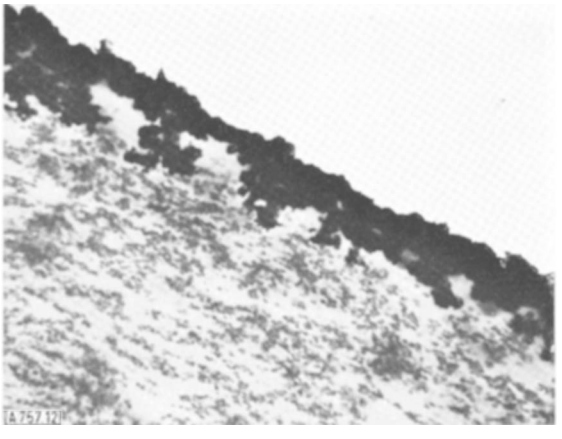


Fig. 12. Electron micrograph of a cross section of the ABS-metal interface (after [13], magnification 9250 ×).

A question of practical importance that now arises is whether plastics other than ABS can give strongly bonded composites on electroplating. On the basis of the theory of mechanical anchorage, it is possible to predict the composition required of a plastic if it is to be capable of being electroplated.

The plastic must consist of at least two phases, one of which must have a cotton-wool like structure with colloidal dimensions[14]. This phase must dissolve much more rapidly than the other phases in an etching medium. The phases that are less soluble in the etching solution must be coherent and mechanically stable. It must also be possible to deposit nuclei for chemical metalization on the etched surfaces, particularly in the holes.

Other plastics have in fact been electroplated; the peel values were similar to those found for ABS, and in some cases even higher. Figures 13 to 15 show three

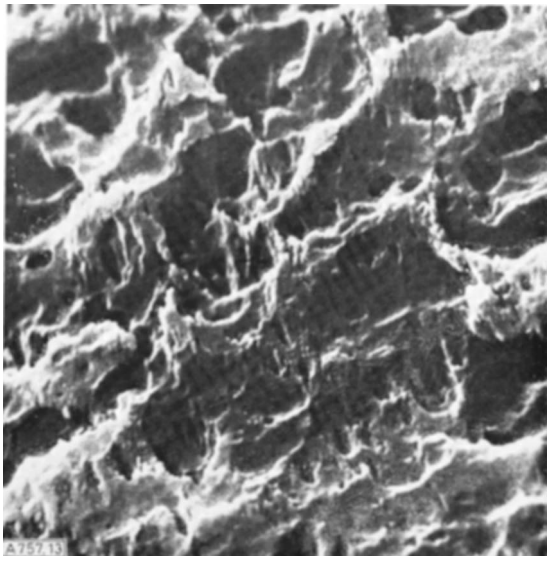


Fig. 13. Electron-scan micrograph of etched modified PPN (after [19], magnification 6000 ×).

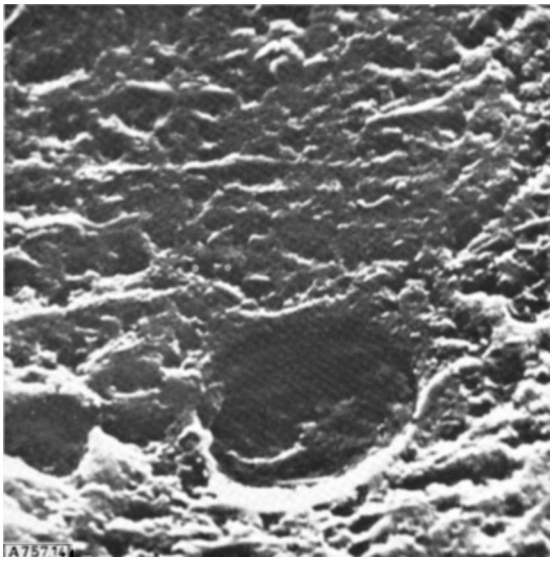


Fig. 14. Electron-scan micrograph of etched modified PPO (after [19], magnification 6000 ×).

[19] *G. Woldt*, Trans. Inst. Metal Finishing *47*, 236 (1969).

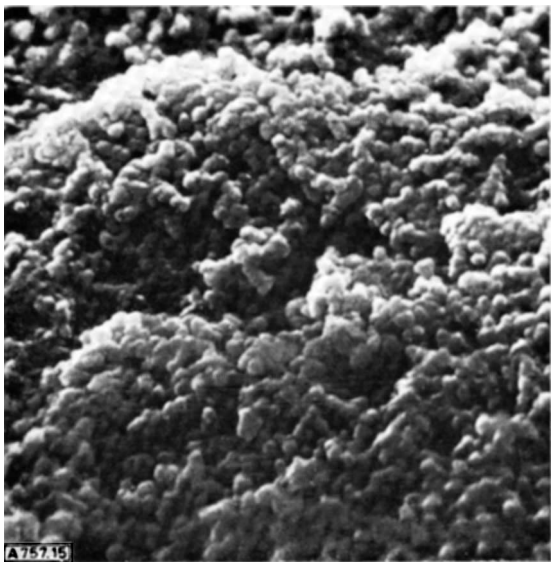


Fig. 15. Electron-scan micrograph of etched adhesive (after [20] magnification 6000 ×).

electron-scan micrographs of electroplatable plastics that have received optimum etching: modified polypropylene (PPN), modified polyphenylene oxide (PPO), and an adhesive for the production of printed circuits by an additive process [20]. These plastics were modified by copolymerization and by introduction of organic or inorganic fillers. The etched surfaces show a distinct similarity to that of optimally etched ABS; they are relatively uniformly roughened, and the light borders of the holes clearly show the presence of undercuts in which the metal can anchor.

Thus, on the basis of present knowledge, one can say that, to give good adhesion of electrodeposited films, a plastic must contain at least two phases, though the difference between the phases may be merely that one is crystalline while the other is not. In accordance with the mechanical adhesion model (snap fastener theory), the phase that can be dissolved out chemically must be uniformly distributed in the surface zones of the injection molded article.

If these requirements are satisfied, a number of further simple conditions must be observed in the injection molding process. The nature and number of gates must be such as to ensure that the articles produced will be as free as possible from strains and orientations. Care should be taken to follow the raw material producer's recommendations on predrying of the granulate, mass and mold temperatures, injection pressure, and injection rate. The article must be ejected from the mold without the aid of mold release agents. The objects must naturally be of a suitable design for electroplating [21].

4. Applications

The number of operations and tanks required is shown in Table 1. A large plant should have a fully automated transport system. The construction of the containers, which have capacities of up to 3000 l, depends on their contents. Lead-lined sheet steel tanks are used for strongly acidic etching solutions, PVC-polyester laminate tanks for the more dilute solutions, and glass fiber reinforced polyester tanks for rinsing water. The decontamination of the waste water is carried out separately. Accessories required are immersion heaters in some places, filter pumps, fume-extraction equipment, and (in the electroplating section) rectifiers. The jigs carrying the articles are passed in succession into the baths, where they remain for fixed times.

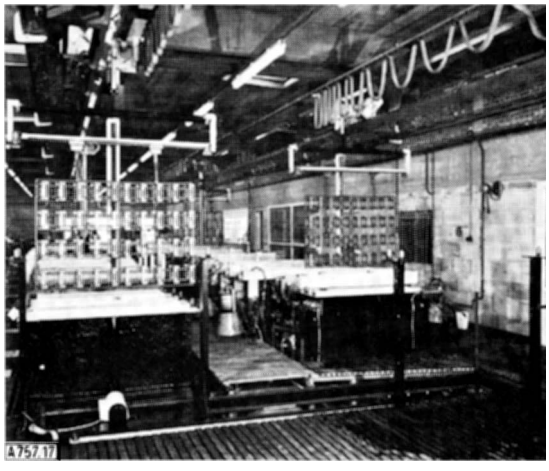


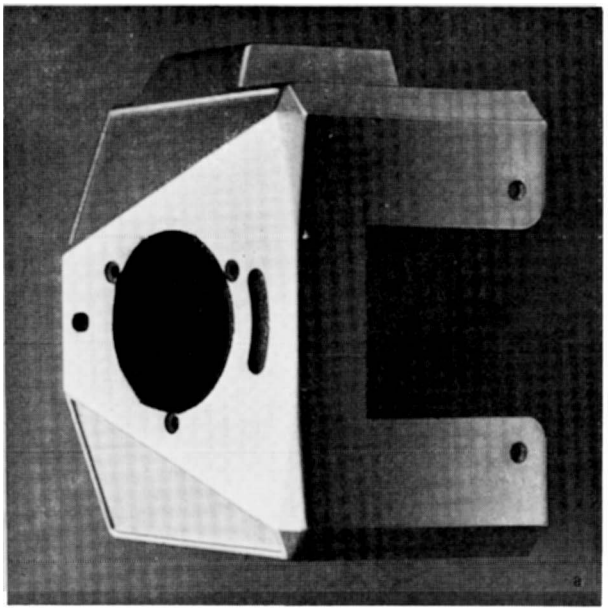
Fig. 16. Fully automated continuous plant for plating plastics with copper, nickel, and chromium located at the Overpelt-Plascobel S. A. Belgium.

The electroplating of plastics has already found applications in the automobile, audio, furniture, clock-making, photographic, household goods, fancy goods, and textile industries. We shall now describe a few examples selected from the many uses.

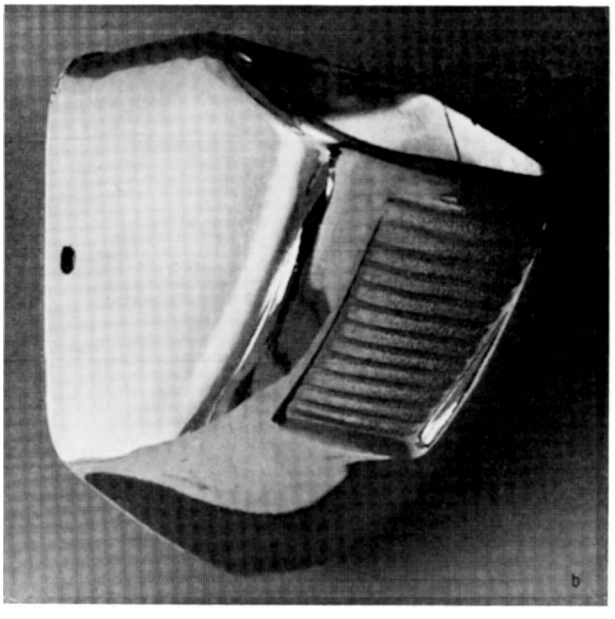
Figure 17c shows an outside mirror for an automobile. The mechanical polishing required when the part is made of metal is unnecessary when plastic is used; the same is true of the armrest fixture (Fig. 17b) and the miniature radio cover (Fig. 17h). The possibilities available to the mold designer are illustrated by the door knob (Fig. 17d) and the clock case (Fig. 17i). In this connection, there is greater variety in the design of clothes buttons (Fig. 17f). The camera front plate in Figure 17g is completely electroplated, though only the chromium plated edges are visible after the application of a black film and assembly. Since there is no need for polishing, this construction is cheaper than production of a front plate from zinc die castings or light metal. The exposure meter housing shown in Figure 17a can be injection molded cheaply in one piece. It is dull nickel plated and chromium plated. The processing of bathroom fittings made of plastic has also proved particularly economical (Fig. 17e). Other applications are navigation light housings for motor boats, radiator grills, automobile rear light housings, thermos flasks, perfume bottles, and mixing valves for bathroom fittings, to name but a few.

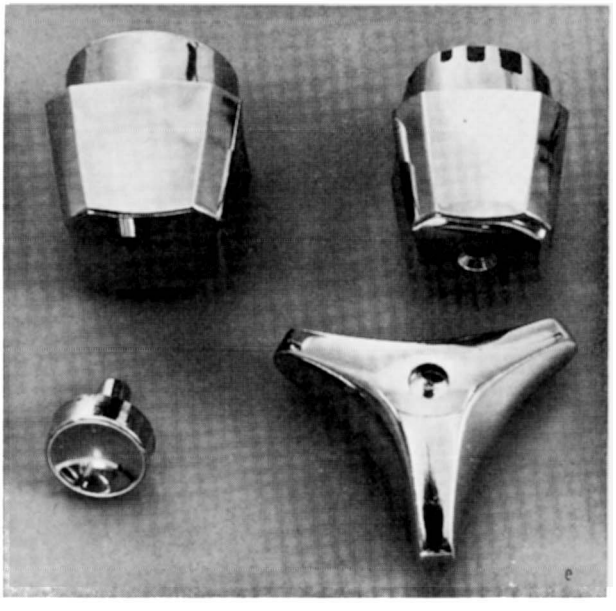
The applications are not confined to large objects, which must be fixed to jigs. Small articles can also be

[20] *H.-J. Ehrich*, Galvanotechnik *61*, 14 (1970).
[21] *P. Spiess*, Ingenieur Digest *7*, No. 9 (1968).

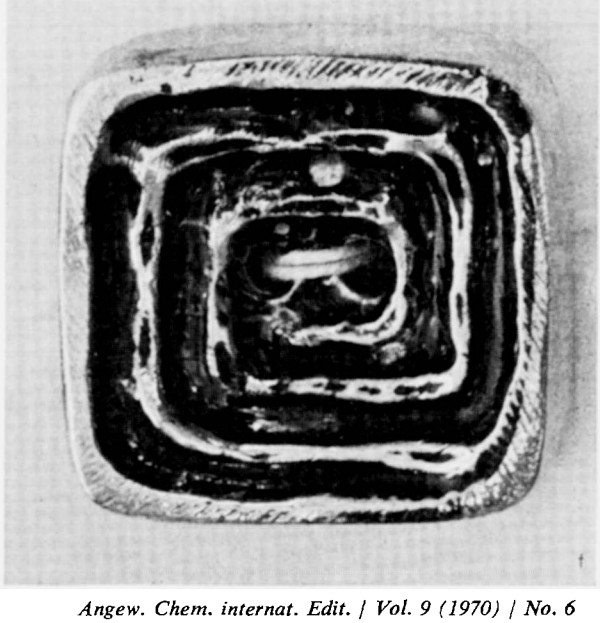




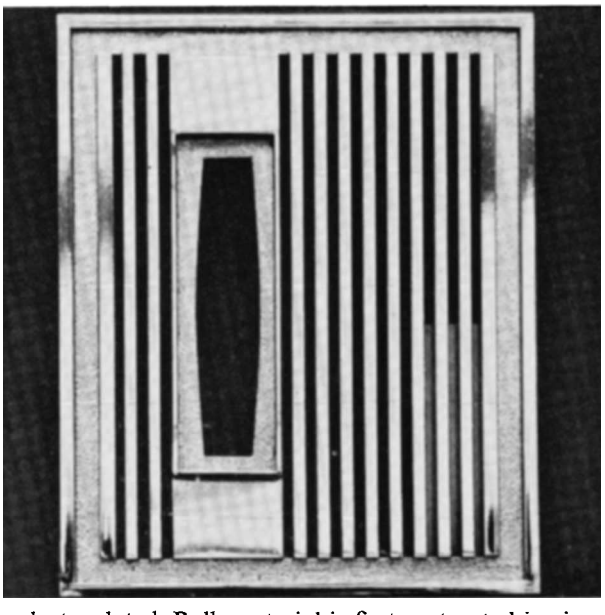












electroplated. Bulk material is first pretreated in sieve baskets. After being made conductive, the articles are copper plated, nickel plated, silver plated, or gold plated electrochemically in barrels. However, this requires a special barrel in which reliable current transfer is ensured by several cathode contacts. This



prevents the light plastic parts from floating away from the contacts.

These examples illustrate the magnitude to which the electroplating of plastics has grown within a few years. By rationalization of the process and improvement of reliability, even in the operation of the electroless metalizing baths, which has not until now been much used in industry, the confidence of the user was won, and a new field of application was opened up both for plastics processing and for electroplating.

As a readily obtainable and cheaply producible composite material, metalized plastic will be a material of the future, if only because of the rapidly expanding production of plastics. The continuous rapid growth of the plastics industry has now been in progress for 30 years. The consumption of plastics in the USA per head of population has increased by 413% since 1953. The consumption of plastics in the Federal German Republic is at present higher (34.1 kg/head of population) than in any other country. In 1980, German industry will process more than 5 million tonnes of plastics. We believe that the future will belong to the composite of plastic and metal.

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Phototropic Glass

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Phototropic glass darkens on exposure to light and returns to its original state in the absence of light. The most extensively investigated of these glasses contain grains of silver halide having sizes > 50 Å. A discussion of theoretical principles is followed by a review of the very broad scope of the phenomenon.

1. Phototropy and Phototropic Materials

Phototropy is the reversible change between states having different absorptions that is induced by light (photons), or more generally by electromagnetic radiation. Photochromy is a special case of phototropy in which at least one of the states absorbs visible light.

Phototropy, as a photochemical phenomenon, obeys the Grothus-Draper law, *i.e.* only the light absorbed by the phototropic substance is effective. Under continuous exposure, the color changes until an equilibrium is reached between the forward and the reverse reactions.

Phototropy is reversible. When the light is switched off, the system returns to its original state:

$$\text{colorless} \underset{\text{absence of light}}{\overset{\text{exposure}}{\rightleftharpoons}} \text{colored}$$

The wavelength of the light causing a change in the light transmission and the rate at which the process takes place depend on the nature of the substance and on the temperature. A temperature rise displaces the absorption band to longer wavelengths. Higher temperatures also accelerate the regeneration reaction, which proceeds simultaneously with the color reaction and opposes the phototropic process.

Many inorganic compounds, of *e.g.*, mercury[1], copper[2], zinc, and chromium, molybdenum, and tungsten[3], exhibit phototropic behavior in the solid state or in solution. When the mineral sodalite $Na_8[Al_6Si_6O_{24}]Cl_2$ is exposed to X-rays it turns blue; the colorless state is regenerated on heating to 450 °C. (For reviews on organic and inorganic phototropic materials, see[4–7].)

Several authors have described inorganic glasses having phototropic properties. Phototropic glasses must not be confused with photosensitive glasses, in which irreversible images are produced as in photographic plates. Phototropic glasses are sometimes called "photochromic" in the American literature.

Cohen and *Smith*[8] studied the change in the transmission of sodium silicate glasses containing traces of europium.

A more comprehensive description of these processes in silicate glasses with variable transmissions is given by *Cohen*[9]. On exposure to light in the presence of titanium or iron, glasses containing cerium, europium, and other lanthanides exhibit color changes due to changes in valency. The variable transmission-absorption band in silicate glasses at 2.16 eV is attributed to the presence of traces of Ti^{3+} ions formed by reduction of Ti^{4+}. The required electron results from the photo-oxidation of Ce^{3+} or Eu^{2+}. This reaction is reversible.

Bishay and *Arafa*[10] observed a thermally reversible photochemical reaction in borate glasses containing arsenic or manganese on exposure to ^{60}Co radiation. *Sakka*[11] described the phototropy in alkaline earth metal tungstates sensitized with bismuth. *Stroud*[12] investigated the reversible formation of color centers in silicate glasses containing cerium.

Swarts and *Presseau*[13] reported the phototropy of reduced silicate glasses with a color center at 570 nm. Similar studies have been carried out by *Swarts* and *Cook*[14] on reduced silicate glasses containing iron. A phototropic effect has also been described for glasses containing germanium sulfide[15].

The first evidence of the existence of phototropic glasses of the type with which we are concerned here was obtained in 1964. *Stookey* and *Armistead*[16] described a borosilicate glass containing silver halides as phototropic components. The silver halides, which were present with a particle size of the order of > 50 Å and in a volume concentration of 500 ppm, decompose

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[1] *A. Murray*, US-Pat. 2503758 (1950); US-Pat. 2503759 (1950).

[2] *A. G. Gulko*, US-Pat. 3081699 (1953).

[3] *E. Lind*, German Pat. 1166795 (1964).

[4] *R. Exelby* and *R. Grinter*, Chem. Reviews *65*, 247 (1965).

[5] *G. Jackson*, Optica Acta *16*, 1 (1969).

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[7] *G.-H. Brown* and *W. G. Shaw*, Rev. pure appl. Chem. *11*, 2 (1961).

[8] *A. J. Cohen* and *H. L. Smith*, Science (Washington) *137*, 961 (1962).

[9] *A. J. Cohen*, C. R., VII[e] Congr. int. Verre, Bruxelles 1965, *1*, 111.

[10] *A. Bishay* and *S. Arafa*, Physics Chem. Glasses *6*, 134 (1965).

[11] *S. Sakka*, J. Amer. ceram. Soc. *52*, 69 (1969).

[12] *J. S. Stroud*, J. chem. Physics *37*, 836 (1962).

[13] *E. L. Swarts* and *J. P. Presseau*, J. Amer. ceram. Soc. *48*, 333 (1965).

[14] *E. L. Swarts* and *L. M. Cook*, C. R., VII[e] Congr. int. Verre, Bruxelles 1965, *1*, 23.

[15] *A. Forber* and *A. M. Reid*, Brit. Pat. 233932 (1961), Pilkington Brothers Ltd.

[16] *W. H. Armistead* and *S. D. Stookey*, Science (Washington) *144*, 150 (1964).

on exposure to light in the same way as in the photographic process. *Garfinkel*[28] has used an ion-exchange process to introduce light sensitive silver halides into the surface of glass.

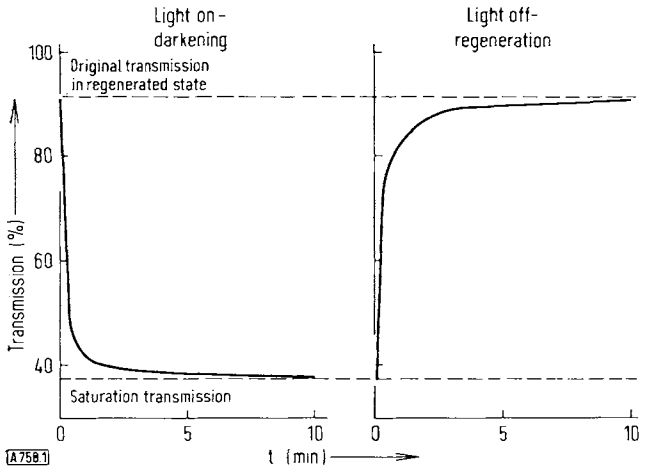


Fig. 1. Darkening and regeneration of a phototropic glass containing silver halides at 545 nm as a function of time (glass no. 7 in Table 1). Left: decrease in transmission during stimulation with xenon light (8000 lx); right: increase in transmission when the stimulation light is switched off. Temperature 20 °C, thickness 2 mm.

The phototropic process can be described with the aid of Figure 1, which shows the behavior of a phototropic glass as a function of time on constant illumination and after the stimulating light is switched off. The blackening process is shown on the left [*]. On exposure to light, the transmission decreases very rapidly to the saturation transmission value (*i.e.* the optical density or extinction or darkening increases). If the stimulating light is switched off after 10 min, the sample is regenerated, as shown on the right, until the original transmission of 92 % is restored.

2. Composition and Structure of Phototropic Silver Halide Glasses

The reversible darkening of pure silver halide crystals under the influence of stimulating radiation was described by *Pohl*[17] in 1938. *Armistead* and *Stookey*[16] discovered that the addition of silver salts and halides to a glass having melting temperatures between 1250 and 1450 °C gives a glass that has phototropic properties after subsequent heat treatment.

A wide range of phototropic glasses of various compositions based on silver halides have been reported since then, so that it is now hard to say what glasses *cannot* be made phototropic by addition of silver halides. The arbitrarily chosen list in Table 1 is based on the uses of the glasses, which impose different requirements as to transparency, chemical stability, melting behavior, and shaping. In glasses of this type, one can in general distinguish between the carriers of

[*] Unless otherwise specified, all experimental values in Tables and Figures refer to a glass thickness of 2 mm.

[17] *R. W. Pohl*, Physik. Z *39*, 36 (1938).

Table 1. Examples of the composition of phototropic glasses based on silver halides (values in wt-%).

	1	2	3	4	5	6	7
SiO_2	62.8	54.0	51.0	10.5	0.8	–	–
B_2O_3	15.9	16.0	19.5	30.3	46.5	54.0	55.0
Al_2O_7	10.0	9.1	6.8	14.9	22.3	22.8	8.0
Na_2O	10.0	3.0	1.7	–	3.5	5.1	–
K_2O	–	1.4	–	3.5	1.6	1.3	–
Li_2O	–	2.3	2.5	–	–	–	0.3
PbO	–	4.3	4.7	23.9	0.2	–	29.6
ZrO_2	–	1.9	4.6	3.2	2.2	–	–
BaO	–	6.6	8.0	1.0	1.7	–	2.0
MgO	–	–	–	8.1	7.7	14.9	2.0
P_2O_5	–	–	–	0.8	0.3	0.6	–
Ag_2O	0.41	0.27	0.65	0.5	0.26	0.3	0.55
Cl	1.7	0.5	0.69	1.2	2.6	0.2	0.4
Br	–	0.5	0.11	2.1	2.3	0.5	0.7
F	2.5	0.1	–	–	8.8	0.3	1.4
CuO	0.016	0.03	0.016	0.008	0.04	0.01	0.03
	103.326	100.00	100.266	100.008	100.80	100.01	99.98

the phototropy, *i.e.* the silver halide components, and the glass matrix, whose composition and thermal history also influences the phototropic properties during the segregation of the silver halide-rich phase, but merely acts as a "solvent" for these segregates in the final annealed glass.

The segregates, which are formed by heat treatment of the initially homogeneous glass, determine the phototropic properties of the glass. Views differ on the structure of the segregate regions; their size is normally between 50 and 300 Å.

Smith[18] found segregate regions of different sizes on examination of electron micrographs of fracture surfaces of transparent and translucent phototropic glasses. For particles having a diameter of 100 Å separated by an average distance of 600 Å, there are 4×10^{15} particles per cm^3. *Smith* was able to identify crystalline silver chloride by X-ray diffraction.

Bereznoj and *Il'cenko*[19] studied phototropic lithium silicate glasses with an excitation maximum at 430 nm. For a constant excitation time, they observed a darkening that was proportional to the previous heat treatment, *i.e.* to the size of the segregate regions. With constant heat treatment, so that all the segregate regions are of the same size, the darkening varies with the number of segregate regions. The silver halide-rich phase separates out between 560 and 600 °C in this particular glass; the authors refer to silver halide crystals.

Robredo[20] has described crystals having a diameter of 50 Å that are responsible for the phototropic effect. *Krauth* and *Oel*[55] found values of between 100 and 400 Å by electron microscopy for the diameter of the silver halide regions.

Hammel and *McGary*[21] published electron micrographs of carbon replicas of freshly fractured and variously etched glass surfaces. These micrographs of

[18] *G. P. Smith*, J. Mater. Sci. *2*, 139 (1967).

[19] *A. I. Bereznoj* and *L. N. Il'cenko*, Izvest. Akad. Nauk SSSR, Neorgan. Mater *4*, 584 (1968).

[20] *J. Robredo*, Bull. Soc. franç. Céram. *65*, 51 (1964).

[21] *J. J. Hammel* and *T. E. McGary* in *J. M. Mitchell et al.*: Reactivity of Solids. Wiley, New York 1969, p. 695.

relatively highly tempered glasses containing silver chloride show that the segregates grow from 100 to 1000 Å with increasing annealing time at a constant temperature. The volumes of segregates and their percentage contributions in samples that had received different tempering treatments were deduced from the line broadening in X-ray diffraction.

The same authors observed an endothermic effect during the segregation of the phototropic regions, this effect occurring between 419 and 456 °C for glasses that contain only silver chloride, and between 392 and 429 °C for glasses that contain only silver bromide.

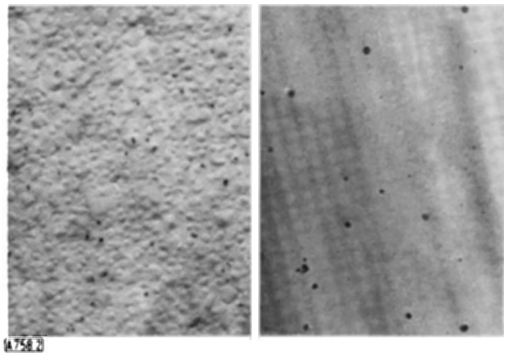


Fig. 2. Electron micrographs of phototropic glasses containing silver halide. Left: glass no. 2 in Table 1; annealed for 2 h at 610 °C, fracture surface etched for 60 sec in 2 % HF, carbon-platinum direct replica, magnification 12000×. Right: glass no. 7 in Table 1; annealed for 1 h at 570 °C, ion-etched, transmission photograph, magnification 48000×.

Figure 2 shows electron micrographs of phototropic glasses containing silver halides. Besides the phase separation in the glass itself, the silver halide-rich segregates (80–100 Å) are clearly recognizable owing to their silver content.

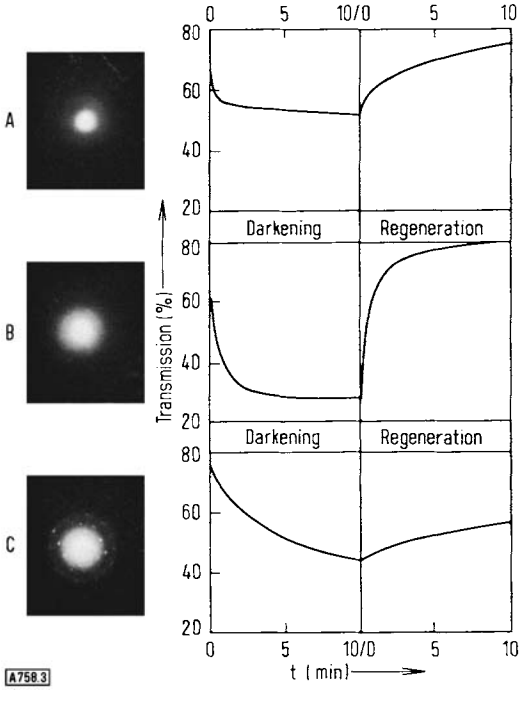


Fig. 3. Electron diffraction diagrams and kinetics of the phototropy of glass containing silver halide after different heat treatments. Glass no. 7 in Table 1. Sample A 40 min at 565 °C, sample B 180 min at 565 °C, sample C 900 min at 585 °C. Measurement of the phototropy at 545 nm and 20 °C during and after excitation with xenon light (8000 lx).

It can be shown in the case of glass no. 7 in Table 1 that the silver halide-rich segregates need not be macrocrystalline to ensure good phototropic properties in the glass. Electron diffraction diagrams for relatively large silver halide segregates and the darkening and regeneration behavior measured previously in the same samples are shown in Figure 3.

Electron diffraction diagram A, which shows no sign of a crystalline structure, but only weak diffractions due to the glass, is associated with medium darkening values and a medium regeneration rate. Tempering of this glass for a long time gives sample B, whose electron diffraction diagram again shows no clear sign of a crystalline structure. However, the phototropy is much better than in sample A. The saturation transmission is lower, *i.e.* the glass becomes darker for the same exposure, and it is regenerated much more rapidly. Sample C, whose electron diffraction diagram shows the first signs of a crystalline structure, is obtained when a glass of the same composition is tempered for a longer time and at a higher temperature. However, the phototropy is considerably poorer than in sample B.

Some of the processes involved in this thermal aftertreatment of the glass and the formation of the light-sensitive silver halide phase can also be deduced from the transmission curves.

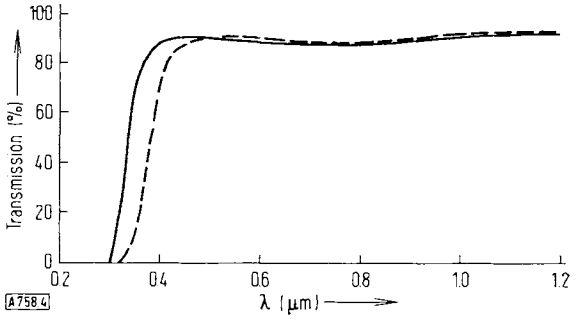


Fig. 4. Transmission curves of untempered glass containing silver halide (——) and of the same glass after tempering for 1 h at 603 °C (- - -) (glass no. 2 in Table 1).

Figure 4 shows a comparison of the transmission curve of the untempered non-photosensitive raw glass (glass no. 2 in Table 1) with that of the heat-treated phototropic final product. The raw glass has an absorption edge (50 % transmission) at 340 nm and an absorption maximum at 775 nm, which is responsible for the blue color of the glass and can be attributed to the Cu^{2+} ion.

After annealing, the color of the glass changes to green. The Cu^{2+} absorption at 775 nm remains unchanged, but the short-wave absorption edge is displaced by about 50 nm to longer wavelengths. This new absorption in the blue part of the visible region and the Cu^{2+} absorption in the red give the green color of the annealed glass. It is reasonable to suppose that the new absorption is due to the silver halide segregates formed during annealing of the glass.

Pure silver halide crystals are characterized by their UV absorption. The long-wave edge of the strong absorption of AgCl (measured for thin vacuum-deposited films at 293 °K) occurs at about 270 nm, and that of AgBr at 325 nm. Weak absorption tails extend far into the visible. The absorption is displaced to longer wavelengths with increasing particle size. The color of the AgBr itself shows a distinct change from white to yellowish with increasing grain size. The UV

absorption of the silver halides is explained by transitions of electrons from the valency band into the conduction band. Sharp bands superimposed on this absorption background can be attributed to exciton processes, in which the electron does not pass into the conduction band, but couples with a defect electron and migrates through the crystal lattice as an exciton.

In silver-free and halogen-free melts of the phototropic matrix glass, the absorption edge is not displaced by annealing, and the blue Cu^{2+} color accordingly persists on heat treatment. The same is true of a matrix glass containing silver and fluorine, of glasses that are free from bromine but contain silver and other halogens (F, Cl), and of phototropic glasses that do not contain silver. Glasses that contain all the components mentioned except chlorine, on the other hand, show the displacement of the absorption edge into the visible region, and the associated color change from blue to green, on annealing.

For a constant glass composition (*e.g.* glass no. 2 of Table 1), the position of the absorption edge depends on the annealing treatment. The edge is displaced to longer wavelengths with rising temperature and increasing annealing time. The same dependence is observed with increasing Ag(Br) concentration.

It thus appears to have been verified experimentally that no displacement of the absorption edge occurs without AgBr segregates in the phase separation during the heat treatment of the raw glass. The absorption of AgCl segregates lies in the region of the UV absorption of the glass itself, and so cannot influence the absorption edge and the color of the glass. The displacement of the absorption edge on heat treatment (annealing) can be explained by the increasing size of the segregate.

The detection of silver halide segregates in glass from the transmission curves agrees with the predictions based on electron microscope studies. According to *Armistead* and *Stookey* [16], *Smith* [22], and our own investigations, the segregates containing heavy metal can be detected in the electron micrographs only after heat treatment. If the silver halide segregates grow larger than 300 Å because of excessively high heat-treatment temperatures, they act as scattering centers (Rayleigh) for visible light. Phototropic glasses containing segregates larger than 2000 Å are distinctly cloudy.

In all phototropic glasses, in addition to the segregation of the silver halide-rich phase, phase separation is observed in the matrix glass. The silver halide segregates as a third phase. The fact that the segregation of the silver halide phase and the phase separation in the matrix glass often occur simultaneously may be attributed to the change in the solubility of the silver halides in the newly formed glass phases.

Evidence of this is provided by investigations by *Doremus* [23] on the diffusion of silver ions in a borosilicate glass with a tendency toward phase separation, the basic composition of which was very close to that of phototropic glasses. This glass consisted of a borosilicate phase containing about 95 % of the total sodium and a silicate phase containing 5 %. The measured diffusion rates show that the silver ions diffuse much more slowly in the silicate phase, *i.e.* they are bound more strongly in this phase. The solubility of the silver ions may therefore be assumed to be increased in this phase. The silver halide concentration is thus increased in this phase. A silver halide lattice that is strongly distorted by the components of the glass matrix can therefore be formed. The degree of microcrystalline order in the silver halide-richer phase cannot yet be stated precisely. The phototropic behavior of the light-sensitive segregates in the glass is described by most investigators in terms of models involving a more or less imperfect lattice.

It may be assumed that on slow segregation of these silver halide phases, not only does the size of the regions increase but the structure inside the segregation zones also changes on prolonged heating at high temperatures, after the manner of an aging process. It is not surprising, therefore, that signs of crystallinity are observed even in particles having a diameter of 1000 Å [21].

The compositions of the silver halide-rich segregation phases in two glasses are shown in Table 2. After annealing, the composition of the separated phase can be examined with the microprobe. The heat treatment in this case is such that the phase separation zones become much larger than 1000 Å. Whereas silver, the halogens, and the bivalent ions (mainly Ba^{2+}) are distinctly enriched, only components of the matrix glass that are also involved in phase separations in other glasses are found.

Table 2. Overall compositions of two glasses in wt-% and qualitative compositions of the segregated phases.

Sum (%)		Segregated phase	Sum (%)		Segregated phase
SiO_2	57	some SiO_2	B_2O_3	45	—
B_2O_3	15	—	PbO	30	some PbO
Al_2O_3	10	some Al_2O_3	Al_2O_3	15	—
RO	7	much RO	RO	5	much RO
PbO	4	—	R_2O	2	some R_2O
R_2O	5	—	ZrO_2	3	—
ZrO_2	2	—	Ag_2O	0.1	much Ag_2O
Ag_2O	0.1	much Ag_2O	halogens	0.2	much halogen
halogens	0.2	much halogen			

3. Models for the Kinetics of Phototropy

The phototropy of a glass is characterized by two properties of the material, *i.e.* the decrease in transmission (darkening) that can be achieved on exposure to light and the rate at which the glass lightens again on protection from light, *i.e.* the regeneration rate. The darkening on exposure is measured as the saturation transmission. This is the constant transmission value reached after the initial rapid decrease on prolonged exposure (cf. Fig. 1). Approximate values are used in practice to avoid excessively long measuring times.

A model has been developed by *Araujo* and *Stookey* [24] and by *Smith* [22] for the phototropic process. This model is capable of describing the darkening of phototropic glasses as a function of the light intensity. The rate of darkening, *i.e.* the change in the concentration of color carriers per unit time (dc/dt), is proportional to the intensity of the incident stimulating light I_d and to the number of light-sensitive silver halide centers A. While the glass is being darkened, the reverse reaction

[22] *G. P. Smith*, IEEE Spectrum *1965*, 39.

[23] *R. H. Doremus*, Physics Chem. Glasses *9*, 128 (1968).

[24] *R. J. Araujo* and *S. D. Stookey*, Glass Ind. *1967*, 687.

with formation of the silver halide is also taking place. This reverse reaction is proportional to the darkening c that has already occurred. Two effects must be distinguished in the reverse reaction; these are optical bleaching and thermal bleaching.

Pohl[17] described photochemical processes in silver halides and mentioned that light absorbed by the color centers, like elevated temperatures, has a regenerating action.

Optical bleaching is the removal of silver by absorption of visible light in the wavelength range 550–750 nm. The absorption of light quanta of this energy leads to the transfer of electrons from the silver into the conductivity band of the halide lattice. Optical bleaching may be compared to the Herschel effect in photography.

In the model proposed by *Araujo* and *Stookey*[24] and by *Smith*[22], the optical bleaching is also assumed to be proportional to the light intensity I_f in the above range of wavelengths. It is clear that the reverse reaction due to light absorption in the visible region increases with increasing darkening c. The absorption of this light is particularly effective in the fully exposed state, owing to the strong absorption band in this region. Thermal bleaching, *i.e.* the recombination of Ag and halogen to form the halide as a result of the thermal motion of the ions, electrons, and defect electrons, clearly plays an important part in deciding the equilibrium state, *i.e.* the saturation transmission. The overall darkening rate[24,22] is given by:

$$dc/dt = k_d I_d A - (k_f I_f + k_t) c \qquad (1)$$

where k_d, k_f, and k_t are the rate constants for darkening, optical bleaching, and thermal bleaching, respectively. In the equilibrium state, with $dc/dt = 0$, the saturation concentration c_s of the darkening silver centers (or the saturation transmission) is obtained from eq. (1)[22].

$$c_s = \frac{k_d I_d A}{k_f I_f + k_t} \qquad (2)$$

The values of the constants in the equation are determined by the structure, number, and size of the photosensitive silver halide regions.

For example, if the constant k_t for thermal bleaching tends toward zero, the color center concentration c_s in the equilibrium state becomes independent of the light intensity, since the ratio of stimulating light and optically bleaching light is constant. If the constant k_t is relatively large, on the other hand, it becomes rate-determining, and the color center concentration c_s is proportional to the stimulating intensity I_s (see Fig. 5).

The above model can be made to fit the experimental data by dividing the elementary phototropic process into surface or interfacial effects and volume effects.

A more advanced model has been proposed by *Araujo*[25], according to which the optical bleaching process

[25] *R. J. Araujo*, personal communication.

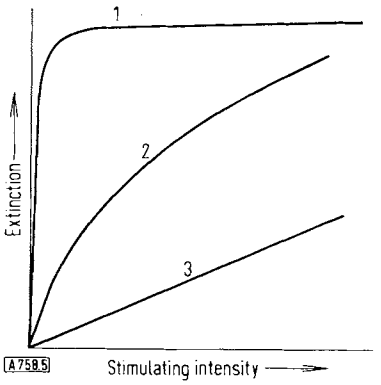


Fig. 5. Stimulating intensity *vs.* resulting darkening for glasses with different values of the constant k_t for thermal bleaching (schematic) after *Araujo* and *Stookey* [24].
Ordinate: Extinction reached in equilibrium state of saturation transmission.
1, very slow thermal bleaching, C_s = const.
2, phototropic glass $C_s = \frac{k_d I_d A}{k_f I_f k_t}$
3, very fast thermal bleaching, $C_s \approx I_s$.

can always be treated as a first order reaction. On the other hand, the thermal bleaching cannot be described by a simple first-order equation, and must be assumed to be of n-th order. In general, the rate constant k_t and the n-th order reaction can be attributed to a diffusion process. The dependence of the regeneration time on the exposure time as deduced from this model has been confirmed experimentally.

The time dependence of the transmission during recovery in the absence of light can be described surprisingly well by a simple diffusion model based on Tammann's rule for the growth of surface layers. Apart from the first increase (decrease) in the extinction on illumination (recovery), which is apparently determined by electronic processes[26], the time dependence of the extinction can be expressed in the form of straight lines as $\varepsilon = f(\ln t)$. According to this model[27], the time dependence of the recovery rate is explained by the increasing length of the diffusion paths of the silver atoms and ions. The small silver particles that are present after prolonged recovery recombine more slowly than the large silver regions that are still present shortly after screening from the light. The diffusion of the silver appears to be of great importance to the models discussed here. Since there is little diffusion of the halogen atoms and halide ions in the silver halide lattice, owing to their size, the key to the factor controlling the regeneration rate lies in the formation of a halide lattice that promotes the diffusion of silver.

The diffusion of silver in silver halide occurs mainly *via* Frenkel defects, *i.e. via* interstitial sites and lattice holes. Self-diffusion *via* interstitial silver ions predominates above 150 °C, and diffusion by means of holes in the silver lattice below this temperature. The number of holes is strongly dependent on doping with foreign materials.

[26] *G. Gliemeroth*, Int. Commission on Glass, Annual Meeting, Toronto 1969.
[27] *K. H. Mader*, unpublished.
[28] *H. M. Garfinkel*, App. Optics 7, 789 (1968).

An insight into the electronic process in the darkening can be gained by experiments in the microsecond range.

Figure 6 shows an arrangement for measurements with a powerful flashlight (1), which emits a measuring beam (2) and a reference beam (3). These beams proceed to the photodiodes (8) and (9) respectively. Photons reaching the photodiodes give the same optical signal when the samples (4 and 5) are alike. At the start of the experiment these samples consist of non-phototropic glass. The electrical signal from the photodiodes passes to a twin-beam oscillograph. Figure 7a shows a calibration plot with ordinary window glass in both beams. Both photodiodes, and hence both channels of the oscillograph, receive the same signal, and both curves coincide.

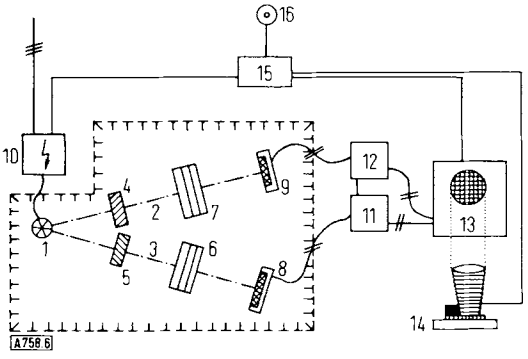


Fig. 6. Measuring arrangement for the determination of the intensity-time behavior of phototropic glass. 1. Flash tube, 2. measuring beam, 3. reference beam, 4. phototropic sample, 5. reference sample (window sheet glass), 6. + 7. filter system. 8. + 9. photodiodes. 10. high-tension unit. 11. + 12. adjusting systems. 13. oscillograph. 14. camera, 15. trigger system, 16. initiator for flash. The unit indicated (1 and 4—9) is thermostated.

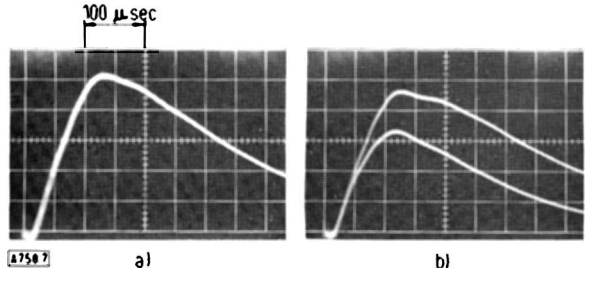


Fig. 7. Intensity-time diagram (photograph of the oscillograph screen) of the darkening at 545 nm of a glass containing silver halides under the action of a flash. a) Calibration measurement: window glass is placed in both beams, and the traces of the two oscillograph channels coincide. b) Glass no. 5 in Table 1 is placed in the measuring beam, and window glass in the reference beam.

Figure 7b shows the intensity-time diagram with a phototropic glass in the measuring beam and non-phototropic material in the reference beam. The light intensity passing through the phototropic glass per unit time decreases in proportion to the darkening effect in the phototropic glass.

If zero time is taken to be the moment when the intensity curve of the reference beam shows its first ascent, the intensity curve of the reference beam corresponds to the photon energy falling on the phototropic glass at any instant. The intensity of the light after passage through the phototropic glass is shown by the lower curve. It is thus possible by this twin-beam method to obtain comparable values even when the energy of the flash unit varies slightly. The difference between the two curves is the light energy absorbed by the phototropic glass.

Figure 8 shows the darkening intensity time functions for four phototropic glasses. Comparison of this darkening behavior in the short time range with the long-time plots for the same glasses (Fig. 9) shows that the rates of darkening of glasses a and b, which have the lowest saturation transmission in Figure 9, do not agree. This discrepancy can be explained by assuming that in the short-time experiments, the diffusion component of the rate constant k_t is of no importance at least in the part evaluated.

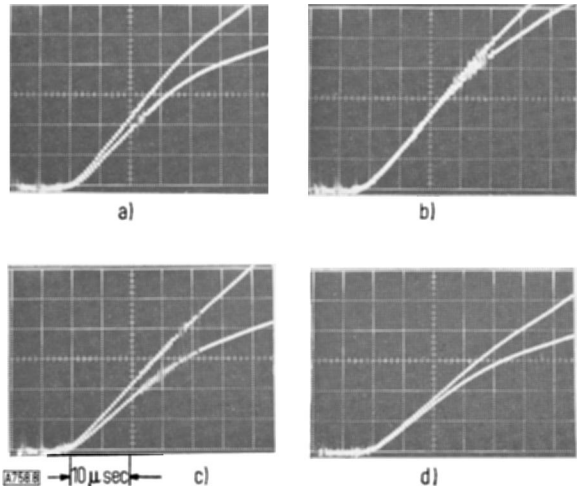


Fig. 8. Intensity-time diagram (photograph of the oscillograph screen) of the darkening at 545 nm of four phototropic glasses under the action of a flash at 20 °C. Horizontal scale 5 µs cm^{-1}. a) Glass 53—01—1989; b) glass 53-01-0491: c) glass 9416; d) glass C 16/4.

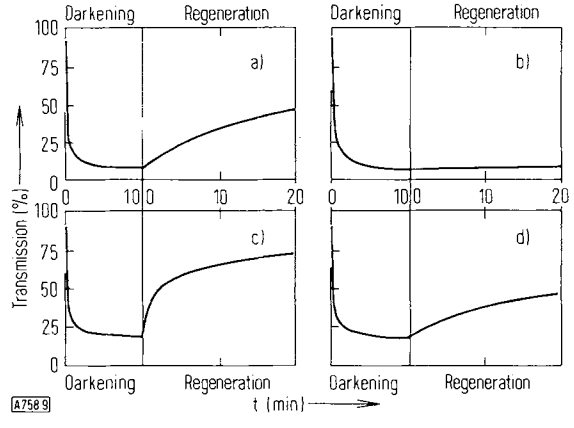


Fig. 9. Darkening and regeneration of phototropic glasses containing silver halides at 545 nm as a function of time on stimulation for 10 min with xenon light (8000 lx) and subsequent regeneration. Temperature 20 °C. For a—d see caption to Fig. 8.

It is only the rate constant k_t that causes any deviation from the reciprocity law governing the response of a photographic emulsion. According to this law, a constant density is obtained if the product of the time and the intensity is constant.

According to *Megla*[29] the rate constant k_t, *i.e.* the rate constant for thermal bleaching of phototropic

[29] *G. K. Megla*, Appl. Optics *5*, 945 (1966).

glasses, influences the darkening effect because the change in the optical density ΔD during the exposure can be described, not by a simple function

$$\Delta D = f(I \times t) \quad (3)$$

but by the equation

$$\Delta D = f(I \times t^p) \quad (4)$$

During the darkening process, the exponent p is smaller than 1; the thermal bleaching retards the increase in the optical density. On bleaching of the phototropic glass, p becomes greater than 1, since the thermal bleaching now accelerates the decrease in the optical density. Since the exponent, which represents the influence of the rate constant k_t on the thermal bleaching, is diffusion-controlled, it must be temperature-dependent.

4. Temperature Dependence

The temperature dependence, which results from that of the rate constant, is found in all the individual processes of the phototropic effect. The relationship between the saturation transmission and the temperature is particularly clear.

Strong darkening can be achieved at low temperatures, and the recovery is extremely slow. The recovery is strongly accelerated with rising temperature, and the saturation transmission at equilibrium simultaneously decreases. Most phototropic glasses no longer react above 80 °C.

Energy considerations connected with the fundamental photographic process (*Bodenstein* – silver seed theory 1941) showed that 30 to 60 kcal/mole would be required for the formation of atomic silver in the photodecomposition of silver bromide. On the other hand, the formation of crystalline silver aggregates on crystallization centers inside the silver bromide should be exothermic to the extent of 2 kcals/mole. This agrees qualitatively with thermodynamic data based on electrochemical measurements on the system Ag/Ag halide [30].

The exothermic character of the photolysis in phototropic glass is in agreement with the model of crystalline silver segregates. Activation energies of −2 to −10 kcal/mole are found by measurements between 0 and 80 °C. The strong temperature dependence (Fig. 10) of the phototropic process in glass is partly due to the decrease in the mobility of the silver ions and the decrease in the lattice vibrations.

A very important fact is that owing to the reduced thermal motion in the lattice, shallow energy troughs become active, and the finite probability of finding charge carriers in these troughs at normal temperature is very small. The time spent by the electrons and

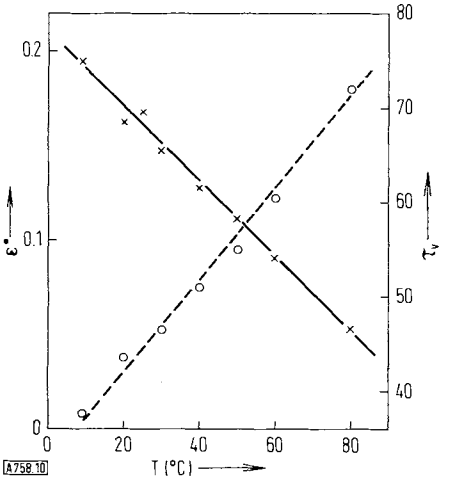


Fig. 10. Temperature dependence of the extinction ε^* and of the transmission τ_V of glass no. 2 in Table 1 at 545 nm. The experimental points were determined by stimulation with xenon light (8000 lx) until the saturation transmission was reached.

defect electrons in sites with shallow energy troughs generally increases with falling temperature. The higher photon yield measured at low temperatures contrasts with the reduced mobility of the interstitial silver ions Ag_i^+. The greater saturation absorption must therefore be explained by the greater probability of finding the electrons in deep energy troughs. Thus if the decrease in the rate of diffusion of the silver ions in the interstitial sites with falling temperature is faster than the increase in the time spent by the electrons in low-energy sites, the reaction between the electrons and the interstitial silver ions to form silver atoms is favored, while the recombination with defect electrons (*e.g.* in bromine atoms) is repressed. This factor is active in the pronounced retardation of the recovery process at low temperatures. These considerations are arguments from analogy that follow from experimental and theoretical studies on the fundamental photographic process.

5. The Phototropic Reaction

The process that occurs on exposure of a phototropic glass to light can be represented schematically, on the basis of the photosensitivity of silver halides, by the following equations:

$$Br^-(Cl^-) + h\nu \rightarrow Br^0(Cl^0) + e \quad (5)$$

$$Ag^+ + e \rightarrow Ag^0 \quad (6)$$

$$Cu^{2+} + e \rightarrow Cu^+ \quad (7)$$

$$Cu^+ + Ag^+ \rightarrow Ag^0 + Cu^{2+} \quad (8)$$

$$Cu^+ + Br^0 \rightarrow Cu^{2+} + Br^-$$

$$Ag^0 \rightarrow Ag^{\square} \quad (9)$$

Unexposed phototropic glass has a slight greenish color. This disappears on exposure to light, the im-

[30] *K. Meinig, G. Metz,* and *J. Teltow,* Physica Status solidi (Berlin) *2,* 1556 (1962).

[31] *J. Eggers, G. Haase,* and *R. Matejec*: Grundlagen der photographischen Processe mit Silberhalogeniden. Akad. Verlagsges., Frankfurt/M. 1968.

pression of color then being due to the silver segregates formed on decomposition of the light-sensitive silver halide segregates. The number and size of the silver segregates depends *inter alia* on the number, size, and structure of the silver halide segregates.

Silver atoms Ag^0 are deposited in accordance with equations (6) and (8), and grow together at the outer and inner grain boundaries of the halide phase to form larger aggregates, probably microcrystalline Ag□ [eq. (9)].

Figure 11 shows the transmission curves of an annealed phototropic glass (glass no. 2 in Table 1) in the unexposed and in the exposed state. The minima in the transmission curves at 1.45, 2.2 and 2.8 μm are bands due to the OH content of the glass, and are independent of the state of exposure of the phototropic glass. The broad absorption at 0.75 μm is due to the Cu^{2+} ion. It seems reasonable to attribute the strong absorption band with a maximum at 0.58 μm to the silver formed on exposure to light. Clear parallels would thus exist with the elementary photographic process, which has already been studied in detail.

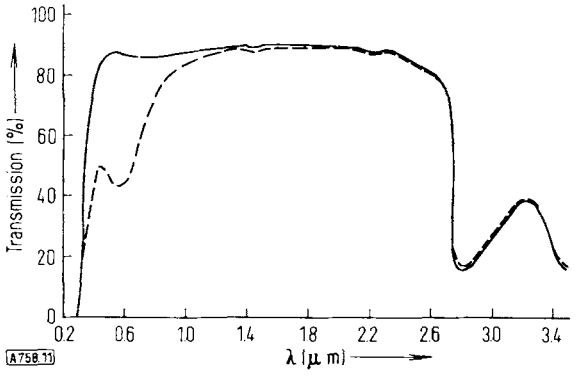


Fig. 11. Spectral transmission distribution for phototropic glass containing silver halide in the unexposed state (——) and after excitation for 20 min with xenon light (8000 lx) (- - -). Glass no. 2 in Table 1, temperature 20 °C.

6. Darkening Effect and Color in the Exposed State

In the photochemical decomposition of pure AgBr, *Hilsch* and *Pohl*[32] showed that exposure to light in the long-wave tails of the AgBr absorption leads to the development of a colloidal silver absorption band with a maximum between 0.6 and 0.8 μm. On the basis of *Rayleigh*'s views, *Mie*[33] calculated the dependence of the position of the maximum on the size of the colloidal silver particles for spherical silver particles in water.

Löhle[34] studied the shape and position of the absorption bands of silver colloids in AgCl crystals. With increasing exposure, the maxima become more intense and migrate from 520 toward 570 nm. Calculations and experiments on colloidal silver particles in gelatin and water have been reported by *Klein* and *Metz*[35]. The absorption curves calculated for the silver particles on the basis of *Mie*'s theory exhibit satisfactory agreement with the experimental curves. The absorption maxima are found to move to longer wavelengths with increasing particle size. Since the size of the silver particles is in the region of the wavelength of visible light, the colloidal "solutions" appear to be colored. On photolytic decomposition of silver compounds in gelatin, the color of the silver changes from yellow through red to blue with increasing particle size.

The silver formed on exposure of photographic layers to light is also colloidal, and exhibits absorptions that are proportional to the particle size between 600 and 800 nm.

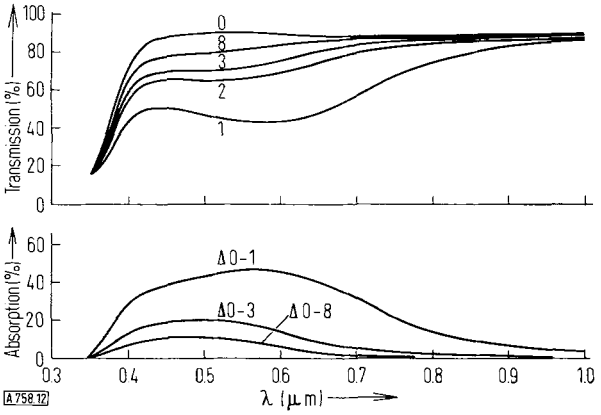


Fig. 12. Transmission curves of glass no. 2 in Table 1 for the excitation states 0 to 8 (top) and the absorption curves found from these by substraction (bottom), temperature 20 °C.

The above results cannot be freely applied to silver in phototropic glass, partly because the optical constants are different; nevertheless, substantial qualitative agreement is found. Figure 12 shows the transmission curves of a phototropic glass in the unexposed and in the exposed state. Subtraction of two curves gives the absorption curve (Δ curve) of the colloidal silver particles formed on exposure. The strong broadening of the absorption bands of the colloidal silver can be explained by the presence of a particle size distribution. As the glass becomes lighter again, the transmission minimum is displaced to shorter wavelengths and the extinction decreases. The color of the glass shown in Figure 12 changes from blue to red. As the glass becomes lighter, the size of the silver particles that have segregated in the glass must clearly decrease as a result of diffusion and recombination with halogen. The maximum of the size distribution moves toward smaller particles, and the integral absorption simultaneously decreases.

If the dependence on particle size found for colloidal silver in gelatin (refractive index $n_D = 1.5$) is assumed to be valid also for the silver particles in glass ($n_D = 1.523$), it can be estimated from the displacement of the absorption maxima on exposure to light and on recovery that the silver particles that separate out have a diameter of 40 to 100 Å. This roughly corresponds to the size of the silver halide regions as found from the electron micrographs. The requirements for quantitative agreement are not satisfied. Moreover, *Mie*'s theories and the absorption curves calculated from them are strictly valid only for spherical particles of uniform size, whereas we must expect a wide particle size distribution in phototropic glass.

[32] *R. Hilsch* and *R. W. Pohl*, Z. wiss. Photogr., Photophysik Photochem. *30*, 255 (1931).

[33] *G. Mie*, Ann. Physique *25*, 377 (1908).

[34] *F. Löhle*, Nachr. Ges. Wiss. Göttingen, math.-physik. Kl. *1933*, 271.

[35] *E. Klein* and *H. J. Mez*: Mitteilungen aus dem Forschungslabor Agfa. Springer, Berlin 1955, Vol. III.

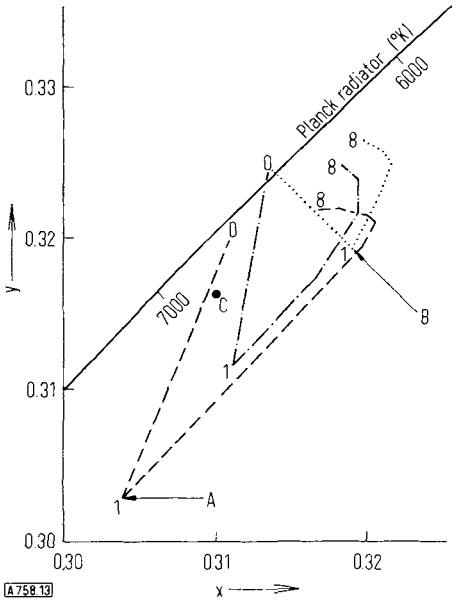


Fig. 13. Color shifts of a phototropic glass containing silver halide in the color chart representation in accordance with the German standard DIN 5033. Color in the unexposed state = 0, color at saturation transmission after exposure to xenon light (8000 lx) = 1. The differently shaded curves denote products obtained by various tempering treatments of glass no. 2 in Table 1. The numbers refer to the transmission curves of Fig. 12. For A, B and C, see text.

Figure 13 shows the color shifts occurring in phototropic glasses directly in a color chart representation in accordance with the German standard DIN 5033. The colors of the glasses are fixed by the x and y coordinates. The greater the change in the color of a glass during the darkening and recovery processes, the longer are the curves described in the color chart.

The colors of the unexposed phototropic glasses all lie in the white region of the color chart. The greatest color change occurs on exposure to light (curve segments 0-1); the glass moves away from the curve for the black body (Planck radiator). Depending on the size of the silver particles formed on exposure to light, the color changes *e.g.* toward blue (curve A) or purple (curve B). During regeneration, all colors move toward red (see curve segments 1–8). The visual transmission $\tau_{v,C}$, based on the nature of the light C, must be imagined to be plotted on the z axis above the plane of the paper. Between 0 and 1, the glasses are situated on the descending part of the curve in Figure 1 (exposure). The color (x and y coordinates) and the transmission (z coordinate) of the segment (1–8) correspond to the regeneration part of the curve in Figure 1.

It can also be seen from Figure 13 that the recovery is always associated with a color shift toward red. The magnitude of the shift increases with increasing blueness of the glass on full exposure. As was mentioned earlier, this behavior can be readily explained by the size of the colloidal silver particles that separate.

7. Wavelength of the Stimulating Radiation

The darkening of a glass is caused by a stimulating radiation. *Armistead* and *Stookey*[16] have published curves showing the relationship between the wavelengths that stimulate the darkening and the sensitivity of the glass. The theoretical excitation limits are about 390 nm for glasses containing silver chloride 500 nm for glasses containing silver bromide and silver chloride, and 580 nm for glasses containing silver chloride and silver iodide. Identical curves were published by *Araujo* and *Stookey*[24] and by *Justice* and *Leibold*[36]. However, all these curves appear to have been extrapolated from the properties of the pure crystalline silver halides.

Smith[18] published curves for the spectral sensitivity of the activation of glasses having different compositions. The glasses gave excitation maxima at 340 and 400 nm.

The light-sensitivity of the phototropic glass no. 2 of Table 1 with a high AgBr content is shown in Figure 14. The maximum darkening is obtained with stimulating light having a wavelength of 360 nm. With increasing transmission of the glass, the light-sensitivity falls off toward longer wavelengths.

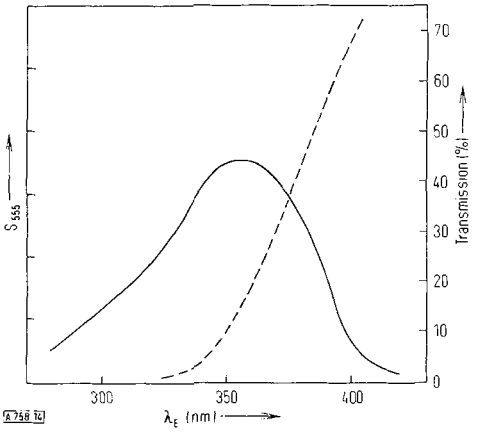


Fig. 14. Spectral position of the excitation maximum (——), determined by the darkening S_{555} at 555 nm resulting from excitation with the wavelengths λ_E, and position of the absorption edge (- - -) of phototropic glass no. 2 in Table 1, temperature 20 °C.

The position of the excitation maxima depends not only on the size and structure, but also on the composition of the silver halide-rich phase, and in fact only on its halide content; it appears to be independent of the type of matrix glass and of the phases that separate out from the matrix glass. Thus by choosing the halides used in the synthesis of the glass, it is possible to produce phototropic glasses with different excitation sensitivities in the short-wave visible and ultraviolet region of the spectrum.

The absorption by pure AgBr and AgCl extends far into the visible region; however, the absorption edge is smaller than 0.01 mm^{-1} above 400 nm at about 25 °C and at silver halide concentrations of less than 1 %. If the silver ions in the silver halide segregates in the phototropic glass are partly replaced by alkali metal, Cd^{2+}, or Pb^{2+} ions, the already low absorption in the long-wave region is displaced further toward shorter wavelengths[30]. Doping of the silver halide

[36] *B. Justice* and *F. B. Leibold*, Information Display, Nov./Dec. 1965, 23.

segregates formed in phototropic glass with components of the glass matrix (alkali metal, lead) is also very probable from what was said above. The reason for the shift of the absorption tails to shorter wavelengths lies in the increased energy difference between the valence band and the conduction band. The optical energy required for the transition from the valence band to the conducting band increases with the concentration of foreign substances in the silver halide lattice.

The fall-off of the darkening curve toward shorter wavelengths is not to be expected in this region because of the strong silver halide absorption. The reduced photosensitivity at wavelengths below 350 nm is due to absorption by the matrix glass itself. In addition to the light-sensitivity, Figure 14 shows the transmission of the phototropic glass as a function of the wavelength. The transmission is only 1 % at 325 nm, and at 290 nm it is less than 0.001 %. Since radiation from the sun begins only at 300 nm, the absorption region below 325 nm is of no interest *e.g.* for the use of phototropic glass in spectacles. Phototropic glasses can be stimulated by high-energy radiation of short wavelength. However, this excitation (X rays, electrons) is usually associated with more or less irreversible disturbance of the phototropic process.

The darkening produced at a constant light intensity also varies from glass to glass under otherwise identical conditions. This agrees with the observation [37] that the darkening in pure and doped silver halide crystals is also a function of the crystallite size, the degree of imperfection, and the concentration of foreign substances [38, 39].

Application of these ideas to the silver halide-rich segregates in phototropic glass provides a simple explanation of the fact that entirely different phototropic glasses can be obtained from the same matrix glass by different tempering. Short tempering times lead to segregates having high degrees of imperfection and high doping levels. Longer tempering times give silver halide segregates with better structures, but these have lower photosensitivities, *i.e.* poorer photon yields. Experiments have shown that for approximately equal crystallite sizes, the saturation transmission attainable on full exposure is strongly dependent on the degree of imperfection and the related doping of the silver halide phase with foreign substances.

8. Intensity of the Stimulating Radiation

Araujo and *Stookey* [24] described the influence of the intensity of the stimulating radiation on the darkening behavior of a phototropic glass. For an excitation wavelength of 400 nm, the intensity was between 10^{-3} and 10^{-5} W/cm². With a glass thickness of 6 mm and the highest intensity of 10^{-3} W/cm², they obtained an optical density of 1.5. Our own investigations have given an optical density of 1.7 at 20 °C with the same excitation intensity and wavelength for other glasses with a thickness of only 2 mm.

The dependence of the saturation transmission on the intensity of the stimulating radiation for a constant spectral composition is shown in Figure 15. The darkening process in a phototropic glass having given composition and structure ends with an equilibrium state that depends, for a constant number of possible color centers, on the number of photons that allow the darkening, as well as on the regeneration rate and the temperature.

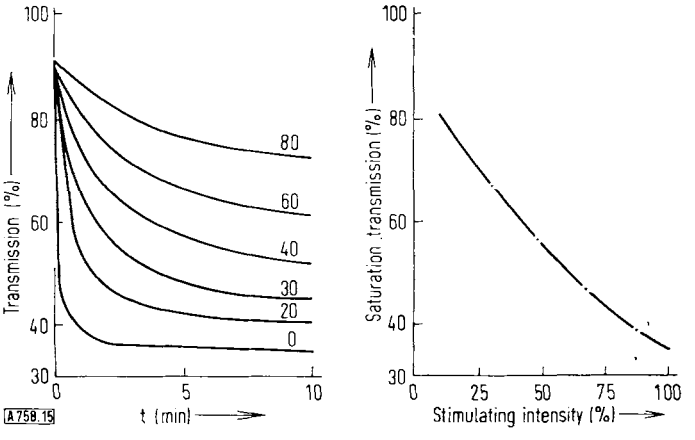


Fig. 15. Dependence of the darkening of a phototropic glass containing silver halide (glass no. 7 in Table 1) on the excitation intensity.
Left: decrease in transmission at 545 nm with time. The stimulation intensity of the xenon lamp (8000 lx) is reduced by rotating sector diaphragms. (The numbers by the curves denote the decrease, in %). Right: dependence of the equilibria of the saturation transmission on intensity, temperature 20 °C.

Figure 15 shows, on the left, the darkening behavior of a phototropic glass as the stimulating beam is stopped down (weakened). The numbers against the curves are the percentage decreases in the intensity of the stimulating light. It can be seen in the right-hand part of the figure that the darkening of a glass decreases with decreasing photon supply. As the number of photons falling on the glass decreases, the time taken to reach equilibrium between darkening and regeneration, *i.e.* the saturation transmission, becomes steadily longer.

Megla [29] determined the energy density of the light of optimum wavelength used. The results show that depending on the nature of the phototropic glass, 4 to 25 times as many photons are required for the bleaching of a previously exposed glass as for the darkening of an unexposed glass. Thus the glasses investigated by *Megla* are not sensitive enough for use *e.g.* as photographic materials in cameras.

A conventional photographic film is more than five times as sensitive as the phototropic glasses currently being produced. Further work is being aimed at much higher sensitivities, approaching the values for photographic films.

[37] *F. Moser, N. R. Nail,* and *F. Urbach,* J. Physics Chem. Solids *9*, 217 (1959).

[38] *J. E. LuValle,* Photogr. Sci. Engng. *8*, 229 (1964).

[39] *G. Kuwabara* and *K. Aoyagi,* Jap. J. appl. Physics, Suppl. 11, I, *4*, 627 (1965).

9. Sensitization of the Stimulation

A few investigations have been carried out on the possibility of sensitizing phototropic glasses. All attempts have been based on concepts regarding the silver halide lattice that have been obtained for pure silver halide crystals or for photographic emulsions [31,38,39]. *Fanderlik* [40], for example, studied the possibility of improving phototropic glasses containing only silver chloride by addition of small quantities of Ag_2S.

In silver halide crystals, disorder involving lattice vacancies and interstitial ions predominates [31]. This Frenkel disorder is confined to the silver part of the lattice ($Ag_{\ddot{o}}$ and $Ag_{\ddot{\square}}$), owing to the size of the halide ions. The imperfection concentration can be strongly influenced by the incorporation of bivalent ions having approximately the same ionic radius. Each bivalent ion incorporated into the silver halide lattice replaces two silver ions, *i.e.* in addition to the foreign ion in a silver lattice site ($Ag^{+}_{\square}$), a silver ion vacancy ($Ag_{\ddot{\square}}$) is also produced to maintain electroneutrality; at the same time, the number of silver atoms in interstitial sites ($Ag_{\ddot{o}}$) decreases.

Table 3. Ionic radii after *L. Pauling* (in Å).

Ag^+	1.26	Cd^{2+}	0.97
Cu^+	0.96	Pb^{2+}	1.21
Li^+	0.60	Ba^{2+}	1.35
Na^+	0.95	F^-	1.36
K^+	1.33	Cl^-	1.81
Ca^{2+}	0.99	Br^-	1.95

These considerations are valid in particular for the incorporation of Ca^{2+} and Cd^{2+} ions into the silver halide lattice, since the ionic radii of these ions favor their incorporation into the silver halide (Table 3). The compositions of the phototropic glasses (Table 1) should also be considered from this point of view. Monovalent foreign ions that replace the silver ions in the lattice ($Ag^{+}_{\square}$) do not displace the imperfection equilibria so much, since they do not introduce any excess charge into the host lattice.

An exception is the Cu^+ ion, which acts as a bivalent ion, and can occupy interstitial sites as well as silver lattice sites. These Cu^+ ions increase the photochemical sensitivity of the silver halide crystals, the increase in sensitivity, at least for low doping levels, being proportional to the Cu^+ concentration [37]. The Cu^+ ions reduce the defect electrons formed on exposure of the Cu^+-doped silver halide to light, and so prevent the reverse reaction of the silver with the halogen [*e.g.* in accordance with eq. (8)]. The resulting additional absorption in the long-wave absorption tails of the silver halides, on the other hand, appears to be less important. The Cu^{2+} ions formed by the capture of defect electrons revert to Cu^+ in the dark as a result of a "fading" process, the rate of which depends on the volume. It is not impossible that the reaction in accordance with eq. (7), *i.e.* the capture of electrons by the Cu^{2+}, explains the rapid bleaching of the absorption at 750 nm on exposure to light. The recovery of the phototropic glass in the dark leads back to the Cu^{2+} ion. The fading mentioned above appears to play only a minor part in the process as a whole. More detailed studies are still in progress.

The Cu^+ ions present in the glass as a result of the equilibrium between Cu^+ and Cu^{2+} must, however, be regarded as a necessary sensitizer for the phototropic process.

An observation corresponding to these discussions that can be used for the sensitization of phototropic glasses has been reported by *Belous* and *Ilmas* [41]. These authors observed a photoamplification effect in silver halide crystals and verified it with the aid of luminescence spectra.

10. Use of Phototropic Glasses

The phototropic effect in glass was first used ophthalmologically in spectacle glass that can vary its transmission for visible light in proportion to the sunlight falling on it [42,43]. The UV absorption of the matrix glass is particularly beneficial in this application, since it ensures that even when the thickness of the glass varies (correcting lenses), stimulation, and hence darkening, occurs mainly in a layer near the surface [44]. The darkening is therefore very uniform over the whole lens. Work in this field is being concentrated mainly on the color in the exposed state and the kinetics of the spectacle lenses [43,45].

Several studies have been carried out on the use of phototropic glasses in conjunction with lasers, which has led *inter alia* to the q switch [46]. In the improvement proposed by *Bojko* [47], the laser substance and the phototropic glass are in direct optical contact; this reduces disturbing reflections.

Another field of application is in image conversion [48,49], where *e.g.* UV light is passed through negatives. The UV light darkens a phototropic glass plate in accordance with the densities in the negative, and the image produced in the phototropic glass in this way can be read by means of an auxiliary light source.

The use of phototropic materials having an inorganic basis in holography and electrical engineering has been described by *Kiss* [50]. *Blue* and *Chen* [51] mentioned the use of phototropic glass for holography and in electronic data processing.

[40] *I. Fanderlik*, 8th International Glass Congress, London 1968.

[41] *V. M. Belous* and *E. R. Ilmas*, Z. prikl. Spektroskopii *9*, 698 (1968).

[42] *S. D. Stookey*, US-Pat. 3252374 (1962), Corning Glass Works.

[43] *G. Gliemeroth*, French Pat. 1538675 (1966), Jenaer Glaswerk Schott & Gen.

[44] *S. Gelius*, Augenspiegel *1968*, 136.

[45] *G. Gliemeroth*, DAS 1284588 (1967), Jenaer Glaswerk Schott & Gen.

[46] *R. D. Maurer*, US-Pat. 3365678 (1964), Corning Glass Works.

[47] *B. B. Bojko*, *N. S. Petrov*, *V. V. Valjavko*, and *I. M. Vaskevic*, Z. prikl. Spektroskopii *6*, 36 (1967).

[48] *G. P. Smith*, C. R., VII^e Congr. int. Verre, Bruxelles 1965, *1*, 108.

[49] *H. Winter*, German Pat. 1212746 (1964), Batelle-Institut eV, Frankfurt/M.

[50] *Z. J. Kiss*, Physics Today *1970*, 42.

[51] *M. D. Blue* and *D. Chen*, Electronics *42*, 108 (1969).

The phototropic properties of the glasses must be modified for this purpose[52].

A phototropic glass for use in holography[29,51,52] must have a high resolution. All phototropic glasses are better in this respect than the best photographic layer, which is tied to the photographic grain. A high writing rate (at least 10^6 bits/s) is required, and the hologram must exhibit good stability over long periods[29]; this requirement is linked with the regeneration time and the activation energy for regeneration[26]. Extinction must also be possible; lasers operating in the near IR region or heat may be used for this purpose[36]. *Baldwin*[53] has published information on the determination of the storage capacity of phototropic glasses for holography.

The use of a conducting film for accelerated regeneration, which is essential for holographic applications, has been described by *Justice* and *Leibold*[36]. The specimens are coated on both sides with a transparent, electrically conducting film of stannic oxide. The applied voltage was 120 V, and the power was approximately 48 W. Specimens with a half life of 500 s were completely regenerated in less than 10 s on application of the electric field.

The use of phototropic glasses in micrography has been described by *DeKing*[54].

Other applications are instrument panels that are controlled by computers and which write the data in the phototropic glass with UV beams[22]. Automobile windshields, window glass, *etc.* have been considered as a potential application of phototropic glass.

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[55] *A. Krauth* and *H. Oel*, Glastechn. Ber. *42*, 139 (1969).

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Ion-Selective Sensors

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Numerous advances have recently been made in the development of ion-selective (glass, solid, liquid) membrane electrode systems. The theoretical principles and practical requirements of such "sensors" are outlined in this article, and an attempt is made to review their possible applications.

1. Introduction

A number of reviews have been published on the selective detection of ions in aqueous and nonaqueous solutions by electrode systems[1–14,220,221,256]. The present position in this field is described below, with special emphasis on the discussion of various sensor systems. The associated membrane phenomena have already been discussed in detail in several publications[2,15–18,220–224].

The sensors to be considered here can be divided into three basic groups, according to the type of membrane:

1. glass membrane
2. solid-state membrane: a. homogeneous solid-state membrane
   b. heterogeneous solid-state membrane
3. liquid membrane: a. electrically charged ligand groups (ion exchangers) as membrane components

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[15] *G. Eisenman*, Analytic. Chem. *40*, 310 (1968).

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[18] *R. P. Buck*, Analytic. Chem. *40*, 1432, 1439 (1968).

b. electrically neutral ligand groups as membrane components.

Figure 1 shows a diagram of a cell assembly for the detection of ions. The membrane, which responds selectively to ions, is normally combined in a unit with the internal filling solution and inner reference electrode (internal reference electrode). Such "sensors" are illustrated in Figure 2 for the membrane types mentioned.

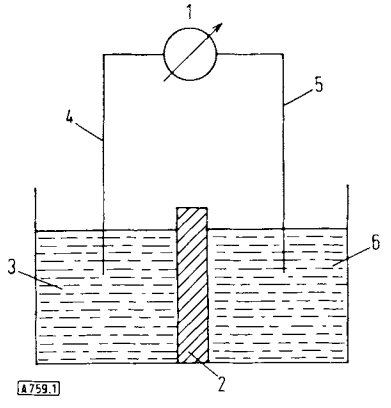


Fig. 1. Membrane electrode cell assembly (schematic).
1: EMF; 2: membrane; 3: internal filling solution; 4: inner reference electrode; 5: reference electrode (external); 6: solution to be measured.

Both the inner solution and the inner reference electrode may in principle be replaced by a direct electrical connection to the corresponding side of the membrane [19–21]. Such systems may occasionally be advantageous for membrane electrodes of types 2 and 3, but are not recommended for glass electrodes in view of the choice of the electrical zero of the cell assembly and the choice of the isopotential pH (intersection of isotherms) [19, 22, 23].

In the glass electrode (Fig. 2A), the ion-selective membrane is usually fused to an inert glass stem, while in solid-state membrane electrodes it is usually cemented to an inert membrane shaft (Fig. 2C,D). For heterogeneous solid-state membranes, *Pungor et al.* [7, 11, 221] use about 30 to 50 wt.-% of ion-selective membrane component (*e.g.* silver halide) having a grain size of 5–10 μm in a silicone rubber matrix. Other matrix materials that have been used are paraffin wax, acrylamides, and polyethylene [24–27].

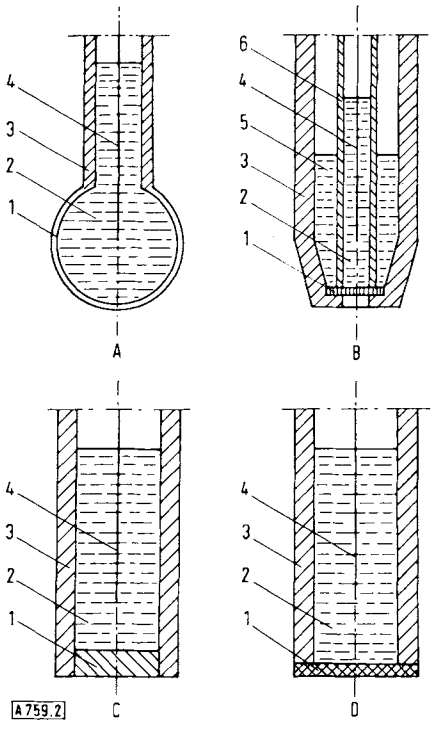


Fig. 2. Membrane electrodes (schematic).
A: *Glass electrode*: 1: glass membrane; 2: internal filling solution; 3: glass stem; 4: inner reference electrode.
B: *Liquid membrane electrode*: 1: filter paper impregnated with ion-selective ligand; 2: internal filling solution; 3: electrode shaft; 4: inner reference electrode; 5: ion-selective ligand; 6: tube to receive internal filling solution.
C: *Electrode with homogeneous solid-state membrane*: 1: homogeneous solid-state membrane; 2: internal filling solution; 3: electrode shaft; 4: inner reference electrode.
D: *Electrode with heterogeneous solid-state membrane*: 1: heterogeneous solid-state membrane; 2: internal filling solution; 3: electrode shaft; 4: inner reference electrode.

In the liquid membrane electrode of Figure 2B, a filter paper impregnated with ion selective ligand acts as the membrane. Any ion-selective component contaminating the solution being measured is replaced from the reservoir 5 (Fig. 2B); this should ensure a long electrode life of the membrane electrode system [28].

For ease of handling of the cell assembly and for working with small samples, it is advisable to combine the ion-selective membrane with the inner reference electrode, the internal filling solution, and the reference electrode that dips into the solution to be measured to form a single structural unit (single-rod cell assembly, combination electrode) [4, 12, 29].

2. Theoretical Considerations

Though liquid junction potentials that depend on the electrolyte of the reference electrode, the sample, the temperature, and other factors arise at the phase boundary between the reference electrode and the sample, it will always be assumed here that the poten-

[19] *R. G. Bates*, cf. [3], p. 1.
[20] Coleman Instruments (Maywood, Ill.), Bull. B 329, No. 1168.
[21] *L. Kratz*: Die Glaselektrode und ihre Anwendungen. D. Steinkopff, Frankfurt/Main 1950.
[22] *D. Wegmann* and *W. Simon*, Helv. chim. Acta *47*, 1181 (1964).
[23] *J. T. Clerc*, *Z. Štefanac*, and *W. Simon*, Helv. chim. Acta *48*, 54 (1965).
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[27] *H. J. C. Tendeloo* and *A. Krips*, Recueil Trav. chim. Pays-Bas *76*, 703, 946 (1957); *77*, 406, 678 (1958); *78*, 177 (1959).
[28] *J. W. Ross*, US-Pat. 3429785 (1969) Corning Glas Works, Corning, N. Y., USA; Brit. Pat. 1107108 (1968).
[29] Orion Research Inc. (Cambridge, Mass.) CAT/961 (1969).

tial of the reference electrode with respect to the sample is constant and independent of the nature of the sample solution (Fig. 1)[4,19,30–34].

2.1. Glass Membranes, Solid-State Membranes (Solid Ion-Exchange Membranes)

Relations based on investigations by *Nicolsky*[35] have been derived from experimental data for the EMF of a cell assembly with a liquid or solid ion-exchange membrane[15–17]. These relations can be formulated as follows for glass and pure solid ion-exchange membranes:

$$\mathrm{EMF}(T) = E_0^{\mathrm{A}}(T) + \frac{n \cdot R \cdot T}{F} \ln \frac{a_1^{1/n} + \left(K_{12}^{\mathrm{Pot}} \cdot a_2\right)^{1/n}}{a_1'^{1/n} + \left(K_{12}^{\mathrm{Pot}} \cdot a_2'\right)^{1/n}} \quad (1)$$

R = gas constant; T = absolute temperature; F = Faraday constant; a_i = ion activities in the sample solution (monovalent ions); a_i' = ion activities in the internal filling solution (monovalent ions); n = constant depending on the ions i and the membrane; K_{12}^{Pot} = selectivity constant (preference of sensor for ion 2 in relation to ion 1).

In sensors having a given inner reference electrode system (a_i' constant), we have

$$\mathrm{EMF}(T) = E_0^{\mathrm{B}}(T) + \frac{n \cdot R \cdot T}{F} \ln \left\{ a_1^{1/n} + \left(K_{12}^{\mathrm{Pot}} \cdot a_2\right)^{1/n} \right\} \quad (2)$$

Figure 3 shows functions of this nature for a glass electrode cell assembly with a high selectivity for sodium ions, one ion being H_3O^+ and the other an alkali metal cation in 0.1 M solution[36]. The selectivity constant $K_{\mathrm{Na^+H^+}}^{\mathrm{Pot}}$ is about 0.18[*] [36], so that for this sensor $(K_{\mathrm{Na^+H^+}}^{\mathrm{Pot}} \cdot a_{\mathrm{H^+}})^{1/n}$ is negligible in relation to $a_{\mathrm{Na^+}}{}^{1/n}$ in aqueous NaCl solutions of medium pH, and a linear relation should accordingly exist between the EMF of the cell assembly and the logarithm of the sodium ion activity of the sample. It can be seen from Figure 4 that this is largely so[36]. The linear regression of the experimental EMF values for the activity range 10^{-1} to 10^{-4} M gives a value of 59.8 mV/pNa$^+$ for the slope of the electrode function, in good agreement with the theoretical value of 59.2 mV/pNa$^+$.

From eq. (1) we obtain in general for a mixture of N monovalent ions with $n = 1$:

$$\mathrm{EMF}(T) = E_0^{\mathrm{C}}(T) + \frac{R \cdot T}{F} \ln \frac{\sum_{i=1}^{N} K_{1i}^{\mathrm{Pot}} \cdot a_i}{\sum_{i=1}^{N} K_{1i}^{\mathrm{Pot}} \cdot a_i'} \quad (3)$$

and

$$\mathrm{EMF}(T) = E_0^{\mathrm{D}}(T) + \frac{R \cdot T}{F} \ln \sum_{i=1}^{N} K_{1i}^{\mathrm{Pot}} \cdot a_i \quad (4)$$

for a given inner reference electrode system.

The selectivity constant K_{ij}^{Pot}, which characterizes the preference of the sensor for the ion j as compared with the ion i, is given by

$$K_{ij}^{\mathrm{Pot}} = \frac{u_j}{u_i} \cdot K_{ij} \quad (5)$$

where K_{ij} is the equilibrium constant of the exchange:

$$J_{\mathrm{solution}} + I_{\mathrm{membrane}} \rightleftharpoons J_{\mathrm{membrane}} + I_{\mathrm{solution}} \quad (6)$$

and u_i and u_j are the mobilities of the ions in the membrane. If the sensor responds to a bivalent ion (a_1) and a monovalent ion (a_2), eq. (3) becomes eq. (7):

$$\mathrm{EMF}(T) = E_0^{\mathrm{E}}(T) + \frac{R \cdot T}{2F} \ln \left(a_1 + K_{12}^{\mathrm{Pot}} \cdot a_2^2\right) \quad (7)$$

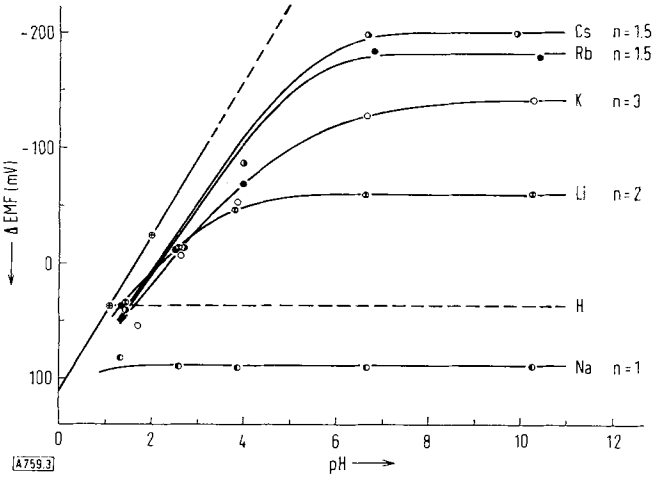


Fig. 3. EMF changes for a Na$^+$ responsive glass electrode in 0.1 M alkali metal ion solutions at various pH values [36].

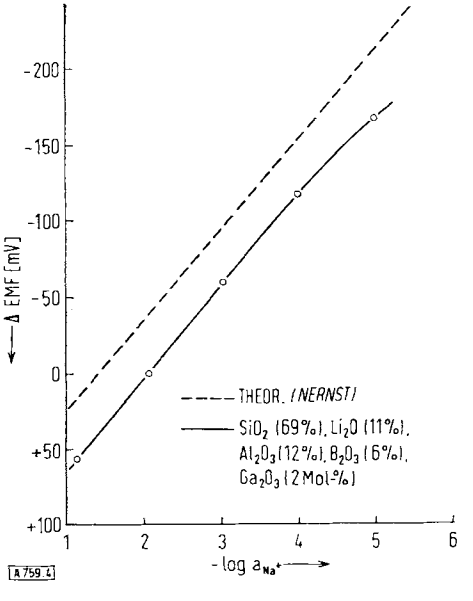


Fig. 4. Electrode function of a sodium-selective glass electrode assembly [aqueous NaCl solutions; cell assembly consisting of a glass electrode and a calomel reference electrode (KCl satd.) with electrolyte bridge (0.1 M NH_4NO_3)] [36].

[30] *I. Feldman*, Analytic. Chem. *28*, 1859 (1956).

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[32] *J. A. R. Kater, J. E. Leonard*, and *G. Matsuyama*, cf. [6], p. 54.

[33] *G. Milazzo*: Elektrochemie. Springer-Verlag, Vienna 1952.

[34] *W. Simon* and *D. Wegmann*, Helv. chim. Acta *41*, 2308 (1958).

[35] *B. P. Nicolsky*, Ž. fiz. Chim. *10*, 495 (1937).

[36] *Z. Štefanac* and *W. Simon*, Analyt. Letters *1*, No. 2, 1 (1967).

[*] If the indices are transposed in the logarithmic term of eq. (1) for $n = 1$, we obtain: $K_{ij}^{\mathrm{Pot}} = 1/K_{ji}^{\mathrm{Pot}}$

For a completely reversible cell assembly, K_{ij}^{Pot} can in principle be determined approximately by carrying out measurements in a solution of the ion i and in a solution of the ion j. If these are *e.g.* 0.1 M solutions of monovalent ions, it follows from eq. (4) (cf. also [37]) that:

$$0.1\ \text{M, Ion i: } EMF_1 = E_0^D(T) + \frac{R \cdot T}{F} \ln (0.1 + K_{ij}^{Pot} \cdot 0) \quad (8)$$

$$0.1\ \text{M, Ion j: } EMF_2 = E_0^D(T) + \frac{R \cdot T}{F} \ln (0 + K_{ij}^{Pot} \cdot 0.1) \quad (9)$$

$$EMF_2 - EMF_1 = \frac{R \cdot T}{F} \ln K_{ij}^{Pot} \quad (10)$$

$$\log K_{ij}^{Pot} = \frac{EMF_2 - EMF_1}{59.2\ \text{mV}} \quad (25\ ^\circ\text{C}) \quad (11)$$

Disturbances of the electromotive behavior of the sensor are to be expected when ions (interfering ions) form soluble products with membrane components (and so destroy the membrane) or give sparingly soluble compounds. In the second case, it is possible to calculate the maximum permissible activity $a_{1,max}$ of the interfering ion 1 from the solubility products $L_{2,3}$ (solubility product of the original membrane material) and $L_{2,1}$ (solubility product of the sparingly soluble compound formed) and the activity a_3 of the ion to be determined:

$$L_{2,1} = a_2 \cdot a_1 \quad (12)$$

$$L_{2,3} = a_2 \cdot a_3 \quad (13)$$

$$a_{1,max} = \frac{L_{2,1}}{L_{2,3}} a_{3,max} \quad (14)$$

Similarly, *Pungor* and *Tóth* [9] express the selectivity constant of heterogeneous solid-state membranes in terms of the solubility products L_{kj} and L_{ki} of the sparingly soluble membrane components:

$$K_{ij}^{Pot} = \frac{L_{ki}}{L_{kj}} \quad (15)$$

The arguments for ion-exchange membranes should be applicable only in part to solid membrane electrodes [15].

2.2. Liquid Membranes

2.2.1. Electrically Charged Ligands

Sandblom, Eisenman, and *Walker* [15–17] have derived a relation for the EMF of a cell assembly consisting of a liquid ion-exchange membrane electrode (Type 3a) and an external reference electrode.

$$EMF(T) = E_0^F(T) + \frac{R \cdot T}{F \cdot z_i} \left[\ln \frac{\Sigma u_i k_i a_i}{\Sigma u_i k_i a_i} - \int 1 - \int 2 \right] \quad (16)$$

$$k_i = \exp\left(- \frac{\mu_i^0 - \mu_i^0(m)}{R \cdot T} \right) \quad (17)$$

z_i = valency of the ion i; μ_i^0 = standard chemical potential of the ion i in solution; $\mu_i^0(m)$ = standard chemical potential of the ion i in the membrane phase.

[37] *K. Srinivasan* and *G. A. Rechnitz*, Analyt. Chem. *41*, 1203 (1969).

Eq. (16) is valid only under the following conditions:

1. the ligands are situated exclusively in the membrane;
2. there are no coions in the membrane;
3. equilibrium exists between the ion i and the ligand at all points in the membrane;
4. associates and ion aggregates of higher order do not occur;
5. the activities can be equated to the concentrations inside the membrane;
6. the system is at zero current.

For certain special cases, the integrals over the thickness of the membrane in eq. (16) can be neglected or can be easily calculated [17]. Thus in the steady state, $\int 2$ is equal to zero, owing to the disappearance of the entire ligand flow. If the concentration of the free ligand is negligible, $\int 1$ will also be zero, and eq. (16) reduces for a given internal electrode system of the sensor to

$$EMF(T) = E_0^G(T) + \frac{R \cdot T}{F \cdot z_i} \ln \sum_{i=1}^{N} u_i k_i a_i \quad (18)$$

in analogy with eq. (4). According to equation (18) the selectivity of the membrane is given mainly by the solvent used to dissolve the ligand. According to *Eisenman* [225] similar circumstances should hold for systems with completely dissociated ligands.

If on the other hand the ligand is mainly in the undissociated mobile form, eq. (16) can be replaced (cell assembly with a given internal electrode system) in the limiting case [*] by

$$EMF(T) = E_0^H(T) + \frac{R \cdot T}{F} \ln \left(a_1 + \frac{u_{2S}}{u_{1S}} K_{12} \cdot a_2 \right) \quad (19)$$

where u_{1S} and u_{2S} are the mobilities of the complexes of the ligand with ions 1 and 2 respectively. For this limiting case, therefore, the equilibrium constant K_{12} is a measure of the selectivity constant (cf. [37]).

In the ideal case, it is accordingly possible to produce liquid membrane sensors having widely different selectivities with components having suitable K_{ij} values [38]. The selectivity of glass and solid membrane electrodes, on the other hand, depends on the product of the exchange equilibrium constant K_{ij} and the mobility ratio of the ions in the membrane [eq. (5)]. In view of the low mobility of Ca^{2+} in glasses, therefore, it will be difficult to find glass electrodes with an extremely high preference for this ion over alkali metal ions [2].

2.2.2. Electrically Neutral Ligands

Eisenman, Ciani, and *Szabó* [220, 222–224] derived the following equation for the EMF of a liquid-membrane electrode of the electrically neutral ligand type and a given internal reference electrode system:

[*] In the limiting case in question, $u_{1S} \approx u_{2S}$.

[38] *C. J. Coetzee* and *H. Freiser*, Analytic. Chem. *41*, 1128 (1969).

$$E(T) = E_0^I(T) + \frac{R \cdot T}{F} \ln \left(a_1 + \frac{u_{2S} k_{2S} K_{2S}}{u_{1S} k_{1S} K_{2S}} a_2 \right) - \frac{R \cdot T}{F} \ln (1 + K_{1S}\, a_1 + K_{2S} a_2) \quad (20)$$

u_{1S}, u_{2S}: Mobilities of electrically charged complexes within the membrane;

k_{1S}, k_{2S}: Distribution coefficients of the complexes between sample solution and membranes;

K_{1S}, K_{2S}: Equilibrium constant of the interaction of the cations with ligand in the sample solution.

Equation (20) holds only under the following conditions:

1. Two monovalent cations with the activities a_1 and a_2 are in the sample solution;

2. The concentrations of all the electrically charged species within the membrane are so small as compared to the concentration of the complexed cations that only the flux of the complexes has to be considered to account for the electric current in the integration of the flux equation;

3. The activities of the complexed cations within the membrane as well as the complexed cations and the ligands in the sample solution are equal to the corresponding concentrations;

4. The fluxes of the complexes do not disturb the equilibrium at the membrane boundary;

5. The concentration of electrically neutral complexes and higher associates within the sample solution may be neglected;

6. The system is at zero current.

In equation (20) the second logarithmic term may be neglected relative to the first if the concentrations in the sample solution are so small that the complex formation in it may be neglected. Furthermore, the constants of the first logarithmic term in equation (20) can be expressed as a ratio of two equilibrium constants of the following salt extraction:

$$I^+_{(aqueous)} + X^-_{(aqueous)} + S_{(organic)} \overset{K_I}{\rightleftarrows} IS^+_{(organic)} + X^-_{(organic)} \quad (21)$$

$$\frac{u_{1S} k_{2S} K_{2S}}{u_{1S} k_{1S} K_{1S}} = \frac{u_{2S} K_2}{u_{1S} K_1} \quad (22)$$

Equation (20) therefore gives in analogy to equation (1)

$$EMF(T) = E_0^J(T) + \frac{R \cdot T}{F} \ln \left(a_1 + \frac{u_{2S} K_2}{u_{1S} K_1} a_2 \right) \quad (23)$$

Since in most cases $u_{1S} \approx u_{2S}$ [223] the selectivity constants of liquid-membrane sensors with electrically neutral ligands are mainly given by the ratios of the equilibrium constants K_1 and K_2 which again depend on the ligands and other possible components of the membrane.

3. Sensor Systems

Glass [39], solid [40,41], and liquid membrane electrode systems [39,42,43] have been known for some time, but apart from glass protodes, as can be seen from the literature (Table 1), they have for obvious reasons only recently come into wide use. Table 1 is the result of an attempt to make a list (by no means complete) of publications on the detection of individual ions by means of ion-selective sensors. The reader is referred in particular to some outstanding reviews in connection with glass electrodes [2–4, 31, 220].

Manufacturers often designate electrodes according to the ions for which they are supposed to be used. These designations should not be taken too seriously. So called "calcium electrodes" (liquid membrane electrodes) prefer Zn^{2+} [43] and "K^+ glass electrodes" are usually more sensitive to H^+ [2]. The most selective sensor available at present is undoubtedly the glass protode, which has $K^{Pot}_{H^+X^+}$ values of 10^{-13} (X^+ = alkali metal cation) [44].

It can be seen from Table 1 that the LaF_3 homogeneous solid-state membrane (single-crystal) sensor developed by *Frant* and *Ross* [45] has proved to be generally applicable for the detection of F^-. Its main limitations appear to be that OH^- ions interfere in most cases at high pH values (> about 8.5), owing to the selectivity constant $K^{Pot}_{F^-OH^-} = 10^{-1}$, and uncertainties can arise at low pH values (< about 5) as a result of the formation of HF and HF_2^-.

On the other hand, apart from the fundamental work of *Pungor et al.* [7–9, 11, 221], only relatively few publications on the use of heterogeneous solid-state membrane electrodes have appeared [46–48].

According to theoretical considerations, homogeneous and heterogeneous silver iodide membrane electrodes and Ag/AgI electrodes should respond similarly to I^-. This is in fact so, as is shown in Figure 5; the observed differences are due to the different histories of the electrodes and to differences in the liquid-junction potentials. The selectivities of adequately conditioned homogeneous and heterogeneous membrane electrodes and electrodes of the second kind with the same ion-selective components agree. Deviations are found only with redox systems. The main advantage of the silver halide solid-state membrane electrodes over the silver/silver halide electrodes is that the former is less sensitive to redox systems; difficulties are to be expected if strongly reducing components lead to the deposition of silver on the membrane. Homogeneous solid-state membrane electrodes appear to have a longer life, presumably because of the permeation in heterogeneous solid-state membrane electrodes (cf. [46]).

[39] *M. Cremer*, Z. Biol. *47*, 562 (1906).

[40] *H. J. C. Tendeloo*, J. biol. Chemistry *113*, 333 (1936).

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[42] *R. Beutner*, Amer. J. Physiol. *31*, 343 (1912).

[43] *F. W. Orme*, cf. [3], p. 376.

[44] *W. M. Baumann* and *W. Simon*, Helv. chim. Acta, *52*, 2054 (1969)

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[47] *P. Hirsch-Ayalon*, Electrochim. Acta *10*, 773 (1965).

[48] *G. A. Rechnitz*, *Z. F. Lin*, and *S. B. Zamochnick*, Analyt. Letters *1*, No. 1, 29 (1967).

Table 1. Literature survey.

Ion/Component	Glass membrane	Solid-state membrane		Liquid membrane
		homogeneous	heterogeneous	
H^+, OH^-	[2, 14, 58–86, 194]		[8, 67–69, 179]	[250]
Li^+	[2, 70, 244]	[139]		
F^-		[45, 84–139, 186, 212, 234–237, 262–265]		
Cl^-		[41, 168–171, 202, 268, 269]	[8, 46, 173, 176–178, 246, 267]	[37, 167, 172]
Br^-		[41, 192, 202, 214]	[9, 46, 176, 179, 246]	
I^-		[41, 184, 202, 214, 241, 270, 271]	[8, 9, 46, 174–184]	
Na^+	[2, 36, 64, 70–78, 82, 107, 167, 169, 185, 243]			[141, 208]
K^+	[2, 50, 64, 70, 78–80, 245]			[53–56, 215, 216, 227–230, 250]
Rb^+	[2]			
Cs^+	[2]			
Tl^+	[2, 244]			[250]
Sr^{2+}	[2]			
Cd^{2+}	[2]	[239]		[250]
Mg^{2+}	[2, 64]			[82, 99, 141, 208]
Ca^{2+}	[2, 64]	[24, 40. 166, 217]	[24]	[6, 24, 38, 43, 49, 64, 82, 99, 140–165, 208, 252, 253, 257–261]
Ba^{2+}	[2]		[68]	
Ni^{2+}			[177]	
Cu^{2+}		[213, 240]		[188, 250]
Ag^+	[2, 81, 244]	[190, 202, 214, 242]		[250]
S^{2-}		[189, 190, 191, 193, 202, 274]	[9, 176, 254]	
CN^-		[187]	[9, 175, 185, 187]	
Zn^{2+}				[43, 250]
Pb^{2+}		[201]		[250]
SCN^-		[192, 214]	[246]	[206, 255]
BF_4^-				[200]
ClO_4^-			[246]	[37, 205, 207]
NO_3^-			[246]	[37, 195–199, 247–249, 272, 273]
SO_4^{2-}		[201, 217]	[8, 48, 68, 69, 177–179]	
H_2PO_4, HPO_4^{2-}, PO_4^{3-}			[8, 26, 48]	[266]
Al^{3+}		212, 238]		
SiF_6^{2-}			[203, 204]	
MnO_4^-				[205]
$Cr_2O_7^{2-}$				[205]
IO_4^-				[205]
ReO_4^-				[205, 255]
CO_2	[2, 209]			
NH_4^+	[2, 210, 211, 245]			
NH_4^+ (Enzymes)	[83, 231–233]			

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The homogeneous solid-state membrane electrodes with AgCl, AgBr, AgI, and Ag_2S membrane for the determination of Cl^-, Br^-, I^-, S^{2-} or Ag^+ and CN^- function mainly by the transport of silver ions in the membrane. By mixing these membrane components with components of larger solubility and a common ion, electrodes for further ions may be obtained. A mixed crystal electrode with $CuS-Ag_2S$ and $CdS-Ag_2S$ membrane for example responds to Cu^{2+} and Cd^{2+} respectively [201, 213, 226]. The electrode response for the divalent cation in these cases is coupled with the Ag^+ electrode function by the sulfide ion.

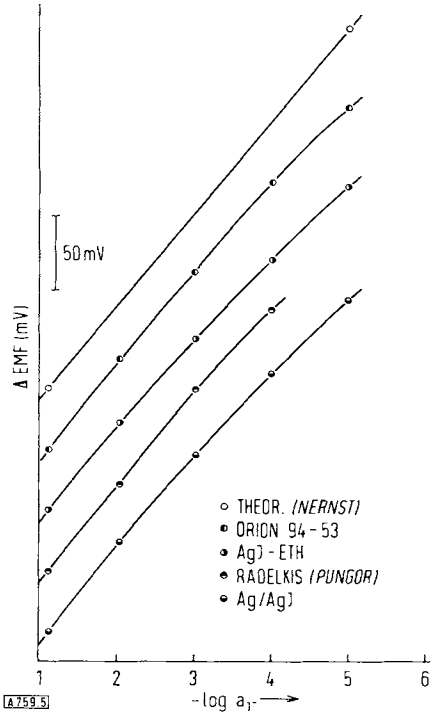


Fig. 5. Electrode function of iodide sensors [aqueous KI solutions; cell assembly consisting of ion-selective sensor and calomel reference electrode (KCl satd.)]. The membrane of the sensor AgI–ETH is a compressed membrane of purified AgI.

Though the nature of the inner solution of the electrode, according to eq. (1), (2), (18), and (20), should influence only the electrical zero point $E_0(T)$ of the cell assembly, it has been found that many sensors work best when the composition of their internal filling solution is similar to that of the sample solution (cf. also [49]). Sensor designs should accordingly allow easy adaptation of the electrode fillings to the measurement problem. Electrode systems with exchangeable membranes are illustrated in Figure 6. The arrangement of the membrane in the liquid membrane electrode prevents the inclusion of air bubbles at the lower end of the sensor (Fig. 6b). Sealing of the membrane is effected by pressure.

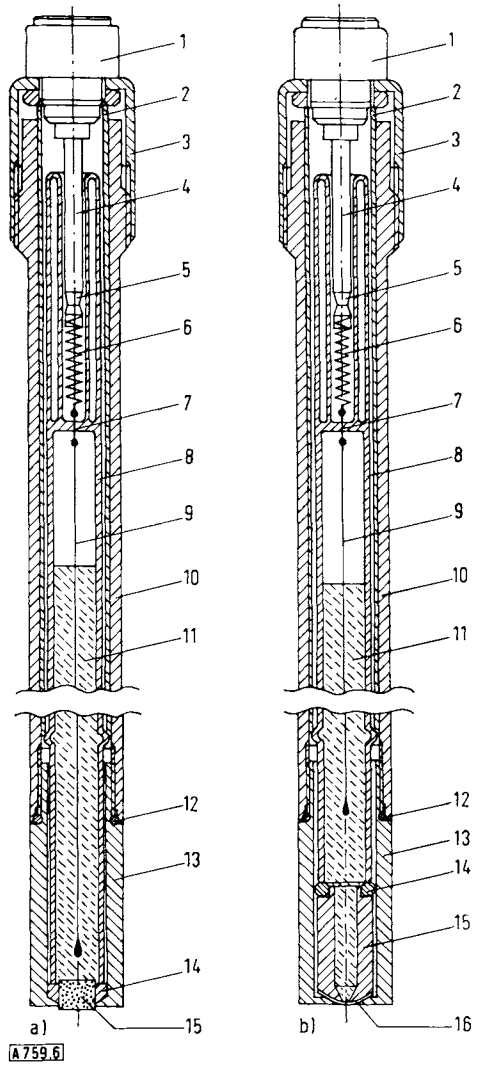


Fig. 6a.) Sensor with exchangeable solid-state membrane.

1: Plug for inner reference electrode system and electrical screening; 2: screening; 3: metal cap; 4: contact pin; 5: silver contact; 6: metal spring; 7: platinum duct; 8: glass insert; 9: inner reference electrode; 10: electrode shaft (plastic); 11: internal filling solution; 12: O ring; 13: membrane support (plastic); 14: silicone rubber sealing ring; 15: homogeneous solid-state membrane. The membrane 15 is held by sealing ring 14. This is done by screwing 3 firmly onto 10 by the screening 2 and the glass insert 8.

b) Liquid membrane sensor.

14: O ring; 15: hollow cylinder (plastic) pressing on membrane 16; 16: liquid membrane (filter paper impregnated with ion-selective ligand). The membrane 16 is fixed by the hollow cylinder 15 and the O ring 14. This is done by screwing 3 firmly onto 10 by the screening 2 and the glass insert 8.

Apart from their use in pH measurement, glass electrodes (mainly having the composition NAS_{11-18} or NAS_{27-4}) are also used for the determination of sodium and potassium ion activities [2, 3]. The glass electrodes for the measurement of Na^+ activities have

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$K^{Pot}_{K^+Na^+}$ values of up to 10^4 [2, 36]; on the other hand, selectivities for K^+ over Na^+ of only about 10 can be obtained in glass electrodes for routine use [2, 3, 50]. Glass electrodes are therefore suitable for the determination of potassium ions *e.g.* in blood serum only if the influence of the sodium ions present in the sample on the EMF of the measuring cell is taken into account. Corrections of this nature are doubtful, in view of the dependence of the $K^{Pot}_{Na^+K^+}$ values on the ion concentration and on the pretreatment of the electrode [51, 52] (cf. [46]). However, liquid membrane electrodes of type 3b with considerably higher selectivities for K^+ over Na^+ than can be obtained with glass electrodes can be produced with the aid of certain antibiotics that selectively complex K^+ [53–56]. Thus valinomycin dissolved in diphenyl ether on Millipore filter [*] gives liquid membrane sensors (Fig. 6b) having a theoretical linear electrode function to potassium ions in the range 10^{-1} to 10^{-5} M (Fig. 7) with selectivities for K^+ over Na^+ of ≈4000 (cf. Table 2), and electrode resistances of about 1 MΩ [55, 56, 227]. With activity changes of one order of magnitude, the potentials generally approach in less than 30 sec to within ±0.5 mV of a steady value, and normally to within ±0.2 mV in one minute, this value being maintained to within an average of ±1.4 mV over 150 hours with routine use of the electrode in solutions of various KCl concentrations (10^{-1}–10^{-4} M).

Table 2. Selectivity constants $K^{Pot}_{M^+K^+}$ for the valinomycin membrane electrode (25 °C; diphenyl ether).

M^+	Rb^+	K^+	Cs^+	NH_4^+	Na^+	Li^+	H^+
$K^{Pot}_{M^+K^+}$	0.52	1	2.6	84	3800	4700	18000

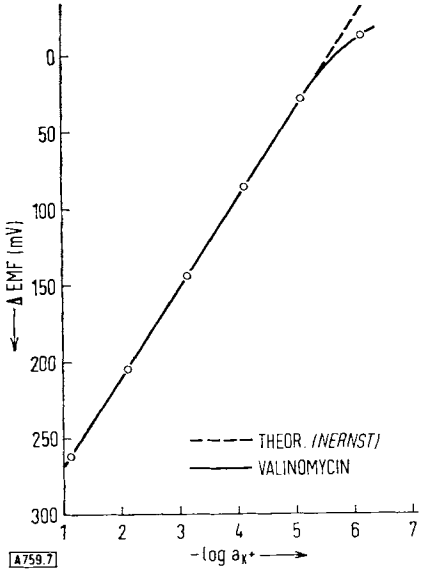


Fig. 7. Electrode function of the valinomycin liquid membrane electrode (25 °C). [Aqueous KCl solutions; cell assembly consisting of membrane electrode in accordance with Fig. 6b and calomel reference electrode (KCl satd.) with electrolyte bridge (0.1 M NH_4NO_3)].

[*] Type MF; Millipore Filter Corp., Bedford/Mass.

4. Error Considerations

A trivial error calculation shows that small uncertainties in the EMF measurement must lead to appreciable percentage errors in the determination of the ion activity or concentration (Table 3). Though short-term reproducibility to within 0.001 pH unit can in

Table 3. Errors Δa_i in the determination of the ion activity due to uncertainties ΔE in the EMF measurement (25 °C).

ΔE (mV)	$\frac{\Delta a_i}{a_i} = \frac{zF}{RT} \cdot \Delta E$ in % for ions having valency z =		
	1	2	3
10	38.92	77.85	116.77
1	3.89	7.79	11.68
0.1	0.39	0.78	1.17
0.01	0.04	0.08	0.12

principle be achieved with glass electrode cell assemblies [57], much larger deviations are found in practice. Uncertainties of 0.03 to 0.05 pH unit have been found in pH measurements on blood samples, presumably as a result of fluctuations of the liquid-junction potentials [32]. This corresponds to errors of 6.9 to 11.5 % in the determination of the hydrogen ion activity. Standard deviations of <1 % can be achieved in the determination of Na^+ concentrations [51]. Reproducibilities of this order can also be obtained with some liquid membrane electrodes (Fig. 7). At present the valinomycin liquid-membrane electrode makes determinations of K^+ in undiluted blood serum possible which are at least as reproducible as those performed by flame photometry [228, 229].

Heterogeneous solid-state membrane electrodes at least occasionally exhibit permeation of the membrane by components of the electrode filling solution or of the test solution [46], which is probably one cause of long-term changes in the electrode potential. In permeation experiments with ^3H and ^{131}I, homogeneous solid-state membrane electrodes (AgI–ETH) were found to have membrane permeabilities of the same order as that of a Teflon membrane with similar dimensions (zero current). The permeability of the membrane can thus be ruled out as a cause of long-term changes in the potentials of the electrodes examined. Silver halide electrodes occasionally exhibit large fluctuations of potential as a result of changes in the intensity of the light [218, 219].

5. Present Situation, New Directions

Although by now at least 37 ions and components (Table 1) may be selectively detected by membrane electrode systems, there are at present only few analytically valuable sensors commercially available. These may be used either for the direct potentiometric determination of the activity of a given ion in a mixture of ions or for the indirect determination by potentiometric titration.

Because of the restricted ion mobility in the membrane phase, glass as well as solid-state membrane electrodes have strict limitations in respect to selectivity (see Section 2). These limitations do not hold for liquid-membrane electrodes. This advantage, however, has its price in a relatively short life-time of the sensor and a sometimes disturbing contamination of the sample solution by membrane components. At present liquid-membrane electrodes for NO_3^-, Ca^{2+}, K^+ as well as $[Ca^{2+} + Mg^{2+}]$ (water hardness) seem to be finding acceptance in a wide range of analytical applications. Especially high selectivities are to be expected for liquid-membrane sensors with certain biologically active materials (antibiotics) as membrane components. Unfortunately our knowledge in connection with the correlation of the structure of organic compounds with their ion specificity is still relatively poor [56, 225].

Extremely high selectivities are obtained if an enzymatic degradation of the components to be determined can be used. The enzyme-carrying matrix is sandwiched between the sample solution and a sensor which detects one of the degradation products [83, 231–233]. There is no doubt that by now only a few possibilities for the production of ion selective sensors have been pointed out. There is therefore a real hope that research in this area will drastically influence analytical chemistry in the widest sense.

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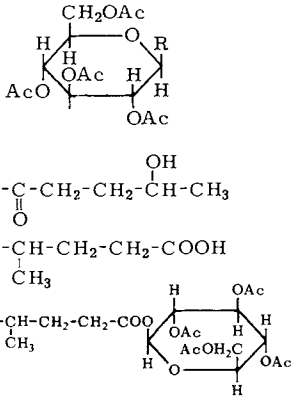
COMMUNICATIONS

New Methods for Preparation of Glycosides [1] [**]

By *Günter Wulff, Gerhard Röhle,* and *Wolfgang Krüger* [*]

Dedicated to Professor R. Tschesche on the occasion of his 65th birthday

Reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with the silver salt of 4-hydroxyvaleric acid in benzene gives the glucosyloxy-acid *(2)* and the 1-*O*-(glycosyloxyacyl)glucose *(3)* as well as the very unstable 1-*O*-acylglucose *(1)*.



(1), R = -O-C(=O)-CH$_2$-CH$_2$-CH(OH)-CH$_3$

(2), R = -O-CH(CH$_3$)-CH$_2$-CH$_2$-COOH

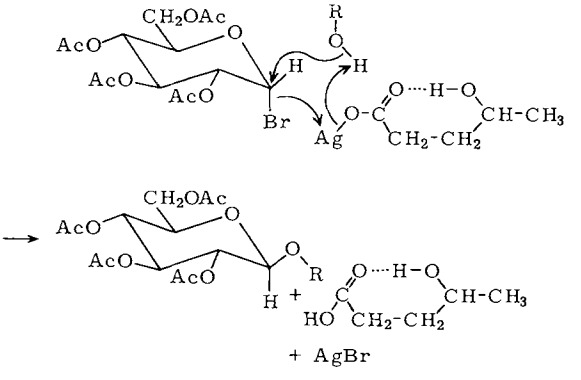
(3), R = -O-CH(CH$_3$)-CH$_2$-CH$_2$-COO-

Silver salts of other 4- and of 5-hydroxyalkanoic acids give analogous products. Moreover, silver salts of 2-, 3-, and 6-hydroxyalkanoic acids afford corresponding products, but here the 1-*O*-acylglucoses are appreciably more stable.

Thus glucosylation of the alcoholic hydroxyl group of the hydroxyalkanoic acids occurs to a considerable extent in this reaction. We have therefore investigated the possibility of glucosylating added alcohols similarly. We found that, in the presence of silver salts of 2-, 3-, or 4-hydroxyalkanoic acids, or of 1,3- or 1,4-dicarboxylic acids, alcohols react with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in ether to give good yields of 2,3,4,6-tetra-*O*-acetyl-β-D-glucosides. Silver 4-hydroxyvalerate proved particularly favorable for use in this reaction. Thus, for instance, we obtained cholesterol β-D-glucoside in 58 % yield (only 33 % [2] or 43 % [3] by the Königs-Knorr method and 45 % by *Kochetkov*'s method [4]) and a 65 % yield of tigogenin β-D-glucoside (45—50 % by the Königs-Knorr method).

The new method is extremely simple and mild: one merely stirs the readily available silver salt and, *e.g.*, 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in dry diethyl ether for 30 min at room temperature or for 4 h at −10 °C; and since no water is produced there is none to remove. 4-Cholestenol, for example, gives almost wholly 3,5-cholestadiene by the usual methods, whereas we obtained the glucoside in 36 % yield. The reaction is clearly applicable also to alcohols of various types [5]; and other *cis*-halogenoses, *e.g.*, 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide and 2,3,4-tri-*O*-acetyl-β-D-arabinopyranosyl bromide, react analogously.

The reaction is highly solvent-specific; it occurs best in diethyl ether. Studies of anion-dependence, of the products, and of the kinetics are in accord with a trimolecular synchronous mechanism.



+ AgBr

This reaction occurs to any considerable extent only on the surface of solid bifunctional anions of specific structure. Such anions include those of 2-, 3-, and 4-hydroxyalkanoic acids and of certain dicarboxylic acids in which neighboring group effects limit the formation of 1-*O*-acylglycoses in favor of glycoside formation by way of a trimolecular transition

state. The Königs-Knorr synthesis in the presence of silver carbonate probably occurs analogously.

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[**] Glycoside Synthesis, Part 1. – This work was supported by the Deutsche Forschungsgemeinschaft.

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[5] After conclusion of this work, Professor *B. Helferich* informed us that he had obtained ethyl β-D-glucoside from 2,3,4,6-tetra-*o*-acetyl-α-D-glucopyranosyl bromide and ethanol in the presence of silver salts of dicarboxylic acids (unpublished work).

Crystalline π-Radicals Containing Lead – Isotropic ^{207}Pb-ESR Hyperfine Structure

By *Hartmut B. Stegmann*, *Klaus Scheffler*, and *Fritz Stöcker* [*]

Dedicated to Professor Eugen Müller on the occasion of his 65th birthday

Attempts to prepare solutions of paramagnetic organolead compounds — in particular by dissociation of hexaaryldiplumbanes [1] — have so far been unsuccessful. We have now been able to isolate lead-containing radicals as products of the reaction of 2-amino-4,6-di-*tert*-butylphenoxyl *(1)* with diaryllead dihalides. Reaction of the aminoaroxyl *(1)* with, *e.g.*, di-*p*-tolyllead dichloride in ethanol affords violet-brown crystals, m.p. 143—145 °C. Elemental analysis and mass spectrum suggest structure *(2)*. While solid *(2b)* gives an intense ESR signal exhibiting exchange narrowing, its solution in benzene gives a multicomponent spectrum.

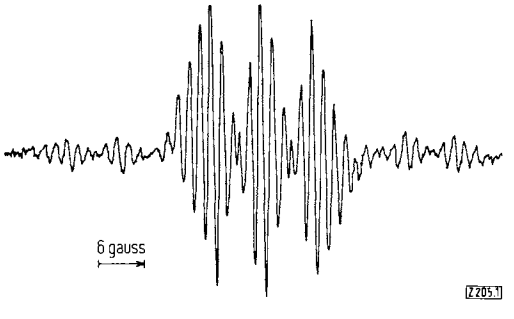
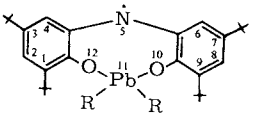


Figure: ESR spectrum of the di-*p*-tolyllead radical *(2b)* in benzene at room temperature.

The central section of the hyperfine structure (HFS) of this spectrum (see Figure) can be interpreted in terms of magnetic coupling of the free electron with two pairs of protons and one ^{14}N nucleus. The less intense components lying on the left- and right-hand sides can be attributed to further coupling with a ^{207}Pb nucleus. This isotope ($I = 1/2$) has an abundance of 22.62% in natural lead. The observed spectrum agrees very well with this figure, as is shown by the successful simulation (CDC 3300) of an enlarged spectrum.

The isotopic spectrum is masked by the main spectrum only in the central region, which corresponds to the 77.38% of nonmagnetic lead nuclei present; thus if both groups of satellites are taken into consideration, the whole ^{207}Pb HFS can be observed. Exact measurements show that the distances between the satellite centers and the center of gravity of the whole spectrum differ in the upfield and downfield directions. This asymmetry is attributable to a second order shift such as has already been detected quantitatively for radicals containing tin [2].

In agreement with other findings, the ESR spectra show the new organolead derivatives to be 11,11-disubstituted 1,3,7,9-tetra-*tert*-butyldibenzo[*d*,*g*]-[1,3,6,2]dioxazaplumbocin-5-yls. The coupling parameters were initially assigned by analogy with the corresponding tin compounds [2].



(2)

ESR data for the radicals *(2)* (gauss), recorded in benzene at room temperature; ΔH = line width.

(2)	$a^{(2)}_{H_{4,6}}$	$a^{(2)}_{H_{2,8}}$	$a^{(1)}_{N}$	$a_{^{207}Pb}$	g	ΔH
(a), R = C_6H_5	1.62	3.24	7.05	41.68	2.00081	0.76
(b), R = *p*-CH_3–C_6H_4	1.62	3.12	7.14	40.54	2.00093	0.70

As expected, the substituent R has only a limited effect on the coupling constants. The exceptional line broadening (≈ 0.7 gauss) is probably due either to an unresolved proton HFS or to unfavorable relaxation conditions. Since the spectra remain essentially unchanged between —70 and +120 °C, the line broadening cannot be due to mechanical movement. The *g* factors of compounds *(2a)* and *(2b)* are remarkably small, owing to interaction of the free electron and the Pb nuclei which has also been determined from the HFS spectra.

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[1] Cf. *e.g.*, *E. Müller*, *F. Günther*, *K. Scheffler*, and *H. Fettel*, Chem. Ber. *91*, 2888 (1958); *G. Bähr* and *G. Zoche*, *ibid. 88*, 542 (1955); *R. Preckel* and *P. W. Selwood*, J. Amer. chem. Soc. *62*, 2765 (1940); *U. Belluco*, *G. Tagliavini*, and *P. Favero*, Ricerca sci. Rend. Suppl. *A 32*, 98 (1962); Chem. Abstr. *57*, 13786 (1962).

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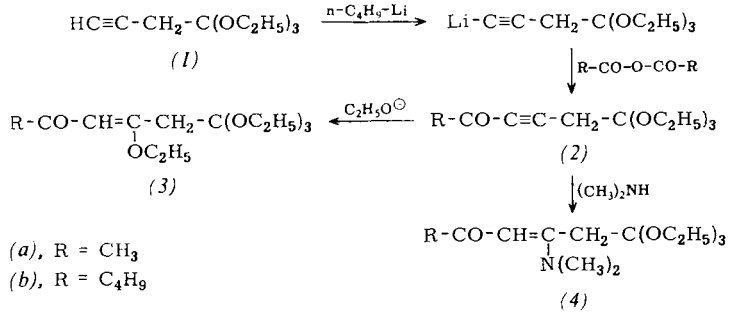
Preparation of Triethyl Ortho-3-butynoate and its Conversion into 5-Oxo-3-alkynoate Esters and into Derivatives of 3,5-Dioxoalkanoate Esters [1] [**]

By *Rolf Finding* and *Ulrich Schmidt* [*]

Dedicated to Professor Eugen Müller on the occasion of his 65th birthday

In triethyl ortho-3-butynoate (4,4,4-triethoxy-1-butyne) *(1)* (which we obtained from propargylmagnesium bromide and tetraethyl orthocarbonate) masking of the carboxyl group as orthoester protects it from attack by alkali-metal acetylides and prevents rearrangement of the acetylenic linkage to the α,β-position or to an allenic unit. The orthoester can thus be

metalated and then acylated to afford triethyl 5-oxoortho-3-alkynoates *(2)*, which can be converted into enol ethers of 3,5-dioxoalkanoic esters *(3)* by base-catalyzed addition of alcohols. Dimethylamine adds almost quantitatively to *(2)* giving triethyl 3-(dimethylamino)-5-oxoortho-3-alkenoates *(4)* which yield copper(II) complexes of the β-polycarbonyl compounds on treatment with a solution of copper(II) acetate in aqueous acetic acid. The reaction sequence *(1)* → *(2)* → *(3)* or *(4)* permits extension of a carboxylic acid chain by two acetyl units. The structures of compounds *(1)*—*(4)* are in agreement with their NMR spectra.



(1)

(2)

(3)

(4)

(a), R = CH_3
(b), R = C_4H_9

Cpd.	n_D^{20}	B.p. (°C/torr)
(1)	1.4261	73—75/10
(2a)	1.4510	132—135/10
(2b)	—	156—160/10
(3a)	1.4586	60/0.001 [a]
(3b)	1.4624	80/0.001 [a]
(4a)	1.5003	70—80/0.001 [a]

[a] Bath temperature on distillation from a bulb-tube.

Triethyl 5-oxoortho-3-hexynoate (2a) from triethyl ortho-3-butynoate (1)

A solution of propargylmagnesium bromide[2] (43 g) in ether (160 ml) is dropped slowly under N_2 into a solution of tetraethyl orthocarbonate (48 g) in anhydrous ether (80 ml) at −30 °C (internal temperature). When the temperature is slowly raised, an exothermic reaction sets in at 25 °C; external cooling is applied to prevent the temperature rising above 30 °C; after 30 min the mixture is hydrolyzed by saturated NH_4Cl solution, whereafter working up gives *(1)* (17.3 g).

The orthoester *(1)* (6.9 g) is metalated in tetrahydrofuran (30 ml) and ether (60 ml) under nitrogen and at −60 °C by an equivalent amount of a 2 N solution of butyllithium in light petroleum. The mixture is allowed to warm to 0 °C and then dropped into a solution of acetic anhydride (5 g) in ether (50 ml) kept at −60 °C. Allowing the resulting mixture to warm to room temperature, shaking it with saturated NH_4Cl solution, and then distillation afford *(2a)* (4.0 g).

Triethyl 3-ethoxy-5-oxoortho-3-hexenoate (3a)

The product *(2a)* (2.3 g) in ethanol (2 ml) is dropped into a solution of Na (0.23 g) in ethanol (10 ml) cooled to 0 °C and after a few min is warmed to room temperature. After 30 min, addition of H_2O (50 ml), extraction with ether, and distillation afford *(3a)* (1.25 g).

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[**] This work was supported by the Austrian Forschungsrat.

[1] β-Polycarbonyl Compounds, Part 6. — Part 5: *A. Hochrainer, S. Hellweger, W. Silhan,* and *U. Schmidt*, Mh. *99*, 2153 (1968).

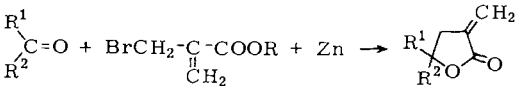
[2] *M. Gaudemar*, Ann. Chimie [13], *1*, 161 (1955).

A Simple Synthesis of α-Methylene γ-Lactones

By *Elisabeth Öhler, Klaus Reininger,* and *Ulrich Schmidt*[*]

Dedicated to Professor O. Hromatka on the occasion of his 65th birthday

Studies of syntheses in the lysergic acid series have revealed a simple route leading to the hitherto difficultly accessible α-methylene γ-lactones[1]. In tetrahydrofuran, α-(bromomethyl)acrylic esters *(1)*[2] readily form organozinc compounds which react with aldehydes and ketones to give methylene lactones *(2)* in very good yields. A single step technique in which the bromo ester is treated with zinc in the presence of the carbonyl compound has many advantages. Many higher and polycyclic ketones give almost quantitative yields [*e.g.* 1-benzoyl-5-oxo-1,2,2a,3,4,5-hexahydrobenz[*cd*]-indole gives *(3)*, m.p. 190—195 °C][3]. Formaldehyde affords a mixture of α-methylenebutyrolactone and γ-hydroxy-α-methylenebutyric ester in low yield.

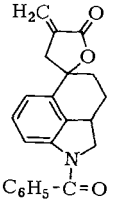


(1) *(2)*

R^1	R^2	Yield (%) [a]	M.p. (°C)	B.p. (°C/torr) [b]
$-(CH_2)_4-$		66		70/0.3
$-o-C_6H_4-(CH_2)_3-$		75	53—55	105-110/0.001
CH_3	CH_3	42		100-110/18
C_6H_5	CH_3	78		80-90/0.001
C_6H_5	C_6H_5	100	105—107	
C_6H_5	H	100	49—54 [c]	80/0.01
i-C_3H_7	H	76		120/13
$C_6H_5-CH=CH-$	CH_3	92		130/0.001

[a] Based on carbonyl compound.
[b] Bath temperature on bulb-tube distillation.
[c] Described as an oil in ref. [1b].

(3)



General procedure:

A solution of bromomethylacrylic ester *(1)*[2] (50 mmoles) in anhydrous tetrahydrofuran (30 ml) is added dropwise with vigorous stirring under nitrogen to a mixture of granulated zinc (3.5 g, 53.5 mmoles, 20 mesh) and the carbonyl compound (45 mmoles) in anhydrous tetrahydrofuran (15 ml). Once the reaction has started, addition is adjusted such that the temperature does not rise above 40—50 °C. The reaction mixture is stirred for about an hour at 50 °C, cooled, and

poured onto ice-cold dilute hydrochloric acid. Depending on the solubility of the lactone *(2)*, the mixture is extracted with ether or methylene chloride, or the solid lactone is filtered off. The solution is washed with aqueous $NaHCO_3$ solution and with water, dried over Na_2SO_4, and finally distilled. Some methylene lactones, especially those bearing small substituents, polymerize very readily, often during distillation.

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[1] a) *E. R. H. Jones, T. Y. Shen*, and *M. C. Whiting*, J. chem. Soc. (London) *1950*, 230; *E. R. H. Jones* and *M. C. Whiting*, Brit. Pat. 640489 (1950); Chem. Abstr. *45*, 642 (1951); *W. J. McGraw*, US.-Pat. 2624723 (1953); Allied Chemical and Dye Corp.; Chem. Abstr. *47*, P 11233 (1953); b) *E. E. van Tamelen* and *S. Rosenberg-Bach*, J. Amer. Chem. Soc. *77*, 4683 (1955); c) *ibid. 80*, 3079 (1958).

[2] β,β-Dibromoisobutyric acid was prepared according to *A. F. Ferris*, J. org. Chemistry *20*, 780 (1955). Ethyldiisopropylamine was used for removal of HBr.

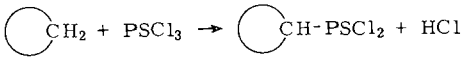
[3] *Note added in proof*: The corresponding reaction of β'-bromotiglic ester with ketones to give α-methylene-β-methylbutyrolactones has recently been reported by *A. Löffler, R. Pratt, J. Pucknat, G. Gelbard*, and *A. S. Dreiding* [Chimia *23*, 413 (1969)].

Cycloalkanephosphonothioic Dichlorides by Photochemical C–P Linkage

By *Ulrich Schmidt* and *Alfred Ecker* [*]

C—P linkage by irradiation of hydrocarbons and phosphorus compounds has hitherto only been accomplished in the reaction of phosphorochloridic diester, phosphonochloridic ester, and phosphinic chloride with cyclohexane[1]. Since compounds containing the O=P—Cl group absorb below 220 nm, irradiation must be carried out with deuterium lamps; reaction times of several weeks are therefore required, even for the preparation of mmole amounts.

We have now found that S=P—Cl derivatives are better suited for photochemical substitution since they absorb at about 260 nm, *i.e.* in the range of maximum intensity of low pressure Hg lamps. Irradiation of mixtures of cyclic hydrocarbons and phosphorothioic trichloride with such a lamp affords cycloalkanephosphonothioic dichlorides. Toluene reacts at the methyl group.



With cyclohexene and $PSCl_3$ *addition* occurs to give the cyclohexanephosphonothioic dichloride and three isomeric chlorocyclohexanephosphonothioic chlorides which were identified by a combination of gas chromatography and mass spectrometry; isolation of the chlorocyclohexanephosphonothioic dichlorides by preparative gas chromatography was precluded by rapid destruction of the column packing. No bicyclohexenyl was detected.

R—P(S)Cl_2 [a] R =	Irradiation duration (h)	Yield (%)	B.p. (°C/torr)	M.p. (°C)	n_D
Cyclopentyl	48	22	54/0.2		1.5590 (24 °C)
Cyclohexyl	96	44	70/0.6		1.5622
	48	21 (47 [b])			(20 °C)
Cyclooctyl	46	25	105/0.3	42–43	

[a] The structures of the phosphonothioic dichlorides follow from the mass spectra [*e.g.* $(CH_2)_5CHPSCl_2$: molecular ion at *m/e* 216 (18%). $(CH_2)_5C^+$ 82 (100)].

[b] Based on *reacted* $PSCl_3$.

Approximately 300 ml of a mixture of $PSCl_3$ and hydrocarbon (molar ratio 1 : 5) was irradiated under N_2 in a cylindrical quartz vessel (height 35 cm, diameter 4.5 cm) surrounded by a ring (diameter 8.5 cm) of seven low pressure Hg lamps (Type NN 15/44 VK produced by Quarzlampengesellschaft Hanau, each of 6 W emission at 250 nm). Deposition on the inner wall of the vessel was avoided by continuous brushing. The products were isolated by fractional distillation.

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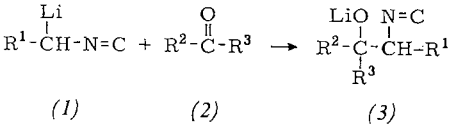
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[1] *Eugen Müller* and *H. P. Padeken*, Chem. Ber. *100*, 521 (1967).

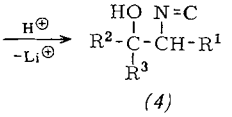
2-Isocyano-1-alkanols from Carbonyl Compounds and α-Metalated Isocyanides[1]

By *Walter A. Böll, Fritz Gerhart, Axel Nürrenbach*, and *Ulrich Schöllkopf* [*]

Reaction of α-isocyanoalkyllithium compounds *(1)* [2] with carbonyl compounds *(2)* followed after about 10 min by neutralization (—70 °C) with glacial acetic acid affords good yields of 2-isocyano-1-alkanols *(4)* (β-hydroxyisocyanides). The compounds *(4)* deserve attention because they can be converted into vinyl isocyanides [3], or hydrolyzed to 2-amino-1-alkanols, *i.e.* the above steps represent a route for the nucleophilic introduction of aminomethyl groups into carbonyl compounds [4].



(1) *(2)* *(3)*



(4)

(4)	R^1	R^2	R^3	Yield (%)
(a)	H	H	C_6H_5	80
(b)	H	CH_3	C_6H_5	75
(c)	$(CH_3)_2N—CH_2—CH_2$	CH_3	C_6H_5	75

The adducts *(3)* [2] occur as intermediates; if benzoyl chloride or acetic anhydride is added instead of glacial acetic acid, the benzoates or acetates of *(4)* [5] are obtained, *e.g.*, in the experiment with isocyanomethyllithium and benzaldehyde, the benzoate (m.p. 57 °C) or the acetate of *(4a)* (m.p. 85–86 °C) is isolated.

1-Isocyano-2-phenyl-2-propanol (4b)

A solution of methyl isocyanide (5.6 ml, 0.1 mole) in dry tetrahydrofuran (20 ml) was added dropwise to a stirred solution of butyllithium (0.105 mole, *i.e.* 66 ml of a 1.6 N solution in hexane) in dry tetrahydrofuran (100 ml) at —70 °C under nitrogen. After 10 min, acetophenone (12.0 g, 0.1 mole) in dry tetrahydrofuran (20 ml) was added to the suspension of isocyanomethyllithium at the same temperature, and after another 10 min the whole was neutralized with glacial acetic acid (6.3 g, 0.105 mole) in dry tetrahydrofuran (10 ml). The reaction mixture was poured into water (0.5 l), extracted

three times with benzene (3 × 50 ml), and concentrated under vacuum. On treatment of the residue with light petroleum (b.p. 50—70 °C), a crystalline precipitate of *(4b)* (9.4 g) appeared. Concentration of the light petroleum solution afforded a further crop of crystals (2.8 g) [m.p. 74—75 °C; IR spectrum (KBr): 2170 cm^{-1} (νNC), 3380 cm^{-1} (νOH)]. — A solution of *(4b)* (5 g) in dioxane (20 ml) was added dropwise (ice cooling) to a mixture of 2 N hydrochloric acid (50 ml) and dioxane (50 ml). After two hours' stirring, work-up at room temperature yielded 1-formylamino-2-phenyl-2-propanol (3.3 g).

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[1] Syntheses with α-Metalated Isocyanides. Part 6. — Part 5: *D. Hoppe* and *U. Schöllkopf*, Angew. Chem. *82*, 290 (1970); Angew. Chem. internat. Edit. *9*, 300 (1970).

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[3] *D. S. Matteson* and *R. A. Bailey*, J. Amer. chem. Soc. *90*, 3761 (1968).

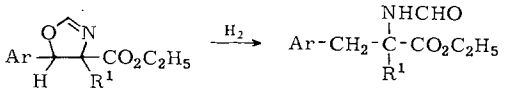
[4] In this connection, see also *F. Gerhart* and *U. Schöllkopf*, Tetrahedron Letters *1968*, 6231; *Th. Kauffmann*, *E. Köppelmann*, and *H. Berg*, Angew. Chem. *82*, 138 (1970); Angew. Chem. internat. Edit. *9*, 163 (1970).

[5] On addition of ethanol, methanol, or water, Δ²-oxazolines are obtained, which are also formed on treatment of *(4)* with alkali.

N-Formylphenylalanine Ethyl Esters by Hydrogenolysis of Ethyl 5-Aryl-2-oxazoline-4-carboxylates [1]

By *Ulrich Schöllkopf* and *Dieter Hoppe* [*]

Phenylalanine and its derivatives (*e.g.* tyrosine, thyroxine, dopa, methyl-dopa, *etc.*) have attracted a great deal of attention because of their biological activity. We have found that *N*-formylphenylalanine ethyl esters *(2)*, R^1 = H, and the α-methyl compounds *(2)*, R^1 = CH_3, can be prepared by hydrogenolysis of 5-aryl-2-oxazoline-4-carboxylates *(1)* [2] with *e.g.* palladium/activated charcoal in ethanol. Compounds *(2)* can be converted into phenylalanines by heating with 20 % hydrochloric acid, while brief heating with potassium hydroxide in ethanol affords *N*-formylphenylalanines.



(1) *(2)*

	Ar	R^1	Hydrogenated [a] (h)	*(2)*, Yield (%)
(a)	C_6H_5	H	3	99
(b)	*p*-CH_3—C_6H_4	H	2	95
(c)	*p*-$CH_3OC_6H_4$	H	12	95
(d)	C_6H_5	CH_3	30	99

[a] With palladium/activated charcoal, room temperature, H_2 at atmospheric pressure.

Cleavage of the C—O bond in *(1)*, R^1 = CH_3, (20 °C, atmospheric pressure, proceeds ten times slower than in *(1)*, R^1 = H; furthermore, substitution in the nucleus, *e.g.* by methoxy groups, lowers the rate of hydrogenolysis. In these cases it is advisable to carry out the hydrogenation at higher temperatures or under pressure.

N-Formylphenylalanine ethyl ester (2a)

A solution of ethyl 5-phenyl-2-oxazoline-4-carboxylate [2, 3] (5.0 g, 23 mmoles) in dry ethanol (50 ml) is shaken at room temperature with 0.25 g of palladium/activated charcoal (10 % palladium, Merck) under hydrogen (normal pressure); in 3 hours 510 ml (22 mmoles) of hydrogen is taken up. After flushing with nitrogen, filtration, and evaporation of solvent there remains 5 g (99 %) of *(2a)* [NMR spectrum (CCl_4): CH_2, τ = 7.0 (*d*, *J* = 7 Hz); CH, τ = 5.2 (m). IR spectrum (film): 3320 cm^{-1} (νNH); 1740 and 1680 cm^{-1} (νCO)].

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[1] Syntheses with α-Metalated Isocyanides, Part 7. — Part 6: *W. A. Böll*, *F. Gerhart*, *A. Nürrenbach*, and *U. Schöllkopf*, Angew. Chem. *82*, 482 (1970); Angew. Chem. internat. Edit. *9*, 458 (1970).

[2] *D. Hoppe* and *U. Schöllkopf*, Angew. Chem. *82*, 290 (1970); Angew. Chem. internat. Edit. *9*, 300 (1970).

[3] The 2-oxazoline must be free from cyanide ions and isocyanide since these poison the catalyst.

Hydrogen Fluoride-Potassium Hydrogen Phosphite (1/1), an Unusual Lattice Compound [**]

By *Hans Falius*, *Dietrich Mootz*, and *Horst Altenburg* [*]

Studies on phosphorofluoridous acid have led to the discovery of the adduct HF · KH[PHO_3] *(1)*, which is stable only in the solid state. It may be readily prepared by the following two methods:

$$\left.\begin{array}{l} HF + KH[PHO_3] \\ KF + H_2[PHO_3] \end{array}\right\rangle \rightarrow HF \cdot KH[PHO_3] \quad (1)$$

(1) is obtained as large colorless monoclinic crystals; d_4^{20} = 2.139 g cm^{-3}, m.p. 96 °C. Unit cell: *a* = 6.692, *b* = 11.040, *c* = 7.841 Å; β = 127.88 °; space group $P2_1/c$ with *Z* = 4.

In the absence of moisture the crystals are stable at room temperature; when kept in glass vessels, however, local attack of the glass surface occurs. In aqueous solution, which shows a strong acid reaction, the compound exhibits only the reactions of its constituent ions; it cannot be reisolated from this solution. The NMR spectra (in methanol and in water) show only one fluorine signal alongside the resonances characteristic of phosphorous acid. The adduct is therefore not a hydrate of potassium phosphorofluoridite $K[PHO_2F] \cdot H_2O$, as was previously assumed. Its IR spectrum closely resembles that of KH[PHO_3].

The properties of "phosphorofluoridous hydrate" described by *Heinz* and *Röhner* [1] suggest that it is also an adduct of composition HF · $H_2[PHO_3]$, for phosphorofluoridous acid is stable and the νPF frequency (about 884 cm^{-1} in the acid) was not observed in the spectrum of this "acid hydrate".

Unlike phosphorofluoridous acid [2], compound *(1)* is immediately oxidized completely to phosphate by iodine in hydrogen carbonate solution. On alkalimetric titration it is neutralized by two equivalents of alkali in two stages. When *(1)* is heated in a vacuum it loses H_2O and HF, loss of weight setting in at 115 °C, to give a mixture containing a little $K[PHO_2F]$ and much $K_2[P_2H_2O_5]$.

Preparation:

1. Equimolar amounts of $H_2[PHO_3]$ and KF are vigorously ground together, the mixture first becoming sticky and then liquid. The syrupy liquid is extracted with hot methanol, filtered, and allowed to cool; yield 30 %.

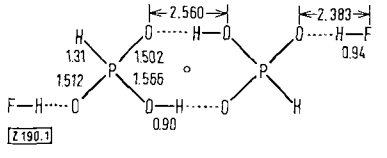
2. A mixture of $KH[PHO_3]$ and 40% HF (molar ratio 1 : 1.5) is evaporated to dryness over P_4O_{10} and KOH in a vacuum desiccator. After a few days, the crystalline mass (or sometimes syrup) is extracted with methanol as above.

Method 1 is superior to the other. Elemental analysis (K, P, F) confirmed the composition of *(1)*; mol. wt. found by alkalimetric titration to be 139 (calc. 140).

The corresponding ammonium compound could not be prepared by the above method; attempted preparation of the sodium compound yielded only the known adduct $NaH[PHO_3] \cdot H_2[PHO_3]$.

X-ray analysis:

Three dimensional intensity data were measured with $Cu_{K\alpha}$ radiation on an automatic single crystal diffractometer[3] ($\Theta/2\Theta$ scan). Several sets of overlapping data had to be recorded for fresh crystals because *(1)* is sensitive to moisture and reacts with glass, as mentioned above. Data reduction resulted in 857 observed independent structure amplitudes which were used for determination of the structure by the usual technique and refinement to $R = 5.6\%$.



The Figure is a schematic representation of two equivalent formula units (without the potassium ions) arranged about a center of symmetry. The positions of the hydrogen atoms and the lengths of the PO bonds (two P—O bonds of 1.502 and 1.512 Å and one P—OH bond of 1.566 Å; standard deviation *ca.* 0.004 Å) provide conclusive proof of the formula $HF \cdot KH[PHO_3]$ (ruling out $KF \cdot H_2[PHO_3]$). Adjacent $H[PHO_3]^-$ ions are linked by equivalent hydrogen bonds O—H · · · O to form centrosymmetric dimers.

The short hydrogen bond F—H · · · O (F · · · O distance = 2.383 Å), which to our knowledge has not previously been reported, is the most interesting feature of the structure.

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[**] This work was supported by the Fonds der Chemischen Industrie and the State of Niedersachsen.

[1] *D. Heinz* and *M. Röhner*, Z. Chem. *9*, 113 (1969).

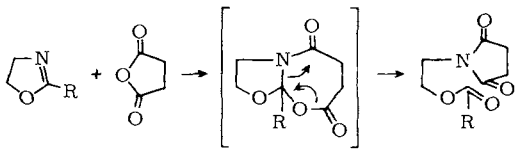
[2] *B. Blaser* and *K. H. Worms*, Z. anorg. allg. Chem. *360*, 117 (1968).

[3] AED designed by *W. Hoppe* of Siemens.

Addition of Maleic Anhydride to 2-Isopropyl-2-oxazoline

By *Rudolf Nehring* and *Wolfgang Seeliger* [*]

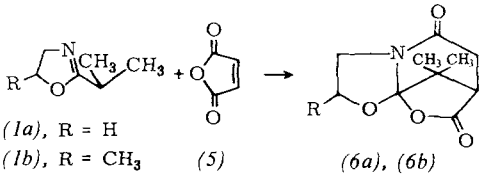
2-Oxazolines *(1)* add anhydrides and chlorides of monocarboxylic acids while undergoing ring scission to give 2-acyloxyethyl-[1] and 2-chloroethyl-*N*,*N*-diacylamines[2]. Reaction with cyclic anhydrides, such as those of phthalic and succinic acid *(2)*[3], affords *N*-(2-acyloxyethyl)-phthalimide and -succinimide *(4)*.



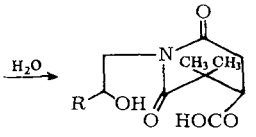
(1) *(2)* *(3)* *(4)*

It may be assumed that the reactive[4] double bond of *(1)* initially adds the anhydride group, which would give the intermediate *(3)* in the case of *(2)*. In this communication we wish to present a well-founded argument for the existence of an intermediate such as *(3)*.

Reaction of maleic anhydride *(5)* with 2-isopropyl- *(1a)* and 5-methyl-2-isopropyl-2-oxazoline *(1b)*, respectively, gave crystalline addition products which were assigned the structures *(6a)* and *(6b)*.



(1a), R = H
(1b), R = CH_3 *(5)* *(6a)*, *(6b)*



(7a)

Their IR spectra showed carbonyl absorption bands at 1780 and 1660 cm^{-1} which are typical of strained γ-lactones and six-membered lactams, respectively. The formulas are further supported by elemental analyses, molecular-weight determinations, and NMR spectra. The exceptional ease of hydrolysis of *(6a)* to *(7a)*, which is converted into α,α-dimethylcarballylic acid and ethanolamine by vigorous hydrolysis, deserves attention.

11,11-Dimethyl-2,10-dioxa-5-azatricyclo[6.2.1.$0^{1,5}$]*undecane-6,9-dione (6a)*

A solution of 2-isopropyl-2-oxazoline *(1a)* (0.8 mole) in dry 1,2-dichloroethane (200 g) was added dropwise to a stirred solution of maleic anhydride *(5)* (78.4 g, 0.8 mole) in dry 1,2-dichloroethane with exclusion of atmospheric moisture. The reaction mixture was boiled for 90 min and, after part of the solvent had been distilled off, allowed to cool, whereupon 119 g of *(6a)* crystallized; a further crop of 9 g was obtained on concentration of the mother liquor (total yield 77%). On washing with dry ethyl acetate, *(6a)* was obtained as colorless crystals (m.p. 178—191 °C, decomp.).

(6b), m.p. 137—139 °C, was prepared analogously in 48% yield.

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[1] *R. C. Elderfield*: Heterocyclic Compounds. Wiley, New York 1957, Vol. 5, p. 388.

[2] *R. Nehring* and *W. Seeliger*, Liebigs Ann. Chem. *709*, 113 (1967).

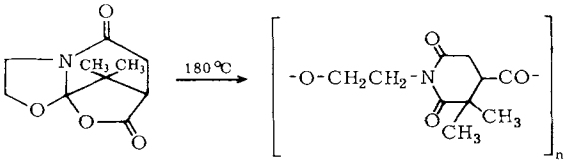
[3] *S. P. Rowland*, US-Pat. 2547494 (1951) and US-Pat. 2547542 (1951), Rohm & Haas Co.

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A New Synthesis of Polyimides

By *Rudolf Nehring* and *Wolfgang Seeliger*[*]

11,11-Dimethyl-2,10-dioxa-5-azatricyclo[6.2.1.0^{1,5}]undecane-6,9-dione *(1)*[1], prepared by addition of 2-isopropyl-2-oxazoline to maleic anhydride, polymerizes when heated to 180 to 200 °C for about 20 min in the absence of moisture.



(1) *(2)*

The reaction affords poly[*N*-(2-hydroxyethyl) α,α-dimethyltricarballyl(α,γ-imid)ate] *(2)* as a transparent plastic of high molecular weight which is soluble in a number of solvents such as DMF, dioxane, DMSO, ethylene chloride, and pyridine. The relative viscosity of the solution was about 2.0 (1 g in 100 ml of chloroform at 25 °C).

During polymerization the γ-lactone carbonyl band of *(1)* (1780 cm^{-1}) disappears in favor of ester bands at 1720 and 1180 cm^{-1}.

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[1] *R. Nehring* and *W. Seeliger*, Angew. Chem. *82*, 468 (1970); Angew. Chem. internat. Edit. *9*, 461 (1970).

A General Synthesis of Pyrimidine Nucleosides[**]

By *U. Niedballa* and *Helmut Vorbrüggen*[*]

The most important method for the synthesis[1] of pyrimidine nucleosides is the Hilbert-Johnson reaction[1a], in which 2,4-dialkoxypyrimidines or the more readily accessible 2,4-bis-trimethylsilyl derivatives of uracils, cytosines[2], and their 2-thio analogs[3] react with protected 1-halo sugars to give predominantly the N^1-nucleosides. Up to now the reaction was usually conducted either by fusion, giving sometimes poor yields, or under milder conditions in boiling benzene in the presence of mercuric salts, which are often difficult to remove.

The Hilbert-Johnson reaction is basically a kind of Friedel-Crafts reaction with formation of a C—N bond. We therefore carried out the reaction in the presence of Friedel-Crafts catalysts and found, in contrast to earlier observations[4], that the above compounds react under mild conditions to give the N^1-nucleosides in good to very good yields.

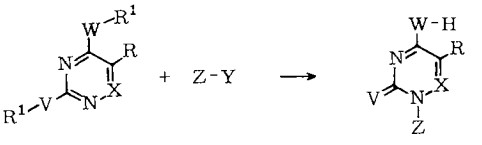
Comparable results were obtained with the Friedel-Crafts catalysts $SnCl_4$, $ZnCl_2$, $TiCl_4$, BF_3—$(C_2H_5)_2O$, and $AlCl_3$ in 1,2-dichloroethane, benzene, acetonitrile, carbon disulfide, and dimethylformamide, but we preferred $SnCl_4$ in 1,2-dichloroethane for the sake of experimental simplicity. Under such conditions the 1-halo sugars can be replaced by the easily accessible and stable 1-alkoxy and 1-acyloxy derivatives of protected sugars. In the presence of a 2α-acyloxy substituent in the sugar component, only the β-anomers of the N^1-glycosides were isolated; the protected derivatives of 2-deoxy-D-ribose and D-arabinose yielded, as expected, mixtures of the α and β anomers. Use of a 10% excess of the pyrimidine component proved advantageous in that we then obtained not only a higher yield but also a purer end product, which in most cases crystallized spontaneously.

Because of the high yields and the simplicity of the procedure pyrimidine nucleosides have thus become readily accessible on an industrial scale.

Experimental:

2,3,5-Tri-*O*-benzoyl-1-acetyl-D-ribofuranose (Z—Y) (2.5 g, 5 mmoles) and the 2,4-bissilyl derivative of 6-azauracil (R = H, R^1 = $Si(CH_3)_3$, V = W = O, X = N) (1.42 g, 5.53 mmoles) in 1,2-dichloroethane (100 ml) were stirred for 4 h at 22 °C in the presence of $SnCl_4$ (0.42 ml, 3.6 mmoles). After addition of saturated aqueous $NaHCO_3$ solution (50 ml) the organic phase was filtered over Celite, dried with Na_2SO_4, and evaporated. The crystalline residue (2.7 g) gave 2.6 g (92%) of 2′,3′,5′,-tri-*O*-benzoyl-6-azauridine, m.p. 192 to 194 °C, after recrystallization from ethanol.

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R^1	V	W	R	X	Y	Z	Catalyst [a]	t (h)	T (°C)	Yield (%)	M.p. (°C)	$[\alpha]_D$ (°)
CH_3	O	O	I	CH	OAc	2,3,5-tri-*O*-benzoyl-D-ribofuranose	1.44	4	22	67	183–184	−112.5 [c]
$Si(CH_3)_3$	O	O	C_2H_5	CH	OAc		0.72	48	22	95	159–160	−96.7 [d]
$Si(CH_3)_3$	O	O	H	N	OAc		0.72	4	22	92	192–194	−71.4 [e]
$Si(CH_3)_3$	O	O	H	N	OAc		0.72 [k]	4	22	83	192–194	−71.4 [e]
$Si(CH_3)_3$	O	O	H	N	OAc		1.44 [l]	5	84	83	192–194	−71.4 [e]
$Si(CH_3)_3$	O	O	NO_2	CH	OAc		0.72	2	22	62	140	−12.2 [d]
$Si(CH_3)_3$	O	O	CH_3	N	OAc		0.72	24	22	77	132–133	−83.5 [f]
$Si(CH_3)_3$	S	NH	H	CH	OAc		1.44	2	22	95	194–195	−36.6 [e]
$Si(CH_3)_3$	S	O	H	N	OCH_3	2,3,5-tri-*O*-acetyl-D-ribofuranose [b]	1.74	15	22	73	101–103	−44.8 [e]
$Si(CH_3)_3$	S	O	CH_3	N	OAc		0.72	3	22	83	156–157	−42.2 [g]
$Si(CH_3)_3$	S	O	H	N	OAc	2,3,4,6-tetra-*O*-acetyl-D-glucopyranose	1.44	6	60	79	225	+18.5 [h]
$Si(CH_3)_3$	O	O	C_2H_5	CH	Cl	2-deoxy-3,5-di-*O*-*p*-tolyl-D-ribofuranose	0.25	2	0	57 [i]	197–198	−90 [c]
$Si(CH_3)_3$	O	O	H	N	Cl	2,3,5-tri-*O*-benzyl-D-arabinofuranose	0.33	15	22	42 [j]	123–124	+65 [e]

[a] mmoles of catalyst/mmole of sugar component. Unless stated otherwise, $SnCl_4$ (in 1,2-dichloroethane) was used as catalyst. [b] NMR and GC give α compound/β compound = 1/4. [c] c = 0.49 in $CHCl_3$. [d] c = 0.60 in $CHCl_3$. [e] c = 1.00 in $CHCl_3$. [f] c = 0.52 in $CHCl_3$. [g] c = 0.51 in $CHCl_3$. [h] c = 1.00 in pyridine. [i] Overall yield 92.7%. [j] Overall yield 74.3%. [k] $SnCl_4$ (in CH_3CN) as catalyst. [l] $ZnCl_2$ (in 1,2-dichloroethane) as catalyst.

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CNDO Calculation of the Inductive Effect of the Methyl Group

By *Herbert Kollmar* and *Harry O. Smith* [*]

MO calculations on hydrocarbons and carbonium ions predict [1,2] an increase in the positive charge at the α position by methyl substituents, a prediction apparently confirmed by ^{13}C-NMR [3]. This finding contradicts the usual assumption that the methyl group exerts an electron-releasing inductive effect.

Various CNDO calculations [4] by our own modified technique [5] have correctly reproduced properties of hydrocarbons and carbonium ions [6]. We have also been able to demonstrate the energetic stabilization of a positive charge by α-methyl substituents and, in particular, can show that, in terms of MO theory, the fact that methyl renders the α position positive is actually responsible for this stabilization.

Table 1 lists the relative heats of formation of a number of carbonium ions; the energies were calculated for complete minimization of the total energy with respect to the geometric parameters (bond lengths and angles).

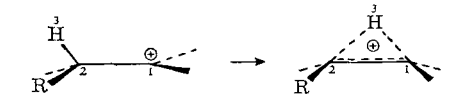
Table 1. Alkylcarbonium ions: Stability and charge distribution.

	Stabilization [a] exp.	calc.	Excess charge on the α-C atom
$C_2H_5^+$ *(1a)*		−13	+0.225
(2a)	− 2	− 3	−0.009
$C_3H_7^+$ *(1b)*	0	0	+0.190
(3b)	24	25	+0.250
(2b)		19	C-1 −0.049
			C-2 +0.066
t-$C_4H_9^+$	41	55	+0.273

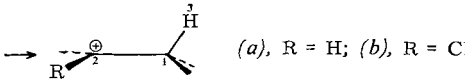
[a] ΔH for the reaction: $R^+ + C_3H_8 \rightarrow n\text{-}C_3H_7^+ + RH$ (kcal/mole).

The tabulated data illustrate the reasonable energetic stabilization of the cation with increasing methyl substitution. The positive charge on the central C atom increases by about 0.02 of a unit charge per methyl group. The significance of the positive charge in the α position for the energetic stabilization of carbonium ions will be demonstrated in the present communication.

Let us consider the 2,1-hydrogen shift in the classical ethyl cation *(1a)* which proceeds *via* the nonclassical bridged ion *(2a)*. The three-center bond in *(2a)* can be formed by steady admixture of the empty p_z orbital on C-1 in *(1a)* with the orbital of the C-2—H-3 bond. The transition should therefore



(1) *(2)*



(3)

(a), R = H; *(b)*, R = CH_3

require negligible activation energy. Our CNDO calculations show structure *(2a)* to be about 10 kcal/mole more stable than *(1a)*, conversion of *(1a)* into *(2a)* entailing no activation energy.

The same process in the case of the 2-methylated ethyl cation (the *n*-propyl cation *(1b)*) leads to *i*-propyl cation *(3b)*. According to our calculations, the energy decreases monotonically during the transition: *(3b)* is 25 kcal/mole more stable than *(1b)*; thus the nonclassical structure *(2b)* is here less stable than the classical *i*-propyl cation. This state of affairs is reflected in the fact that the two C—H-3 bonds vary in strength in *(2b)*, where an H atom is situated above the middle of the C-1—C-2 bond: the H atom is drawn towards C-1. This asymmetry is caused by the methyl substituent on C-2.

In the CNDO formalism the total energy of a molecule can be allotted to bonds and atoms [4]:

$$E = \sum_{A} E_A + \sum_{A>B} E_{AB}$$

The term E_{AB} is a measure of the strength of the chemical bond A—B [7], and can be further resolved according to physical principles. It thus becomes clear (Table 2) that the bond 2—3 is weaker than 1—3 because the positive H atom 3 (charge + 0.205) is more strongly repelled by the more positive of the two C atoms, *i.e.* C-2. This is less obvious from the purely electrostatic bonding components E^S than from the resonance energy contributions (E_R = one-electron resonance energy; E^K = electron exchange energy [7]). However, more detailed analysis shows that the contributions of E^R and E^K to the bonds 1—3 and 2—3 differ only because the positive charge on C-2 is greater than that on C-1.

Table 2. Energy components of the bonds 1—3 and 2—3 in *(2b)*.

	1—3	2—3
E	−0.303	−0.262
E^R	−0.286	−0.271
E^K	−0.100	−0.082
E^S	+0.082	+0.092

Thus a relationship is established between the charge shift induced by the methyl group and the energetic stabilization of a positive charge by an α-methyl substituent: The CH_3 group increases the positive charge in the α position and is, in turn, bonded particularly strongly to a positive center. In alkylcarbonium ions, the methyl groups donate negative charge to the empty p orbital of the central C atom (hyperconjugation). This effect is overcompensated by electron withdrawal from the σ bonds by the methyl group [1]. In methyl substituted π systems, the appearance of a positive charge in the α position is accompanied by the occurrence of a corresponding negative charge in the β position. A methyl substituent therefore has a polarizing effect on a π system [2]. This is exemplified by propene [2], toluene, and also by the ion *(2b)* (see Table 1).

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Crystal Structure of $TeCl_4$: Presence of Tetramers in Solid Chalcogen(IV) Halides

By *Bruno Buss* and *Bernt Krebs* [*]

On the basis of X-ray [1] and spectroscopic studies [2] of possible structures of Group VIB halides in the solid state and the steric effect of the lone pairs of chalcogen atoms, two structural models have been proposed for $SeCl_4$, $TeCl_4$, and $TeBr_4$: one model is ionic and contains $ElX_3^+X^-$ (the cations having C_{3v} symmetry) the other one being covalent and based on ElX_4 (C_{2v}; trigonal bipyramid) by analogy with the gaseous state. No unequivocal evidence in favor of either structure has hitherto been adduced. Relevant knowledge has been limited to the structure of TeF_4 [3].

We have determined the structure of solid tellurium(IV) chloride by a complete X-ray analysis of a twinned crystal. $TeCl_4$ forms monoclinic crystals of space group C2/c having $a = 17.076$ (8), $b = 10.404$ (5), $c = 15.252$ (8) Å; $\beta = 116.82°$; $Z = 16$; $d_{X\text{-ray}} = 2.959$, $d_{exp} = 3.01$ g cm^{-3}. The lattice constants are in good agreement with the known values [1b, 1d]. The structure was determined on the basis of about 3000 independent reflections (recorded with a four circle diffractometer and reduced to a single crystal). Refinement (isotropic) has so far reached $R = 0.09$.

The solid consists of isolated Te_4Cl_{16} units (Figure) with a cubane-like structure [4] and having only van der Waals contacts (Cl · · · Cl) with one another. Each of the Te atoms appears at the apex of an equilateral trigonal pyramid (mean TeCl distance 2.31 Å; σ for individual values 0.006 Å), three terminal Cl atoms forming the base. The coordination of the Te atom is made up to an octahedron by three much more remote bridging Cl atoms (mean TeCl distance 2.93 Å), the Te being displaced from the center parallel to the C_3 axis. The corners of the cubane-like skeleton are occupied alternately by Te and bridging Cl atoms. Mean bond angles are 94.8° for Cl(terminal)—Te—Cl(terminal), 85.1° for Cl(bridge)—Te—Cl(bridge), and 94.7° for Te—Cl(bridge)—Te. The Te_4Cl_{16} unit (exact symmetry C_2) has almost T_d symmetry. While the shorter Te—Cl bonds are ideal (covalent) single bonds, insofar as the bond length corresponds to the sum of the covalent radii, ionic bonding plays a dominant role in the much weaker Te—Cl bridging bonds. Thus the polar resonance structure can be fairly accurately described as an

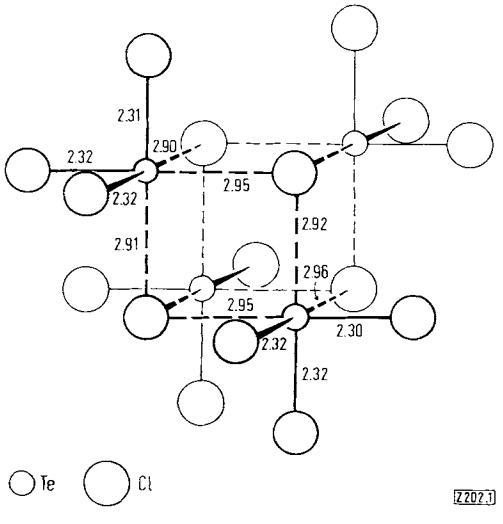


Figure: Te_4Cl_{16} structural unit in solid tellurium(IV) chloride

array of $TeCl_3^+$ ions, of approximate symmetry C_{3v}, and Cl^- ions. $TeCl_3^+$ ions have also been detected in $TeCl_3^+AlCl_4^-$ [2a, 2e], $TeCl_3^+AsF_6^-$ [2e, 5], and $TeCl_3^+SbCl_6^-$ [2e]. The shortest Te · · · Te distances in the tetramer are 4.30 Å, thus ruling out Te—Te bonding. The Cl atoms are approximately close packed (Cl · · · Cl distances 3.38 to 4.21 Å), Te filling 1/4 of the octahedral sites (cf. ref. [1c]).

Interestingly, the Te—Cl bond lengths in the $TeCl_3^+$ groups of $TeCl_4$ (2.31 Å) are much shorter than those found for Te^{IV}—Cl in, *e.g.*, $(CH_3)_2TeCl_2$ (2.51 Å) [6], $TeCl_6^{2-}$ (2.56 Å) [7], or *trans*-$TeCl_4(SC[N(CH_3)_2]_2)_2$ (2.53 Å) [8] (cf. also ref. [9]). A knowledge of the structure of solid $TeCl_4$ permits resolution of apparent contradictions in the properties of the compound, such as its electrical conductivity in the liquid state and its solubility in nonpolar solvents, *e.g.* benzene. A benzene solution of $TeCl_4$ is reported to contain trimers or tetramers [2b, 10]; this can readily be deduced from the structure. Under certain conditions, however, the possibility of an equilibrium with the monomer cannot be discounted [2c, 2e, 2f, 10]. Moreover, the vibrational spectra can now be unequivocally assigned, the twinning interpreted, and characteristic data such as the dipole moment, the high boiling point, the nuclear quadrupole resonance spectrum [11], *etc.* explained. $SeCl_4$ and $TeBr_4$ are isotypic with $TeCl_4$ (cf. also ref. [1c, 1d]).

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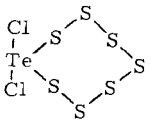
8,8-Dichloro-1,2,3,4,5,6,7,8-heptathiatellur(IV)-ocane [**]

By *Johannes Weiss* and *Manfred Pupp* [*]

Reaction of $TeCl_4$ with polysulfanes affords a compound having the composition Cl_2TeS_7. We have been able to isolate this product as orange crystals that are stable in air and insoluble in the usual solvents; they are, however, slightly soluble in CS_2 (*ca.* 2 g/l). On heating, a black coloration is observed at 95 °C (m.p. 110–112 °C).

Cl_2TeS_7 forms orthorhombic crystals, space group D_{2h}^{16}—Pmnb, $a = 8.82$, $b = 9.01$, $c = 13.28$ Å; $Z = 4$; $d_{X\text{-ray}} = 2.65$ g/cm³.

Preliminary results from an X-ray structure analysis indicate the following structure:



The eight-membered ring has the same "crown shape" as the S_8 ring of the α-[1] and β-modification[2] of sulfur. The Te atom is coordinated as a distorted trigonal bipyramid: The Cl atoms occupy the apices of the pyramids, the lone pair taking up an equatorial position.

Procedure:

A solution of "crude sulfane"[3] (20 g) in CS_2 (0.5 l) is added dropwise to a stirred solution of $TeCl_4$ (20 g) in CH_2Cl_2 (1 l) and CS_2 (0.5 l) at room temperature over a period of 4—5 h. About 18 g of Cl_2TeS_7 is precipitated; concentration of the filtrate to a volume of 200 ml yields another 2 g of product. Purification is by recrystallization from CS_2.

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[**] Interchalcogen Compounds, Part 1.

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A Simple New Synthesis of Arylalkynes

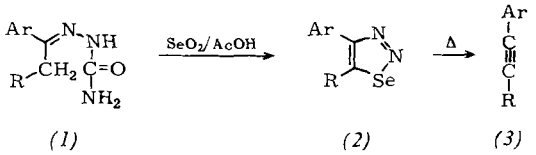
By *Iradj Lalezari*, *Abbas Shafiee*, and *Mohamed Yalpani*[*]

In a previous communication we reported that selenium dioxide oxidation of aryl ketone semicarbazones *(1)* in acetic acid affords 1,2,3-selenadiazoles *(2)*[1]. We now describe experiments which show that compound *(2)* is an intermediate in a new synthesis of aryl derivatives of acetylene.

On attempted recrystallization of 4-phenyl-1,2,3-selenadiazole *(2a)* from water, the compound was found to decompose at elevated temperatures to a volatile substance having a pleasant odor and a red deposit of selenium. Steam distillation of compound *(2a)* gives an oily substance, the IR spectrum of which shows an absorption frequency at 2200 cm^{-1}. This substance reacts readily with aqueous silver nitrate to give a greyish precipitate from which phenylacetylene *(3a)* can be liberated.

A better yield of the arylalkyne *(3)* is obtained when the selenadiazole is mixed with five times its weight of sand, pyrolyzed, and vacuum distilled. Compounds of type *(3)* are also formed by exposing an alcoholic solution of *(2)* to sunlight over a long period of time.

The reaction represents a general method (see Table) for ready conversion of aryl ketones into arylalkynes. The course of reaction for aliphatic ketones is not yet clear.



(1) *(2)* *(3)*

Ar–C(=O)–CH₂–R		*(2)*		Ar–C≡C–R [a]
Ar	R	m.p. °C	yield (%)	yield (%)
(a) C_6H_5	H	76	70	84
p-F–C_6H_4	H	110	73	11
p-Cl–C_6H_4	H	130	65	80
p-Br–C_6H_4	H	143	70	85
p-NO_2–C_6H_4	H	189	65	80
p-CH_3–C_6H_4	H	87	65	70
p-CH_3O–C_6H_4	H	101	50	60
C_6H_5	CH_3	81	68	72
C_6H_5	C_6H_5	125	61 [b]	67 [c]

[a] All arylalkynes were identified by comparison with authentic materials.

[b] SeO_2/dioxane.

[c] Diphenylacetylene was obtained in one step from the selenium dioxide oxidation of deoxybenzoin semicarbazone in acetic acid.

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Silicon-Carbon Compounds with a Carborundum Structure ("Carborundanes"[**])

By *Gerhard Fritz*, *Fritz Diem*, *Helmut Köhler*, *Dieter Kummer*, and *Heinz Scheer*[*]

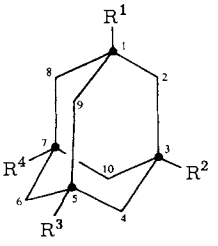
The chief products of pyrolysis of tetramethylsilane and of methylchlorosilanes are compounds having an —Si—C—Si— skeleton ("carbosilanes"); the structure of these readily distillable and sublimable compounds has already been the subject of many reports[1]. Thus, *(1a)* is formed from $Si(CH_3)_4$ and the derivatives *(1b)*—*(1e)* from $(CH_3)_3SiCl$; *(1f)* can be obtained by reaction of *(1b)* with $LiAlH_4$[2].

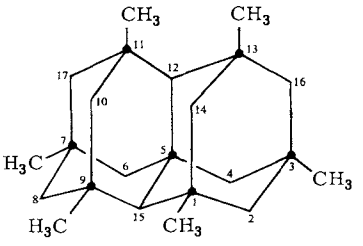
We have now been able to isolate by column chromatography (Al_2O_3, pentane) the compounds *(2)*, *(3)*, and *(4)*, which are present in low concentration in the viscous products of the gas-phase pyrolysis of $Si(CH_3)_4$ at 700 °C; their structures were established by ^{1}H-NMR- and mass spectrometry.

An accurate determination of the mass of *(2)* gave *m/e* = 424.121238 (calc. for $Si_7C_{16}H_{36}^+$ 424.120189). According to its IR spectrum and chemical properties the molecule does not contain Si—H or Si—Si groups; therefore, with the Si : C ratio under discussion, the presence of C—C groups can also be ruled out. This is also the case for *(3)* and *(4)*.

The six CH_3 groups in *(2)* can be differentiated according to their position: the methyl protons attached to the Si atoms 1, 9, 11, and 13 and to 3 and 7 are symmetrically equivalent. The ^{1}H-NMR spectrum (220 MHz) consists of two sharp $SiCH_3$ signals (τ = 9.80 and 9.81), a complex group of Si_2CH_2 signals (10.06 to 10.48) and an Si_3CH triplet (10.91), whose intensities are in the ratio 12 : 6 : 16 : 2. A more detailed analysis of the spectrum, supplemented by a double-resonance experiment, confirmed the structure *(2)*[3].

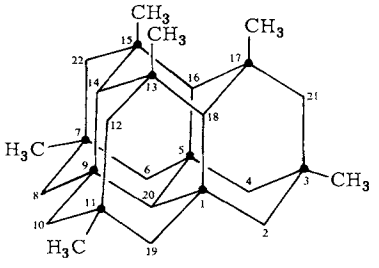
(3): *m/e* = 520.10496 (calc. for $Si_9C_{19}H_{40}^+$ 520.10534). ^{1}H-NMR: two sharp $SiCH_3$ signals (τ = 9.67 and 9.84), a group of Si_2CH_2 signals (10.20, 10.21, 10.28, 10.74), a doublet (10.74), and a quartet (10.84) due to the $SiCH_3$ protons; I_{rel} = 9 : 9 : 12 : 6 : 3 : 1. The 40 protons of *(3)* are distributed over six (3 + 3) $SiCH_3$, nine Si_2CH_2, and four Si_3CH groups. The CH_2 protons at positions 2, 4, 6, 8, 10, and 19

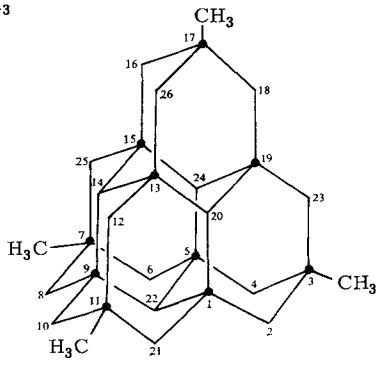




(1a), $R^1 = R^2 = R^3 = R^4 = CH_3$
(1b), $R^1 = R^2 = R^3 = R^4 = Cl$
(1c), $R^1 = R^3 = R^4 = Cl$; $R^2 = CH_3$
(1d), $R^1 = R^4 = Cl$; $R^2 = R^3 = CH_3$
(1e), $R^1 = Cl$; $R^2 = R^3 = R^4 = CH_3$
(1f), $R^1 = R^2 = R^3 = R^4 = H$

(2)





(3) *(4)*

• = Si

and those at 12, 21, and 22 are equivalent. Correspondingly, the Si_3CH protons at positions 14, 16, and 18 are symmetrically equivalent and can be differentiated from the proton on C-atom 20. W-coupling (spin-spin-splitting between protons in a planar $\begin{smallmatrix} H & & H \\ & \diagdown\ \diagup & \\ & Si & \\ C & & C \end{smallmatrix}$ arrangement) of C-20—H with C-14—H, C-16—H, and C-18—H causes splitting of the C-20—H signal into a quartet and conversely of the C-14—H, C-16—H, and C-18—H signal into a doublet; $J = 1.8$ Hz.

(4): *m/e* = 560.08118 (calc. for $Si_{10}C_{20}H_{40}^+$ 560.08227). ^{1}H-NMR: a sharp $SiCH_3$ signal ($\tau = 9.73$), an Si_2CH_2 signal (10.19), and an Si_3CH signal (10.87); $I_{rel} = 12 : 24 : 4$. The methyl protons at positions 3, 7, 11, and 17 are symmetrically equivalent; this is also true of the Si_2CH_2 protons at positions, 2, 4, 6, 8, 10, 12, 16, 18, 21, 23, 25, and 26 and of the Si_3CH protons at positions 14, 20, 22, 24.

These very stable and unreactive new compounds are crystalline, colorless, and sublime without decomposition in a Hg-vacuum [*(2)* at 140 °C; *(3)* at 200 °C; *(4)* at ≈ 200 °C]; they are only sparingly soluble in pentane, benzene, or carbon tetrachloride and moderately soluble in xylene (the solubility decreases with increasing molecular weight).

Nomenclature[**]: *(1a)*: 1,3,5,7-tetramethyl-1,3,5,7-tetrasilatricyclo[3.3.1.1^{3,7}]decane; *(2)*: 1,3,7,9,11,13-hexamethyl-1,3,5,7,9,11,13-heptasilahexacyclo[7.5.1.1^{3,13}.1^{7,11}.0^{5,12}.0^{5,15}]-heptadecane; *(3)*: 3,7,11,13,15,17-hexamethyl-1,3,5,7,9,11,13,-15,17-enneasilaenneacyclo [9.7.1.1^{1,5}.1^{3,17}.1^{7,15}.0^{5,16}.0^{9,14}.-0^{9,20}.0^{13,18}]docosane; *(4)*: 3,7,11,17-tetramethyl-1,3,5,7,9,11,-13,15,17,19-decasilaundecacyclo [9.9.1.1^{1,5}.1^{3,19}.1^{5,19}.1^{7,15}.-1^{13,17}.0^{9,14}.0^{9,22}.0^{13,20}.0^{15,24}]hexacosane.

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[**] Because of the complexity of the official nomenclature we suggest that these compounds be refered to as *carborundanes* – in line with the ideal structure of carborundum (zinc blende type).

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Separation of Nucleosides on Cytidine-Containing Polymer Gels in DMSO/$CHCl_3$ or Water

By *Herbert Schott* and *Gerd Greber*[*]

The separation of nucleosides on thymine- or cytidine-containing gels in DMSO/$CHCl_3$ is possible by reason of Watson-Crick base pairing[1]. We have now synthesized cytidine gels that swell in both organic solvents and in water and which carry a cytidine residue in each structural unit. This was achieved by crosslinking copolymerization of *N*-benzoyl-$O^{x'}$,$O^{y'}$-bis(trimethylsilyl)$O^{z'}$-methacryloylcytidine with *N*-benzoyl-$O^{x'}$,$O^{y'}$-bis(methacryloyl)cytidine[2]. In contrast to the products crosslinked with tetramethylene dimethacrylate[3], in which some structural units do not contain a nucleoside residue, it was possible to separate mixtures consisting of two of the nucleosides adenosine (A), thymidine (T), cytidine (C), and guanosine (G), not only in DMSO/$CHCl_3$ but also in distilled water (Tables 1 and 2).

As shown in Table 1, when the separation of nucleosides is carried out on C-gel in DMSO/$CHCl_3$ the Watson-Crick complimentary guanosine is retarded the strongest and consequently can be separated almost quantitatively from the other nucleosides. This finding and the results of experiments on the separation of other pairs of nucleosides can be explained by the fact that the hydrogen bonds between the base pairs exhibit different degrees of stability[4]. It is already known[5] that pairing of nucleic acid bases in organic solvents takes place predominantly by hydrogen bonding whereas in water

Table 1. Separation of equimolar mixtures of nucleosides on a C-gel in DMSO/$CHCl_3$ (2 : 3) at room temperature. Diameter of column 1 cm.

Column height (cm)	Nucleosides	Total amounts (mg)	Total amounts (ml)	Rate of flow (ml/h)	Separation effect [a]	Elution 1.	Elution 2.
43	TG	25	1.25	24	++	T	G
43	AG	25	1.5	24	++	A	G
100	CG	25	1.5	19	++	C	G
100	TC	50	2.5	19	+	T	C
100	AC	25	1.5	19	—	A	C
100	TA	50	1.25	11.5	—	T	A

[a] ++ almost quantitative separation; + good separation; —— no separation; — slight separation.

Table 2. Separation of equimolar mixtures of nucleosides on a C-gel in water at room temperature (column dimensions 20 cm/2 cm; total amount about 25 mg).

Nucleosides	Total amount (ml)	Rate of flow (ml/h)	Separation effect [a]	Elution 1.	Elution 2.
CG	40	145	++	C	G
TG	40	185	++	T	G
CA	20	165	+	C	A
TA	20	135	+	T	A
AG	40	100	—	A	G
TC	20	200	——		

[a] See footnote [a] in Table 1.

the base stacking effect makes the greater contribution. These different base pairing mechanisms are therefore responsible for the differing adsorption behavior of the same nucleoside mixture on the same gel in DMSO/$CHCl_3$ and in water.

For example, adenosine is so strongly adsorbed on C-gel from water that a separation of adenosine/guanosine in water is hardly quantitative but almost completely so in DMSO/$CHCl_3$. For the same reason the elution sequence of A and C is reversed on going from DMSO/$CHCl_3$ to water. Therefore, base pairing between cytidine and guanidine in our chromatographic system is only specific if it takes place predominantly *via* hydrogen bonding, as is the case in DMSO/$CHCl_3$.

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Haloformyl(perhaloalkyl)-sulfanes and -disulfanes [**]

By *Alois Haas, Hartmut Reinke*, and *Jürgen Sommerhoff* [*]

Haloformyl(perhaloalkyl)-sulfanes *(1)* and -disulfanes *(2)* have not previously been described. Reactions of the haloformyl group, *e.g.* hydrolysis, alcoholysis, aminolysis, and thiolysis, should lead to derivatives of these compounds of interest both as herbicides and for further syntheses. Earlier attempts to obtain chloroformyl(trifluoromethyl)sulfane *(1b)* by irradiation of CF_3SCl and CO did not give unambiguous results [1].

We now report the desired synthesis and unequivocal characterization of *(1b)* and of related formyl chlorides and fluorides.

Chloro(fluoroformyl)sulfane reacts with silver trifluoroacetate in absence of a solvent, in a sealed tube at −10 °C, almost quantitatively according to the equation:

$$CF_3COOAg + ClSCOF \rightarrow CF_3COOSCOF + AgCl \quad (3)$$

Fluoroformyl(trifluoroacetoxy)sulfane *(3)* is a colorless liquid, stable if moisture is excluded and decomposing to CO_2 and fluoroformyl(trifluoromethyl)sulfane *(1a)* when irradiated by UV light [3]:

$$(3) \xrightarrow{h\nu} CF_3SCOF + CO_2 \quad (1a)$$

Aluminum chloride converts *(1a)* in a sealed tube at room temperature into *(1b)* with fluorine-chlorine exchange in the haloformyl group.

Photolytic reaction of thiocarbonyl halides with chloro(haloformyl)sulfanes in a sealed tube at 20 °C is particularly suitable for preparation of analogous compounds of type *(2)*, *e.g.*:

$$F_2CS + ClSCOCl \xrightarrow{h\nu} ClF_2CSSCOCl \quad (2c)$$

$$Cl_{2-n}F_nCS + ClSCOF \xrightarrow{h\nu} Cl_{3-n}F_nCSSCOF \quad (2d),\ n=2;\ (2e),\ n=1$$

$$CF_3SCSF + ClSCOF \xrightarrow{h\nu} CF_3SCClFSSCOF \quad (2f)$$

	B.p. (°C/torr)	M.p. (°C)	^{19}F-NMR δ (ppm) [a]	^{19}F-NMR J_{FF} (Hz)
(1a)	8/760	—	42.0 d (CF_3) −53.0 q (COF)	19.5
(1b)	46.8/760	—	43.1	—
(2a)	65/760	—	46.5 d (CF_3) −41.5 q (COF)	2.0
(2b)	103.9/760	—	46.2	—
(2c)	164/760	−44	34.7	—
(2d)	96.6/760	−76	33.3 d ($CClF_2$) −42.3 t (COF)	2.2
(2e)	143/760	—	26.4 d (CCl_2F) −45.0 d (COF)	2.4
(2f)	158/750	—	38.9 d (CF_3) −44.3 d (COF) 56.0 dq (CClF)	$J_1 = 9.6$ $J_2 = 2.0$
(3)	74/745	—	75.0 (CF_3) −20.0 (COF)	—

[a] CCl_3F as internal standard.

The time required for irradiation (15—40 hours) depends on the degree of fluorination of the reactants. These reactions, which proceed *via* radicals [4], afford complex mixtures of products which can be separated by distillation (1-m spinning band column) and purified by gas chromatography.

(Fluoroformyl)- *(2a)* and (chloroformyl)-(trifluoromethyl)-disulfane *(2b)* are formed from chloro(haloformyl)sulfane and mercury(II) trifluoromethanethiolate:

$$(CF_3S)_2Hg + 2\ ClSCOX \rightarrow 2\ CF_3SSCOX + HgCl_2$$
(2a), X = F
(2b), X = Cl

It is here seen that chloro(chloroformyl)sulfane reacts only monofunctionally. Attempts to replace also the Cl atom of the chloroformyl group by the trifluoromethyl group failed. This accords with findings by *Zumach* and *Kühle*[5] in which ClCOSCl was attacked by thiols only at the *S*-bonded Cl atom.

Compounds *(1)* and *(2)* are water-clear, mobile liquids which are stable in absence of moisture (see Table).

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Direct Synthesis and Reactions of Bromo(pentafluorophenyl)silanes[1]

By *Manfred Weidenbruch* and *Nezam Wessal*[*]

Halo(pentafluorophenyl)silanes, which are of interest for the preparation of novel polysiloxanes, cannot be obtained by reaction of silicon tetrahalides with (pentafluorophenyl)-magnesium bromide or -lithium because, even with a large excess of the SiX_4 components, only tetrakis(pentafluorophenyl)silane is formed[2]. We have now found that a direct synthetic process[3] affords them easily and with a selectivity that is remarkable for perhalogenated compounds.

For instance, bromopentafluorobenzene reacts (optimum temperature: 600 °C) with a catalyst composed of silicon (85%) and copper (15%) to give 60% of dibromobis(pentafluorophenyl)silane *(1)*, b.p. 110 °C/0.6 torr, and 30% of tribromo(pentafluorophenyl)silane *(2)*, b.p. 205–208 °C, together with a little bromotris(pentafluorophenyl)silane, m.p. 83 °C:

$$C_6F_5Br + Si/Cu \xrightarrow{600\,^\circ C} \underset{(1)}{(C_6F_5)_2SiBr_2} + \underset{(2)}{C_6F_5SiBr_3}$$

Conversion of C_6F_5Br amounts to 10–30%, which indicates the advisability of a recycling technique in which the unused C_6F_5Br, b.p. 136 °C, is continuously distilled off fractionally from the less volatile products and returned to the heated catalyst. Decafluorobiphenyl *(3)*, m.p. 68 °C, b.p. 188 °C, is the only by-product formed in detectable amounts; the proportion of *(3)* formed depends on the copper content of the catalyst and produces difficulties if it exceeds 20%. On pure copper C_6F_5Br gives *(3)* quantitatively at 600 °C.

Chloropentafluorobenzene reacts analogously, giving chloro-(pentafluorophenyl)silanes, though the conversion is, as expected, lower because of the greater bond energy of R—Cl than of R—Br. Hexafluorobenzene does not react with the Si/Cu catalyst up to 600 °C.

Applicability of compounds *(1)* and *(2)* to synthesis of further pentafluorophenyl-substituted silanes and polysiloxanes is indicated by the annexed chart of some reactions of *(1)*:

$$\underset{(5)}{(C_6F_5)_2Si(OH)_2} \xrightarrow{120\,^\circ C} \underset{(6)}{[(C_6F_5)_2SiO]_n}$$

$$\underset{(4)}{(C_6F_5)_2SiF_2} \xleftarrow{SbF_3} \underset{(1)}{} \xrightarrow{C_2H_5MgBr} \underset{\text{b.p. 110 °C/0.4 torr}}{(C_6F_5)_2Si(C_2H_5)_2}$$

(H_2O: *(5)* ⇄ *(1)*; H_2O: *(1)* ⇄ *(4)*)

Heating *(1)* or *(2)* with antimony trifluoride leads to the fluorosilanes *(4)*, b.p. 207 °C, and $C_6F_5SiF_3$, b.p. 102 °C, respectively, which, like bromosilanes, react spontaneously with water. Hydrolysis of *(1)* and similarly of *(4)* proceeds *via* the stable silanediol *(5)*, m.p. 120–122 °C, which condenses at the melting point to give the resinous polysiloxane *(6)*, m.p. > 170 °C. On prolonged heating or on storage, *(6)* changes, without alteration in composition, to a silicone that is very resistant both thermally and chemically and has celluloid-like properties, melting at > 350 °C.

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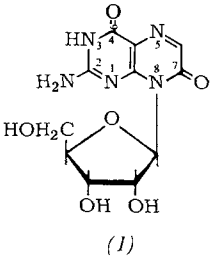
CONFERENCE REPORTS

Synthesis of Pteridine 8-Ribosides

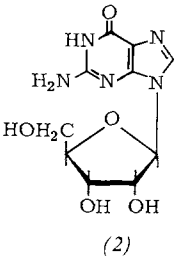
By *Wolfgang Pfleiderer*[*]

The synthesis of pteridine 8-ribosides *(1)*, the structural analogs of the purine nucleosides *(2)*, has been the focal point of our investigations in the field of pteridines for more than twelve years.

Previous investigations on the glycosidation of 7-oxo-7,8-dihydropteridines by the heavy-metal salt method have shown that 7-*O* glycosides are always formed and no *N*-8 glycosides[1]. The analogous behavior of the 2-oxodihydroquinoxalines[2] and of 2-pyrazinone[3] helped to clarify the complex nature of the reaction and showed that the observed selectivity in the direct glycosidation of the pteridine system



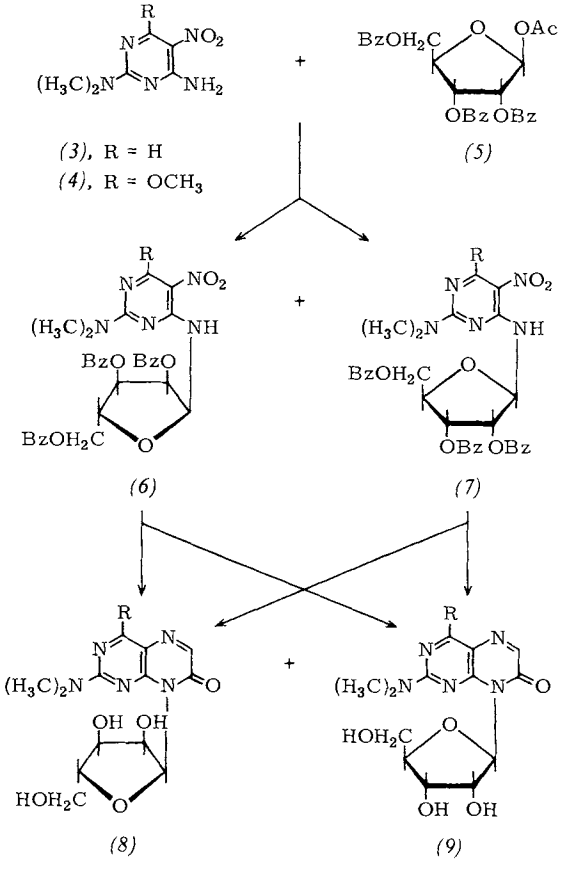
(1)



(2)

under such conditions is determined primarily by two factors steric hindrance and the particular electronic features of the pyrazine system — both of which oppose an $O \rightarrow N$ transglycosidation.

The first definite synthesis of a pteridine 8-glucoside was accomplished in 1964[4] using 4-amino-6-dimethylaminopyrimidine as starting material. The carbohydrate group was introduced into the molecule at the pyrimidine stage; amination at C-5 *via* the benzeneazo derivative followed by cyclization with α-oxo esters completed the synthesis. A further successful variant was found for the synthesis, namely the reaction of 4-chloro-5-nitropyrimidines with 1-aminohexoses to give 4-glycopyranosylamino derivatives which, on reduction and cyclization, afford the 7-oxo-7,8-didydropteridine 8-glycopyranosides[5]. Since attempts to use this method of synthesis in the ribofuranose series failed because of the instability of 1-amino-2,3,5-tribenzoylribofuranose, a new preparative route was developed on the basis of a fusion reaction. For instance, 4-amino-5-nitropyrimidines *(3)* and *(4)* react with fully acylated sugars such as 1-acetyl-2,3,5-tribenzoylribofuranose *(5)* on fusion in the presence of acid catalysts[6]. The 4-amino groups of *(3)* and *(4)* undergo ribosidation in good yield if the reactants are heated for 30 mins at 160 °C in the presence of $ZnCl_2$ as catalyst. Separation of the reaction mixture by layer chromatography showed that a mixture of anomers is formed under such vigorous reaction conditions and that the α-riboside *(6)* is the predominant product in each case. Assignment of the pure ribosides to the α- and β-series was established by analysis of the NMR spectra and by decoupling experiments. No definite conclusions could be drawn from the ORD spectra.



Surprisingly, it was found that the pure anomers *(6)* or *(7)* are partially anomerized to the pteridine-*N*-8-riboside during both the catalytic hydrogenation of the 5-nitro to the 5-amino group and the reaction with glyoxylate. Compounds *(8)* and *(9)* could be separated by preparative layer chromatography.

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[6] *H. Rokos*, Dissertation, Universität Stuttgart 1967.

Recent Work on Insect Sex Attractants

By *Karl Eiter*[*]

The insect sex attractants found so far belong to one of the following classes: Singly or multiply unsaturated, straight-chain or slightly branched alcohols and their esters; olefinic carboxylic acids and their esters; heterocyclic and aliphatic substances resembling terpenes.

The sex attractant of the gypsy moth (*Porthetria = Lymantria dispar*), reported to be (+)-1-hexyl-10-hydroxy-3-*cis*-decenyl acetate and synthesized stereospecifically by *Jacobson et al.*[1] has been prepared by us[2] and by *Stefanovic et al.*[3] in a stereospecifically uniform synthesis and found to posses no biological activity. The explanation offered by the American authors[1], namely that the activity is inhibited by contamination with small amounts of the *trans* compound, was shown to lack any substance since mixtures of the synthetic material with active extracts exhibited a definite activity in an electroantennogram (EAG)[**]. *Jacobson et al.*[1] have further described the synthesis of 1-hexyl-12-hydroxy-3-*cis*-dodecenyl acetate, "gyplure", which is reported to be just as active as the gypsy moth attractant. We have also synthesized this substance stereospecifically and found it to be completely inactive. It follows that the structure given for the gypsy moth attractant cannot be correct.

Isolation and structural elucidation of the sex attractant of the American cockroach (*Periplaneta americana*) were also reported by *Jacobson et al.*; after publication of a total synthesis of this cyclopropane derivative by *Day* and *Whiting*[4], which yielded a biologically inactive product, they later retracted their claims.

The sex attractant of the pink bollworm moth (*Pectinophora gossypiella* S.) is given by *Jacobson et al.*[5] as 10-propyl-5-*trans*,9-tridecadien-1-ol, "propylure". On carrying out a sterically non-uniform synthesis we obtained a product completely lacking activity. *Jacobson*[6] repeated the synthesis and isolated the pure *trans* compound from the mixture of isomers. The presence of 15—20% of the *cis* compound was said to inactivate the attractant completely. This finding is the same as in the case of the gypsy moth attractant and rather unlikely, particularly in view of reports that the activity of propylure in field tests depends on the presence of activators (*N,N*-diethyl-*m*-toluamide : mosquito repellent Autan®)[7] and that 7-*cis*-hexadecenyl acetate, "hexalure", is considerably more active than propylure and is not inhibited by the *trans* compound[8].

In the present state of uncertainty regarding their mode of action, the pheromones of other insects, which are possibly only quantitatively definite mixtures of three or four synergically acting components, can hardly be used as models for studies on the problem whether insect pests can be attracted specifically to some central position. This paramount question of modern pest control still cannot be answered owing to the confusion present in this field of research.

Lecture at Kiel on April 16, and
at Erlangen on May 29, 1970 [VB 238 IE]
German version: Angew. Chem. *82*, 485 (1970)

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Farbenfabriken Bayer,
Wissenschaftliches Hauptlaboratorium
509 Leverkusen-Bayerwerk (Germany)

[**] An electroantermogram is a recording of the electric potential measured on the antenna receptors in the presence of attractant (microelectrodes).

[1] *M. Jacobson, M. Beroza,* and *W. A. Jones,* Science (Washington) *132,* 1011 (1960); J. Amer. chem. Soc. *83,* 4819 (1961).

[2] *K. Eiter, E. Truscheit,* and *M. Boness,* Liebigs Ann. Chem. *709,* 29 (1967).

[3] *D. Stefanovic, B. Grujić,* and *D. Mićić,* Ištita Bilja *73,* 235 (1963).

[4] *A. C. Day* and *M. C. Whiting,* Proc. chem. Soc. (London) *1964,* 368; *1966,* 64.

[5] *W. A. Jones, M. Jacobson,* and *D. F. Martin,* Science (Washington) *152,* 1516 (1966).

[6] *M. Jacobson,* Science (Washington) *163,* 190 (1969).

[7] *W. A. Jones* and *M. Jacobson,* Science (Washington) *159,* 99 (1968).

[8] *N. Green, M. Jacobson,* and *J. C. Katter,* Experientia *25,* 682 (1969).

Problems of Copolymerization in Multicomponent Systems

By *Wolfhart Ring* [*]

The rules governing copolymerization of multicomponent systems are based on simple kinetic premises. From them can be calculated the composition of a copolymer and the distribution of sequences of the same monomer unit as affected by monomer concentration and degree of conversion. Copolymerization parameters ("*r* values") are normally used for characterizing the polymerization behavior, these parameters being valid for a given monomer pair; they are available in tabular form.

The distribution of the sequences often have a great effect on the technological and physical properties of industrial copolymers, and this was discussed for two cases:

1. Ethylene-propane rubber. To repress the crystallization of the product as much as possible, it is desirable that there should be no long sequences (> 10—15) of the two components. The kinetic criterion for a suitable catalyst is as low a numerical value as possible for the product $r_{ethylene} \times r_{propene}$.

2. Styrene-butadiene copolymers — these are important as synthetic elastomers. On radical initiation, the copolymerization properties of styrene and butadiene present no problem in relation to distribution of sequences (short styrene sequences are desirable). However, on anionic initiation, the reactivities of the two monomers are generally so different that discontinuous copolymerization processes are excluded. Kinetiv calculations permit determination of suitable reaction conditions for a continuous process in a steady-state reactor [1].

Radical copolymerization can be discussed from the general standpoint of the relation between structure and reactivity, as shown, for example, in the work of *Bamford* and *Jenkins* [2].

Lecture at Hannover on April 30, 1970 [VB 239 IE]
German version: Angew. Chem. *82,* 485 (1970)

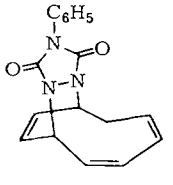
[*] Dr. W. Ring
Chemische Werke Hüls AG
4370 Marl (Germany)

[1] *W. Ring,* Macromolekulare Chem. *75,* 20 (1964).

[2] *A. D. Jenkins,* Advances Free Radical Chem. *2,* 139 (1967).

SELECTED ABSTRACTS

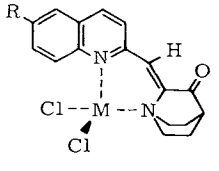
The cycloaddition of *cis,cis,cis*-1,3,5,7-cyclononatetraene to 4-phenyl-1,2,4-triazoline-3,5-dione has been studied by *A. G. Anastassiou* and *R. P. Cellura.* At —78 °C they obtained the adduct *(1)* (m.p. 181—183 °C, yield about 60%) as sole

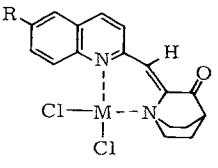


(1)

product. *(1)* could be distinguished from its conceivable isomers by NMR spectroscopy. / Tetrahedron Letters *1970,* 911 / —Kr. [Rd 181 IE]

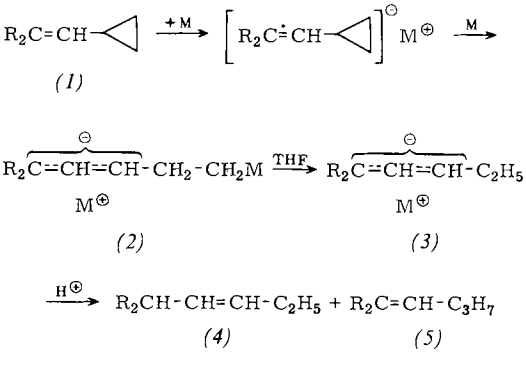
Isomeric nickel complexes from *trans*-2-(2-quinolyl)methylene-3-quinuclidone and its 6-methoxy derivative have been obtained by *D. L. Coffen* and *T. E. McEntee jr.* On admixture of transition metal dichlorides in ethanol with the ligands the complexes *(1), (2), (5),* and *(6)* crystallize. On attempted recrystallization from methylene chloride/ethanol complex *(2)* was converted irreversibly into *(3).* The structures were assigned on the basis of the IR spectra and the fact that Co^{II} forms tetrahedral complexes and Cu^{II} planar ones. The magnetic moments for *(1), (6), (7),* and *(8)* confirm the structures assigned and also indicate contamination of *(8)* with *(6).* / J. Amer. chem. Soc. *92,* 503 (1970) / —Kr. [Rd 183 IE]





(1), M = Co, R = OCH_3 *(3)*, M = Cu, R = OCH_3
(2), M = Ni, R = OCH_3 *(4)*, M = Ni, R = OCH_3
(5), M = Co, R = H *(7)*, M = Cu, R = H
(6), M = Ni, R = H *(8)*, M = Ni, R = H

Addition of alkali metals to 1,1-diphenyl-2-cyclopropylethylene *(1)* has been studied by *A. Maercker.* The deep red THF solution obtained from *(1)* and Na/K alloy afforded a 3 : 2 mixture of the 1,1-diphenylpentenes *(4)* and *(5)* on hydrolysis. As shown by carboxylation of the reaction mixture to

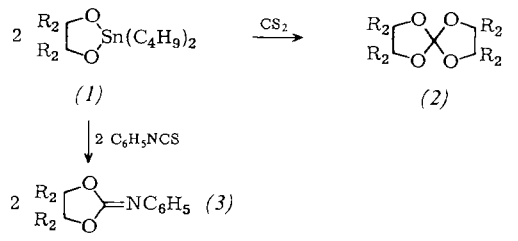


(1), *(2)*, *(3)*, *(4)*, *(5)*

R = C_6H_5

2,2-diphenyl-3-hexenoic acid and 2-ethyl-4,4-diphenyl-3-butenoic acid, *(4)* and *(5)* must arise from the monoanion *(3).* Reaction with lithium gave the same acids together with higher homologs (ethylene taken up from solvent). The Li—C bond in the dianion *(2)*, M = Li, could be detected directly. / Liebigs Ann. Chem. *732,* 151 (1970) / —Kr. [Rd 182 IE]

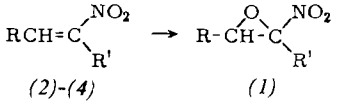
Spiroorthocarbonates *(2)* and cyclic iminocarbonates *(3)* have been obtained on a preparative scale by *S. Sakai, Y. Kobayashi*, and *Y. Ishii* on treatment of cyclic dibutyltin dialkoxides *(1)* with carbon disulfide and phenyl isothiocyanate, respectively. The organometal compound is removed as dibutyltin sulfide. Examples: *(1a)*, R = H, →*(2a)*, R = H,



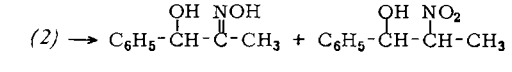
(1) *(2)*

82% yield, b.p. 60—70 °C/0.5 torr; *(1b)*, R = CH_3, →*(3b)*, R = CH_3, b.p. 120—125 °C/0.4 torr (100%). / Chem. Commun. *1970*, 235 / — Kr. [Rd 185 IE]

α-Nitro epoxides (nitrooxiranes) *(1)*, a new group of compounds, were obtained by *H. Newmann* and *R. B. Angier* from nitro olefins and hydrogen peroxide in the presence of alkali. For example, (2-nitropropenyl)benzene *(2)*, R = C_6H_5, R′ = CH_3, *cis*-α-nitrostilbene *(3)*, R = R′ = C_6H_5, and (2-nitropropenyl)cyclohexane *(4)*, R = cyclohexyl, R′ = H, gave the nitro epoxides *(1)* in 67, 85, and 91% yield, respectively. However, for steric reasons *trans*-α-nitrostilbene did not react. The nitro epoxide from *(2)* (as example) behaves towards nucleophilic reagents like an α-halo ketone. With acids, *e.g.* dilute aqueous H_2SO_4, it gives 1-hydroxy-1-phenylacetone and a small amount of diketone. Reducing agents



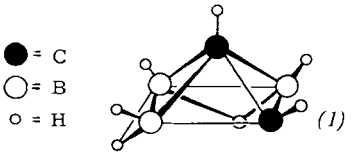
(2)-(4) *(1)*



(5) *(6)*

such as Zn/aqueous acetic acid afford the oxime *(5)*; catalytic hydrogenation over PtO_2 leads to *(5)* and 2-nitro-1-phenyl-1-propanol *(6)*. / Tetrahedron *26*, 825 (1970) / —Ma. [Rd 188 IE]

A new carborane cage system, 1,2-$C_2B_3H_7$, is described by *D. A. Franz* and *R. N. Grimes*. The compound, 1,2-dicarba-*nido*-pentaborane *(1)*, a member of a new class of small carboranes, is isoelectronic and isostructural with pentaborane, B_5H_9. It was obtained in 3—4% yield by gas-phase reaction of tetraborane with an excess of acetylene at 50 °C and was purified by gas chromatography. Its structure was proved by IR, NMR, and mass spectra. It is stable in the vapor phase at 50 °C but in the liquid phase it polymerizes



(1)

rapidly at room temperature. It reacts rapidly with B_2H_6 at 50 °C but not with B_4H_{10}. / J. Amer. chem. Soc. *92*, 1438 (1970) / —Ma. [Rd 189 IE]

Photochemical synthesis of aromatic chloro compounds from aromatic iodo compounds that are readily accessible has been reported by *F. Kienzle* and *E. C. Taylor*. Dilute solutions of the iodo derivatives in CCl_4 were irradiated with light of wavelength 3000 Å, iodine exchange occurring without formation of impurities due to position isomerization. After reaction for 5 hours the conversion amounted to 70—75%; the reaction probably occurs in accord with the scheme:

$$ArI \rightarrow Ar^{\cdot} + I^{\cdot}$$
$$Ar^{\cdot} + CCl_4 \rightarrow ArCl + {}^{\cdot}CCl_3$$
$$2\,I^{\cdot} \rightarrow I_2$$
$$2\,{}^{\cdot}CCl_3 \rightarrow C_2Cl_6$$

Hexachloroethane was isolated in yields of up to 5%. Electron-donating substituents accelerate halogen exchange, electron-attracting substituents decelerate it. Examples are *p*-chloroanisole (96% yield), *o*-chlorophenol (80%), *o*-chlorobenzoic acid (51%). / J. org. Chemistry *35*, 528 (1970) / —Ma. [Rd 190 IE]

Isolation, properties, and reactions of chlorocarbonyl isocyanate *(1)* have been described by *W. Gottardi* and *D. Henn*. On photolysis of gaseous chlorine isocyanate *(2)* with light of > 280 nm in a vacuum, N_2, CO, and phosgene are formed together with an orange product *(1)* which after purification is obtained as a colorless liquid, m.p. —68 °C, b.p. 63 °C. Formation of *(1)* probably occurs by the primary radical-forming reactions:

$$2\,ClN{=}CO \rightarrow (Cl_2N{-}C(O){-}N{=}CO \rightarrow Cl_2N^{\cdot} + {}^{\cdot}C(O){-}NCO$$
$${}^{\cdot}C(O){-}NCO + ClN{=}CO \rightarrow ClC(O){-}NCO + {}^{\cdot}N{=}CO$$

(1) is both an isocyanate and an acid chloride and is thus sensitive to moisture. With less than the stoichiometric amount of water it affords, besides cyanic acid and CO_2, the previously unknown iminodiformyl dichloride, ClCO—NH—COCl, m.p. 88—89 °C. / Mh. Chem. *101*, 11 (1970) / —Ma. [Rd 191 IE]

Spectroscopic evidence for the $H_5O_2^+$ ion in the crystalline dihydrate of perchloric acid at —180 °C is presented by *A. C. Pavia* and *P. A. Giguère*. The absence of certain IR and Raman bands characteristic of H_3O^+ and H_2O confirms the existence of $H_5O_2^+$ ions in that crystal postulated previously on the basis of X-ray diffraction data. The spectra are consistent with a *trans* H_2O—H—OH_2 structure of approximate C_{2h} symmetry. In the deuterated compound IR spectra indicate the existence of $D_5O_2^+$ with the same structure. Unfortunately, the interference of strong ClO_4^- bands prevents identification of all the fundamentals of $H_5O_2^+$. / J. chem. Physics *52*, 3551 (1970) / —Hz. [Rd 193 IE]

Synthesis and attempted automerization of [1-^{13}C]naphthalene are reported by *H. A. Staab* and *M. Haenel*. The Grignard derivative from 1-bromo-3-phenylpropane was converted by $^{13}CO_2$ (from barium [^{13}C]carbonate) into 4-phenyl[1-^{13}C]-butyric acid. Ring closure of the acid chloride to give [1-^{13}C]-tetralone was followed by Clemmensen reduction and dehydrogenation (yield 55% based on barium [^{13}C]carbonate). The ^{13}C enrichment amounted to 50.6%. NMR spectra and the ESR spectrum of the radical anion showed selective α-labeling. No automerization could be detected under the conditions given by *Balaban* and *Fărcaşiu*[1] for [1-^{14}C]-naphthalene (heating with $AlCl_3$ in benzene at 60 °C). / Chem. Ber. *103*, 1095 (1970) / —Kr. [Rd 202 IE]

[1] *A. T. Balaban* and *D. Fărcaşiu*, J. Amer. chem. Soc. *89*, 1958 (1967); Tetrahedron Letters *1968*, 1273.

Adamantane as a matrix for the preparation and conservation of free radicals is recommended by *D. E. Wood* and *R. V. Lloyd*. Some radicals obtained by X-irradiation and found to be relatively stable (half-lives in the order of 10 h at room temperature) are *tert*-alkyl, benzyl, phenoxyl, semiquinone, and tropyl. As adamantane provides a nonpolar matrix with essentially spherical holes, the radicals can easily rotate, and their ESR spectra are normally isotropic at temperatures from −120 to +80 °C. A new class of free radicals was obtained by X-irradiation of aliphatic amines; they are formed by removal of a hydrogen atom *alpha* to the amine group. The average spin density on the trigonal carbon is estimated to be 0.63 in this class of radicals; thus about 1/3 of the spin density is delocalized, presumably on to nitrogen. / J. chem. Physics *52*, 3840 (1970) / —Hz. [Rd 192 IE]

The conductivity of imidazole single crystals was studied by *A. Kawada, A. R. McGhie*, and *M. M. Labes*. The conductivity in the crystallographic *c* direction, the direction of the hydrogen bonds, exceeds the conductivity along the *a* axis by a factor of about 10^3 provided that surface conduction is eliminated. After a sluggish start, electrolysis in *c* direction evolves up to 0.97/2 moles of H_2 per Faraday at the negative electrode. The conduction mechanism is thought to consist in injection of an "L-defect", a proton vacancy in a hydrogen bond. For further supply of charge carriers the imidazole molecules must reorient around an axis in the ring plane perpendicular to the *c* axis. This process accounts well for the relatively high activation energy of 1.7 eV. / J. chem. Physics *52*, 3121 (1970) / —Hz. [Rd 194 IE]

The primary photochemical processes of tetramethyl-*p*-phenylenediamine (TMPD) have been investigated by *J. T. Richards* and *J. K. Thomas* in cyclohexane, ethanol, and water. In cyclohexane, singlet fluorescence with 3.2 ns half-life and the triplet state absorption spectrum were observed; the triplet decays by triplet-triplet annihilation accompanied by delayed fluorescence. N_2O, SF_6, and CO_2 quench the excited singlet state; N_2O also reacts with triplet TMPD forming a charge transfer complex. In ethanol, the singlet fluorescence has a half-life of 5.1 ns; the triplet is also observed, but it decays over several 100 ns. Photolysis of TMPD in water produces, instead of fluorescence and triplet absorption, $TMPD^+$ (Wurster's blue) and hydrated electrons. The energy difference between exciting light (3.6 and 4.75 eV, corresponding to 3472 and 2650 Å) and the ionization potential of gaseous TMPD (about 7 eV) is supplied by the solvation energy of the ions produced. No biphotonic processes were observed with laser excitation. / Trans. Faraday Soc. *66*, 621 (1970) / —Hz. [Rd 195 IE]

BOOK REVIEWS

Chemie heisser Atome (Chemistry of Hot Atoms). By *G. Stöcklin*. Vol. 6 of the "Chemischen Taschenbücher", edited by *W. Foerst* and *H. Grünewald*. Verlag Chemie GmbH, Weinheim/Bergstr. 1969. 1st ed., ix, 284 pp., 49 figures, 53 tables, paperback DM 18.—.

The reactions of "hot atoms", *i.e.* chemical reactions in the range 1—10 eV (0.025 eV corresponds to 300 °K) form a very heterogeneous field of investigation, which is full of controversies. Consequently, existing articles in scientific handbooks are mostly confined to collections of experimental facts and the reproduction of more or less speculative attempted interpretations. A "chemical pocket book" intended both as an introduction for students and as a review for the expert is therefore an undertaking that will undoubtedly be greeted with scepticism at first by the initiated. This merely adds to the respect one acquires for this book on reading it. The author has declined to discuss the pros and cons of the many hypotheses on high-energy reactions, which are so confusing to beginners in particular, but has confined his treatise largely to established facts, or else he expressly points out the hypothetical nature of statements cited. The author has also succeeded in presenting the numerous experimental facts clearly and understandably, despite their diversity.

The reader is first acquainted with the established physical facts concerning hot reactions. This is followed in the second part by experimental observations concerning numerous chemical systems and the most important theories on these observations. Out of a total of perhaps 2000 publications in this field, about 370 have been selected for illustration. Most of these are concerned with the reactions of tritium and of ^{14}C and ^{11}C. The other two topics, *i.e.* "Reactions of hot halogen atoms" and "Hot reactions in inorganic solids", are discussed in less detail, on the grounds (which are only partly valid) that these fields have not yet led to such definite results as the reactions of T and C.

Earlier models that have had an influence on developments are also briefly mentioned. It is gratifying to find that the priorities, which are often blurred in the literature, are correctly represented here (cf. p. 213).

On the whole, the present book can be described as a successful exposition of the "reactions of hot atoms", which lives up to the aims of the series of "pocket books". Physical chemists who are interested in high-energy reactions and organic chemists who are interested in labeled compounds may also find it useful.

Franz Baumgärtner [NB 873 IE]

Citric Acid Cycle. Control and Compartmentation. Edited by *J. M. Lowenstein*. Marcel Dekker, Inc., New York-London 1969. 1st ed., xxi, 366 pp., numerous figures, $ 17.75.

A reader who is not familiar with the trends in biochemistry will perhaps be surprised to find that the present monograph on the citric acid cycle tells him nothing about individual reactions, the coenzymes involved, *etc.*, and does not even contain the well-known diagram of the cycle. The book, which is not intended for beginners, presupposes such (by no means inconsiderable) biochemical knowledge. Details of reaction mechanisms are of no interest in any case in a book whose real theme is stated in the subtitle "Control and Compartmentation" (*i.e.* in the field of cell metabolism insofar as it is related to the citric acid cycle).

The first and longest article (by *G. D. Greville*) presents a sort of "topographical biochemistry" of the cell, in which the localization of the enzymes in the cell compartments, the displacements of the metabolites between these compartments, and the transport problems that arise are discussed. The interplay of these factors leads to a complicated network of interdependent reaction chains, which are separated as far as possible and examined with a view to establishing their importance. This treatment, which takes into account the situation in the intact cell, differs very considerably in some points from the "one-dimensional" picture of the metabolism as shown in essence by our textbooks.

The next two contributions (*D. E. Atkinson*; *P. B. Garland et al.*) try to draw a coherent picture of the control mechanisms that are involved in the synthesis and degradation of citric acid and that connect the citric acid cycle more inti-

mately with the fatty acid metabolism. The variety of the existing or assumed mutual influences is confusing, and imposes on the authors a need for a particularly critical view. Reference is repeatedly made to the difficulty of deducing the situation in the living cell from experiments *in vitro* ("Thus a postulated control mechanism may not in fact control *in vivo* nor may so called "regulatory enzymes" play a regulatory role").

Further contributions deal with the role of α-ketoglutaric acid (*J. M. Tager et al.*) and of the dicarboxylic acids (*M. F. Utter*) in metabolism. An enzyme-kinetic study of inhibition mechanisms of antimetabolites produced by the introduction of fluorine (*E. Kum*) provides the material for the final chapter.

The book is intended primarily for advanced biochemists and for biologists with corresponding interests, who will welcome a book by competent authors in this important field, which summarizes the results of various special lines of investigation (with more than 1000 references, extending up to 1968 in some cases).

To the chemist who possesses the knowledge mentioned above, this book, the title of which is really too modest, offers a source of information on the principal lines of research in modern biochemistry. While chemistry progresses toward a more detailed understanding of the properties of molecules, biochemistry is concentrating increasingly on combining the individual processes into one integrated picture. Since it is no longer concerned with the study of isolated reactions, or even cycles, but mainly with how they are linked and how they influence one another, it has taken an important step toward the true goal of its research.

Carl Martius [NB 876 IE]

Strahlen-Biochemie (Radiation Biochemistry). By *C. Streffer*. Vol. 59/60 of the "Heidelberger Taschenbücher". Springer-Verlag, Berlin-Heidelberg-New York 1969. 1st ed., xi, 196 pp., 69 figures, stitched DM 14.80.

In contrast with irradiation with UV light, in which a certain selectivity of the chemical reactions and biological effects induced by the radiation can be achieved by means of the wavelength used, the action of ionizing radiation on biological objects leads to many radiation-chemical reactions and biological phenomena. In the present pocket book the author has attempted to examine critically the voluminous, but in part very diffuse, material published so far on the basis of biochemistry and to present it in an orderly manner. As is stressed in the preface, research in the field of radiation biology is rapidly advancing, and it is not yet possible to glimpse the causal relationships in many cases. The blame for the rather confusing impression received by those who are not very familiar with the field on reading this book, as well as books on similar topics, cannot therefore be laid on the author, but is due rather to the present state of research.

After an introduction to the principles of radiation research, the changes suffered by the nucleic acids, proteins, and amino acids, carbohydrates, lipids, hormones, and vitamins (including their metabolism), as well as the respiratory chain, the metabolism of energy-rich phosphates, and the electrolyte balance on irradiation are described in a well-ordered manner. The bibliography includes 277 references, mainly to recent publications, with the aid of which earlier publications can be found.

The pocket book is recommended above all to chemists, biochemists, biologists, and physicians who wish to familiarize themselves with the problems of the irradiation of biological objects with ionizing radiations prior to their own scientific studies. *Egon Fahr* [NB 878 IE]

Electron Microscopy and Microanalysis of Metals. Edited by *J. A. Belk* and *A. L. Davies*. Elsevier Publishing Co. Ltd., Amsterdam-London-New York 1968. 1st ed., xiv, 254 pp., 80 figures, Dfl. 47.50.

The scope of the material sciences has recently been so greatly increased by the electron microscope and the microprobe that the use of these two instruments should be known to every materials engineer and metallographer, and to a certain extent also to metal and chemical technologists. The present book is excellently suited to provide a rapid survey of the construction and applications of these instruments. Following an introduction to electron optics by *W. James*, the editors and other well-known electron microscopists present the principles of electron diffraction and specimen preparation (thin films and replicas) and the use of the electron microscope in studies on deformations, strains, and precipitation processes. Further sections, also by renowned authorities, deal with the construction and operation of the microprobe, qualitative analysis using this instrument, and its industrial use.

Despite the large number of authors, the book still retains the character of an independent review of these two important methods for the investigation of solids. The concentrated text is relieved by numerous texture photographs, literature references at the end of each chapter offer an opportunity for further reading in this field, and a subject index facilitates searches and shows the relationships between the various chapters. Though the book is intended primarily for advanced students, it is also a valuable reference work for practising metallurgists, metallographers, and materials engineers. It can be stated quite positively that no previous knowledge of the subject is assumed, and that the practical aspect is stressed, while the theoretical principles are introduced only insofar as they are necessary for an understanding and for successful work. *Günter Petzow* [NB 880 IE]

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Recent Chemistry and Biochemistry of Bile Pigments[**]

By Wolfhart Rüdiger[*]

Bile pigments are not merely waste products of the degradation of hemoglobin, but have specific functions in plants and lower animals, in which they occur in the form of chromoproteins (biliproteins). Chromic acid degradation under controlled conditions is particularly suitable for structural investigations. In the case of the phycobilins (bile pigments of red and blue algae), not only have the structures been established, but the linkages with the proteins have also been located.

1. Formation and Occurrence of Bile Pigments in Vertebrates

Hemoglobin *(1)*, the red blood pigment in man and the vertebrates, is continuously being synthesized and degraded [1,2]. Whereas the formerly complexed iron is retained in the organism and re-utilized for the synthesis of the blood pigment, the degradation products of the complexing agent (porphyrin) are excreted. The first isolable degradation product is bilirubin *(2)*, which occurs mainly in the bile and is the principal pigment of this body fluid. *(2)* is therefore referred to as "the bile pigment", and compounds having the same basic skeleton as *(2)*, irrespective of their occurrence, are known as "the bile pigments".

Bilirubin passes with the bile into the intestine, where it is hydrogenated by microorganisms to form urobilinogen *(3)* and stercobilinogen *(4)*. These are the principal excretion products, which partly change in air into urobilin *(5)* and stercobilin *(6)*; some mesobiliviolin *(7)* and mesobiliverdin [= glaucobilin, *(8)*] are also formed from *(3)*.

Bilirubin *(2)* is also present in small quantities (bound to albumin [3]) in the blood serum of healthy individuals. Under pathological conditions (icterus) its concentration here (and in the bile) is increased; it is then excreted in the urine and deposited particularly in elastin-rich tissues. The further transformation products *(3)*, *(4)*, *(5)*, and *(6)* are also formed in increased quantities under pathological conditions. The detection and the determination of bile pigments are therefore of clinical importance [4].

Instead of *(2)*, the bile of birds and of some reptiles contains the blue-green biliverdin *(9)*, which is readily obtainable *in vitro* by dehydrogenation of *(2)*, but is probably the precursor of *(2)* *in vivo* [5–7]. *(9)* is also found in the serum of some fish [8–10].

2. Occurrence of Bile Pigments in Other Organisms

Whereas the bile pigments of the vertebrates can be described as waste products of the degradation of the blood pigment, this description would be incorrect for most other organisms. Bile pigments frequently occur in plants and lower animals that do not contain hemoglobin or other heme or porphyrin components in corresponding amounts. The pigments are often bound

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[**] Extract from the Habilitation Thesis of *W. Rüdiger*, Universität Saarbrücken 1968.

[1] *R. Lemberg* and *J. W. Legge*: Hematin Compounds and Bile Pigments. Interscience Publ., New York 1949, p. 453ff., 603ff.

[2] Cf. *C. Rimington*, Annu. Rev. Biochem. *26*, 561 (1957).

[3] *T. K. With*: Biologie der Gallenfarbstoffe. Thieme, Stuttgart 1960, p. 124.

[4] Cf. [3], p. 319.

[5] *R. Lemberg*, Biochem. J. *29*, 1322 (1935).

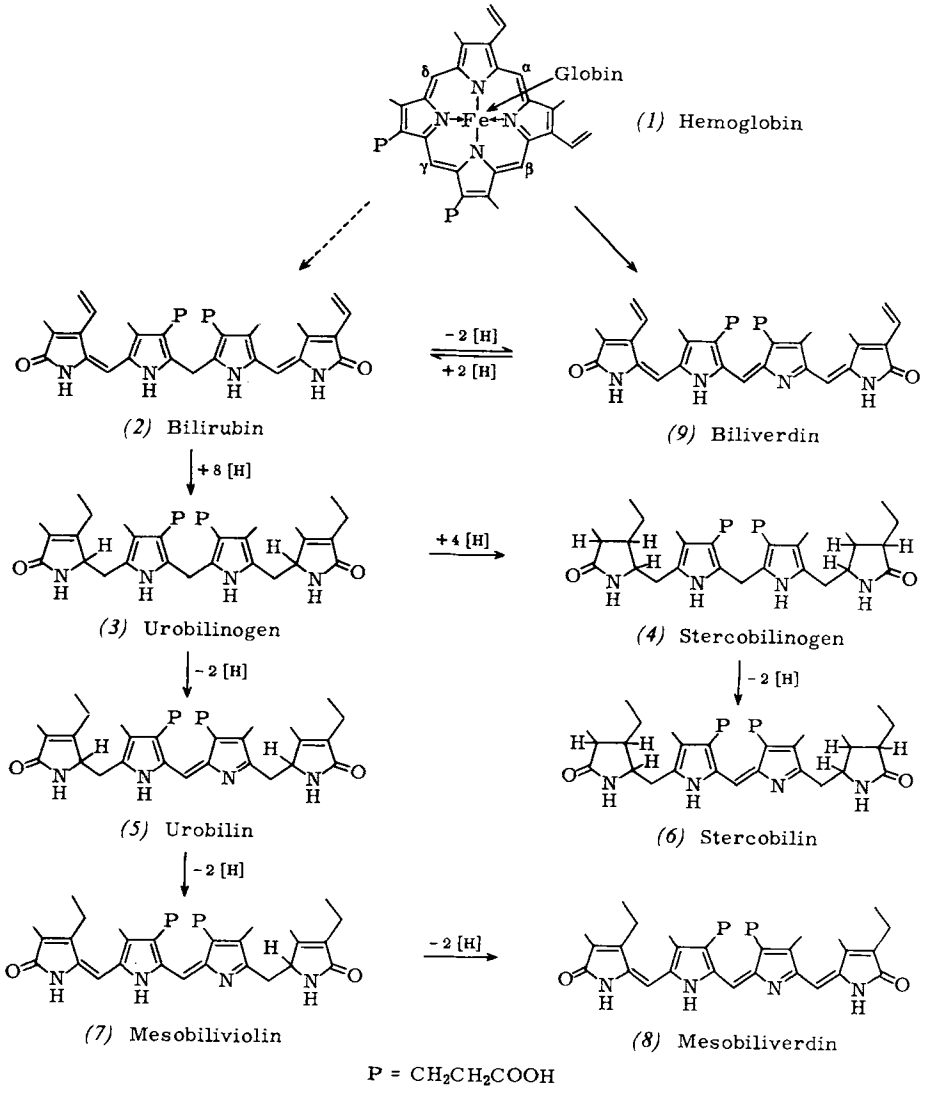
[6] Cf. *R. Lemberg*, Rev. pure appl. Chem. *6*, 1 (1956).

[7] *C. Ó hEocha* in *T. W. Goodwin*: Porphyrins and Related Compounds. Academic Press, London 1968, p. 91.

[8] *L. Abolinš*, Ark. Zool. (2) *13*, 541 (1961).

[9] *Y. Kōchiyama, K. Yamaguchi, K. Hashimoto*, and *F. Matsuura*, Bull. Japan. Soc. Sci. Fisheries *32*, 867 (1966).

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Scheme 1. Formation of bile pigments of the IXα series in man and in vertebrates. "IXα" means derived from protoheme IX by oxidative opening of the α methine bridge.

to proteins (biliproteins); some are known to have specific functions (protective coloring in insects, photosynthetic activity in algae, photoregulation of growth and development in higher plants).

Table 1 lists the occurrence of bile pigments (except in bile and serum). It can be seen that biliverdin IXα *(9)* is the most widespread; other bile pigments are found in only a few animals [biliverdin IXγ *(10)*, aplysioviolin *(11a)*] or plants [phycobilins *(11)* and *(12)* and phytochrome chromophore *(13)*]. Data on the occurrence of other pigments described as bile pigments (of unknown structure) are not included (confusion with carotenoids and ommochromes, see [11–13]).

Table 1. Occurrence of bile pigments outside bile and serum.

Pigment		Animal or Plant	Organ	Ref.
Biliverdin IXα *(9)*		Dog	Placenta	[14, 15]
Biliverdin IXα *(9)*		Bird	Egg-shells	[16, 17]
Biliverdin IXα *(9)*		Fish	Fish-bones	[18–21]
Biliverdin IXα *(9)*	[a]	Fish	Fins, skin	[22, 23]
Biliverdin IXα *(9)*	[a]	Grasshopper	Integument, hemolymphs	[24–28]
Biliverdin IXα *(9)*		Blue coral	Skeleton	[29, 30]
Biliverdin IXγ *(10)*	[a]	Butterflies	Integument	[31, 32]
Aplysioviolin *(11a)*	[a]	Sea hare (Aplysia)	Secretion	[33, 34]
Biliverdin IXα *(9)*	[a]	Legumes	Root nodules	[35, 36]
Phycobilins *(11)*, *(12)*	[a]	Red- and blue algae	Thallus	
Phytochrome chromophore *(13)*	[a]	Higher plants	All parts	[37, 38]

[a] As chromoprotein.

[11] *J. Verne*: Les pigments dans l'organisme animal. Doin, Paris 1926, cited after *M. Fontaine*, Bull. Inst. océanogr. Monaco *1941*, No. 792.

[12] *L. Abolinš*, Acta Zool. *38*, 223 (1957), and p. 235.

[13] Cf. *A. Butenandt, U. Schiedt, E. Biekert*, and *P. Kornmann*, Liebigs Ann. Chem. *586*, 217 (1954).

[14] *R. Lemberg* and *J. Barcroft*, Proc. Roy. Soc. (London), Ser. *B 110*, 362 (1932).

[15] *R. Lemberg* and *J. Barcroft*, Biochem. J. *28*, 978 (1934).

[16] Sea-gulls: *R. Lemberg*, Liebigs Ann. Chem. *488*, 74 (1931); *499*, 25 (1932).

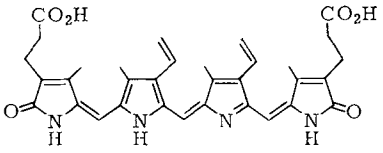
[17] Emu: *R. Tixier*, Ann. Inst. océanogr. Monaco *22*, 343 (1945).

[18] *Zoarces viviparus*: *H. Willstaedt*, Enzymologia (Den Haag) *9*, 260 (1941).

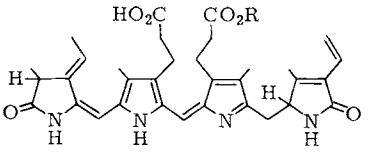
[19] *Katsuwonus pelamis* L.: *D. L. Fox* and *N. Millott*, Experientia *10*, 185 (1954).

[20] *Belone belone*: *W. Rüdiger*, unpublished.

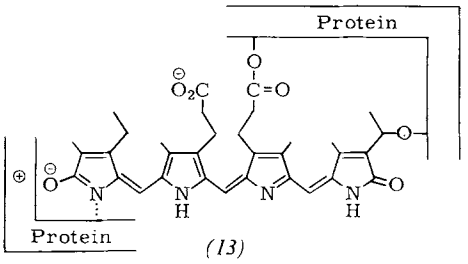
[21] *Cololabis saira Brevoort*: *Y. Tsuchiya* and *T. Nomura*, C. R. Séances Soc. Biol. Filiales *155*, 34 (1961).



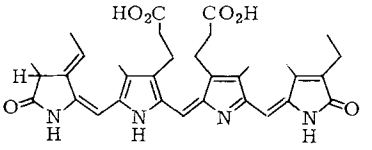
(10)



(11), R = H
(11a), R = CH_3



(13)

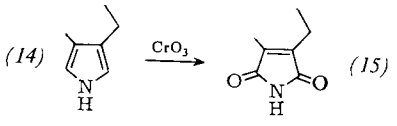


(12)

3. General Methods of Investigation

3.1. Chromic Acid and Chromate Degradation

Pyrrole pigments and some simple pyrrole derivatives, *e.g.* *(14)*, give maleimides on oxidation with chromium trioxide, the substituents in the β positions remaining intact [39].



(14) (15)

The rate of this reaction is pH-dependent [40]. It has been found that bile pigments can be distinguished from other pyrrole compounds (porphyrins, chlorophylls, vitamin B_{12}) by this reaction. This may be illustrated for protoporphyrin [*(1)* without Fe and globin] and biliverdin IXα *(9)*. At the same pH value (in this case pH = 1.7), the extinction of the bile pigment decreases almost 100 times as rapidly as that of the porphyrin ($t_{1/2}$ = 4.5 min and 420 min respectively).

The half lives of these decoloration reactions [40] under the conditions used here are between 0.5 and 20 min for bile pigments; pigments with unsaturated side chains [*e.g. (9)* with its vinyl groups] are decolorized more rapidly than those with saturated side chains [*e.g. (8)* with its ethyl groups]. Porphyrins, chlorins, and corrins are oxidized under the same conditions with half lives ranging from several hours to days.

Degradation with dichromate/hydrogen sulfate (pH ≈ 1.7), referred to below as "chromate degradation", and degradation with chromium trioxide in 2 N H_2SO_4, referred to below as "chromic acid degradation", both have proved suitable for the investigation of bile pigments. The chromic acid degradation is carried out at 20 °C ("non-hydrolytically") or at 100 °C ("hydrolytically").

A given bile pigment gives different degradation products, depending on the conditions used (Scheme 2). Thus the chromate degradation of *(9a)*, the dimethyl ester of *(9)*, yields the pyrroledicarbaldehyde *(18a)* as a new degradation product, together with methylvinylmaleimide *(16)* and hematinimide methyl ester *(17a)*, which is formed in small quantities. *(18a)* is an intermediate in the imide formation. On chromic acid degradation it is converted into the expected imide, *i.e. (17a)* at 20 °C and *(17)* at 100 °C. *(17a)* and *(17)* are also formed directly from the pigment *(9a)*.

Methylvinylmaleimide *(16)* is formed in roughly the same yield under all the conditions mentioned, but is destroyed by chromium trioxide in more strongly acidic media (*e.g.* 6 N H_2SO_4). Since 6—10 N H_2SO_4 had always been used in earlier chromic acid degradations of pyrrole pigments [42–44], *(16)* was not found in these investigations.

Pyrrole-2,5-dicarbaldehydes cannot be derived from the terminal (pyrrolone) rings (I and IV) of the original bile pigment, since they contain *two* of the former bridge C atoms. It has been shown [41] that with pigments of the biliverdin

[22] *L. Abolinš* and *W. Rüdiger*, Experientia *22*, 298 (1966).

[23] *W. Rüdiger* and *L. Abolinš*, Experientia *25*, 574 (1969).

[24] *Mantis religiosa*: *M. Passama-Vuillaume*, C. R. hebd. Séances Acad. Sci. *258*, 6549 (1964).

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[27] *Clitumnus extradentatus*: *W. Rüdiger*, *W. Klose*, *M. Vuillaume*, and *M. Barbier*, Bull. Soc. Chim. biol. *51*, 559 (1969).

[28] *Carausius morosus*: *W. Rüdiger*, unpublished.

[29] *R. Tixier*, Ann. Inst. océanogr. Monaco *22*, 379 (1945).

[30] *W. Rüdiger*, *W. Klose*, *B. Tursch*, *N. Houvenaghel-Crevecoeur*, and *H. Budzikiewicz*, Liebigs Ann. Chem. *713*, 209 (1968).

[31] *W. Rüdiger*, *W. Klose*, *M. Vuillaume*, and *M. Barbier*, Experientia *24*, 1000 (1968).

[32] *M. Vuillaume* and *M. Barbier*, C. R. hebd. Séances Acad. Sci. *268*, 2286 (1969).

[33] *W. Rüdiger*, Hoppe-Seylers Z. physiol. Chem. *348*, 129 (1967).

[34] *W. Rüdiger*, Hoppe-Seylers Z. physiol. Chem. *348*, 1554 (1967).

[35] *A. I. Virtanen* and *J. K. Miettinen*, Acta chem. scand. *3*, 17 (1949).

[36] *W. Rüdiger*, *W. Klose*, and *R. Lichter*, unpublished.

[37] *H. W. Siegelman*, *B. C. Turner*, and *S. B. Hendricks*, Plant Physiol. *41*, 1289 (1966).

[38] *W. Rüdiger* and *D. L. Correll*, Liebigs Ann. Chem. *723*, 208 (1969).

[39] Cf. *H. Fischer* and *H. Orth*: Die Chemie des Pyrrols. Akad. Verlagsges., Leipzig 1934, Vol. 1, p. 39.

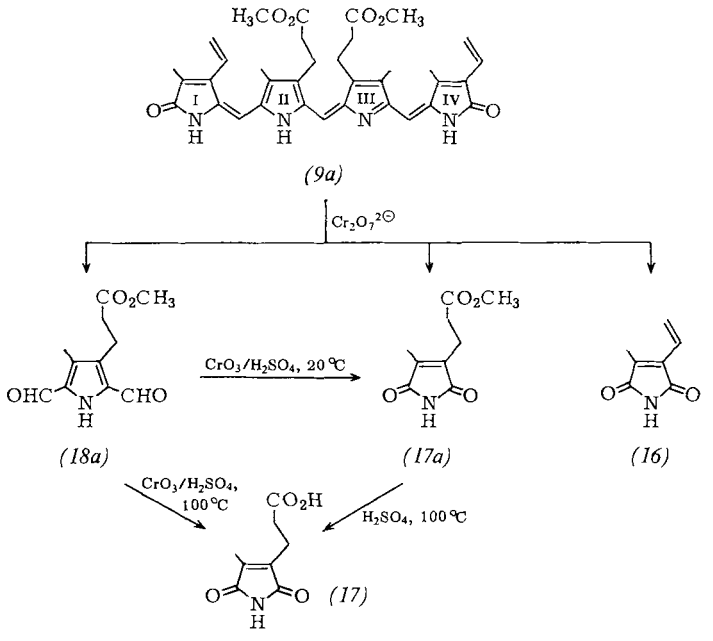
[40] *W. Rüdiger*, Hoppe-Seylers Z. physiol. Chem. *350*, 1291 (1969).

[41] *W. Rüdiger*, unpublished.

[42] *H. Fischer* and *H. Wenderoth*, Liebigs Ann. Chem. *537*, 170 (1939).

[43] *H. M. Muir* and *A. Neuberger*, Biochem. J. *45*, 163 (1949).

[44] *G. E. Ficken*, *R. B. Johns*, and *R. P. Linstead*, J. chem. Soc. (London) *1956*, 2272.



Scheme 2. Chromic acid and chromate degradation of biliverdin IXα dimethyl ester *(9a)*.

type the dialdehydes are derived from *both* inner rings (II and III), while with pigments of the mesobiliviolin *(7)* type they are derived almost exclusively from ring II.

Thus, by identification of the degradation products in the chromate degradation, it is possible to establish not only the nature but in some circumstances also the sequence of the β substituents of a bile pigment ("sequence analysis").

3.2. Separation and Identification

An effective separation method is important not only for the isolation and identification of the degradation products but also for the purification and characterization of the bile pigments. Thin layer chromatography has been found to be suitable, and is superior *e.g.* to column chromatography in the case of the pigments; these two methods are equally good for the degradation products.

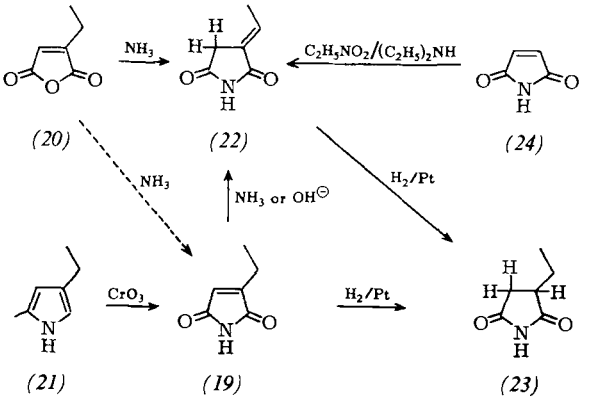
The *bile pigments* are best separated from one another in the form of their dimethyl esters. In the standard developer (benzene/petrol/methanol 9 : 5 : 1)[33], the R_f value increases with the number of conjugated pyrrole rings [*e.g. (5)* < *(7)* < *(8)*]; the pigments containing vinyl groups migrate farther than their analogs with ethyl groups. Even very similar pigments (*e.g.* isomeric urobilins and mesobiliverdins[46]) can be separated by multiple development[45]. Finding the positions of the spots presents no problems, owing to their color; they are characterized by their color and the fluorescence colors of the zinc complexes in UV light[33]. Useful mass spectra can be obtained even with small quantities (approx. 0.1 mg) of the pigments isolated by thin layer chromatography[47].

In the standard developer for the *degradation products* (carbon tetrachloride/ethyl acetate/cyclohexane 5 : 3 : 1)[33,48], succinimides do not migrate so far as maleimides and pyrroledicarbaldehydes; the R_f values for all the degradation products increase with the chain length of the β-alkyl substituent. Difficult separations [*e.g. (15)* from *(16)*] can be effected by multiple development[40]. The color reaction of the imides with chlorine/benzidine[40,49] is sensitive, but not specific; it is advantageous to use the mass spectra of the imides isolated by thin layer chromatography for a sure identification[50]. Pyrroledicarbaldehydes can be detected by spraying with 2,4-dinitrophenylhydrazine[40].

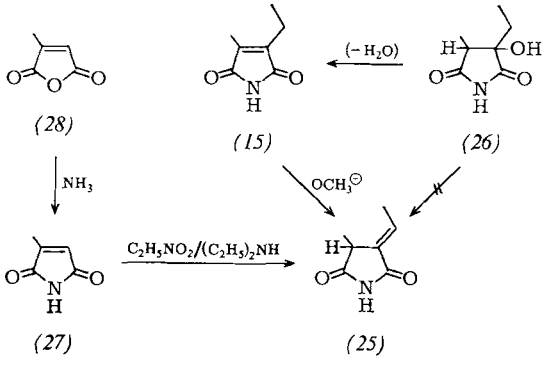
3.3. Synthesis of Comparison Substances

Maleimides and succinimides can be obtained by reaction of the anhydrides with ammonia or urea, and have often been prepared as comparison substances for the degradation products of pyrrole pigments[43,44,51].

Conflicting data were found for ethylmaleimide *(19)*. *Anschütz*[52] had obtained a product having m.p. 141 °C from the anhydride *(20)* with ammonia, whereas the product *(19)* obtained by *Fischer et. al*[53] by chromic acid oxidation of 2-methyl-4-ethylpyrrole *(21)* melted at 80 °C. The product obtained by *Fischer*'s method was found to consist solely of *(19)*, whereas the mixture obtained by *Anschütz* consisted mainly of ethylidenesuccinimide *(22)*[48]. *(22)* was prepared independently from maleimide *(24)* and nitroethane[54].



When heated with alkali (*e.g.* even with ammonia), *(19)* is converted smoothly into *(22)*. A corresponding rearrangement also occurs with the methyl homolog *(15)*, but only when methoxide is used [maximum yield of *(25)* = 5%][54].



Scheme 3. Routes for the synthesis of ethylidenemethylsuccinimide *(25)*.

[45] Cf. *E. Stahl*: Dünnschichtchromatographie. 2. Edit., Springer-Verlag, Berlin 1967, p. 87.

[46] *L. Paulmann*, Diplomarbeit, Universität Saarbrücken 1968.

[47] *H. Budzikiewicz* and *W. Rüdiger*, unpublished.

[48] *W. Rüdiger* and *W. Klose*, Tetrahedron Letters *1966*, 5893.

[49] Cf. *F. Reindel* and *W. Hoppe*, Chem. Ber. *87*, 1103 (1954).

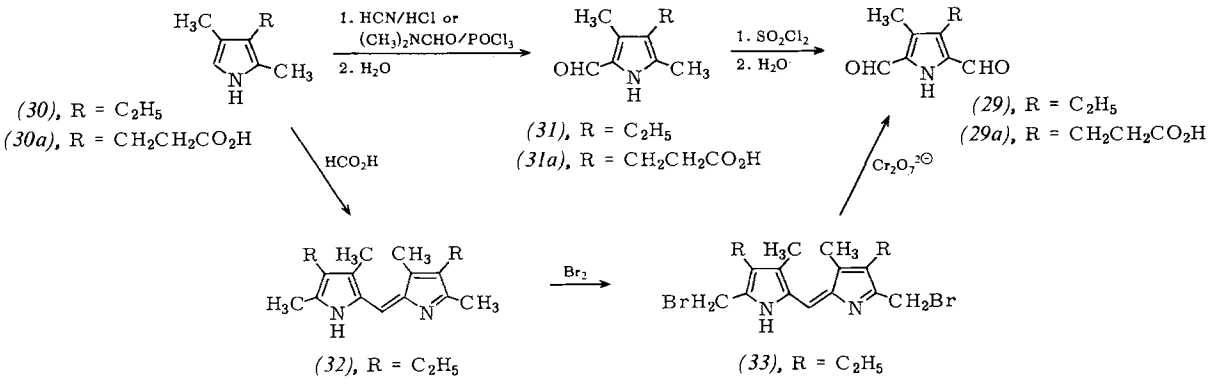
[50] *R. K. Ellsworth* and *S. Aronoff*, Arch. Biochem. Biophysics *124*, 358 (1968).

[51] *W. Küster*, Liebigs Ann. Chem. *345*, 1 (1906), and p. 18.

[52] *R. Anschütz*, Liebigs Ann. Chem. *461*, 155 (1928), and p. 169.

[53] *H. Fischer*, *A. Treibs*, and *G. Hummel*, Hoppe-Seylers Z. physiol. Chem. *185*, 33 (1929), and p. 53.

[54] *W. Rüdiger* and *W. Klose*, unpublished.



Scheme 4. Routes for the synthesis of 3-ethyl-4-methylpyrrole-2,5-dicarbaldehyde *(29)* and the propionic acid derivative *(29a)*.

Routes for the synthesis of this imide, which is a degradation product of aplysioviolin *(11a)* and of the phycobilins *(11)* and *(12)*, are summarized in Scheme 3 [40,41,55].

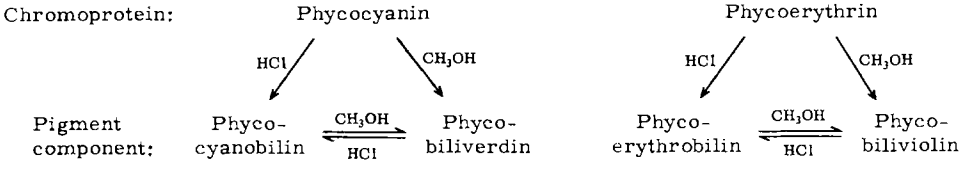
3-Ethyl-4-methylpyrrole-2,5-dicarbaldehyde *(29)* was chosen as a comparison substance for the chromate degradation [56]. The synthesis of this compound from cryptopyrrole *(30)* is shown in Scheme 4 [40,54,56,57]. Analogous reactions with propionic acid derivatives are also possible [54].

4. Chromoproteins of Red and Blue Algae

Red algae (Rhodophytae), blue algae (Cyanophytae), and Cryptophytae are distinguished from other algae by their red and blue pigments. Like the chlorophylls, these are light receptors for photosynthesis [58]. The red pigments are known as phycoerythrins and the blue pigments as phycocyanins. Depending on source and properties, we distinguish between R-, B-, C-, and cryptomonad phycoerythrins and R-, C-, allo-, and cryptomonad phycocyanins [59].

Numerous investigations have already been carried out on the structure of these pigments. *Kylin* [60] was able to crystallize the pigments and to confirm the assumed [61] protein nature by cleavage with pepsin; however, neither this author nor *Lemberg* [62] could obtain protein-free, colored groups with pepsin or with acid. *Lemberg* [63] managed to split off the protein-free bile pigment mesobiliverdin *(8)* from the phycoerythrin of red algae, and this was later [64] identified as mesobiliverdin IXα by X-ray investigations; owing to the color change that accompanies this cleavage, however, mesobiliviolin *(7)* has been considered to be the actual prosthetic group.

Two methods that lead to new bile pigments were described some time ago: 1. Cleavage of the phycobiliproteins with concentrated hydrochloric acid at room temperature yields pigments whose spectra agree with those of the denatured chromoproteins, and which are regarded as the native chromophores phycoerythrobilin and phycocyanobilin [65,66]. 2. Treatment with boiling methanol gives similar bile pigments, which were at first [67] thought to be the protein-free biological precursors of the chromoproteins and named "blue pigment" and "purple pigment", but were later [68] shown to be cleavage products of the chromoproteins. These pigments will be referred to as phycobiliviolin and phycobiliverdin. Phycoerythrobilin and



Scheme 5. Isolation and transformation of phycobilins. 12 N HCl, 30 min at 20 °C; CH_3OH, 24 h at 65 °C.

phycobiliviolin are interconvertible, as are phycocyanobilin and phycobiliverdin [68]. The formation of these bile pigments (phycobilins) from the chromoproteins (phycobiliproteins) is shown in Scheme 5.

4.1. Comparison of Phycobiliviolin with Aplysioviolin

Aplysioviolin *(11a)*, the principal pigment of the defensive secretion of sea hares (Aplysia), is presumably derived from phycoerythrin, which these molluscs

[55] *W. Rüdiger* and *W. Klose*, Tetrahedron Letters *1967*, 1177.

[56] *H. Fischer*, *E. Baumann*, and *H. J. Riedl*, Liebigs Ann. Chem. *475*, 205 (1929), and p. 234

[57] *H. Fischer* and *M. Schubert*, Ber. dtsch. chem. Ges. *56*, 1202 (1923).

[58] Cf. *F. T. Haxo* and *L. R. Blinks*, J. gen. Physiol. *33*, 389 (1950).

[59] On the occurrence of individual types cf. *C. Ó hEocha* in *T. W. Goodwin*: Biochemistry of Chloroplasts. Academic Press, London 1966, Vol. 1, p. 409.

[60] *H. Kylin*, Hoppe-Seylers Z. physiol. Chem. *69*, 169 (1910); *76*, 396 (1911/12).

[61] *H. Molisch*, Bot. Ztg. *52*, 177 (1894); *53*, 131 (1895).

[62] *R. Lemberg*, Liebigs Ann. Chem. *461*, 46 (1928); *477*, 195 (1930).

[63] *R. Lemberg* and *G. Bader*, Liebigs Ann. Chem. *505*, 151 (1933).

[64] *W. Siedel*, Ber. dtsch. chem. Ges. *77*, 21 (1944), and p. 41

[65] *C. Ó hEocha*, Biochemistry *2*, 375 (1963).

[66] *P. Ó Carra*, *C. Ó hEocha*, and *D. M. Carroll*, Biochemistry *3*, 1343 (1964).

[67] *Y. Fujita* and *A. Hattori*, J. gen. appl. Microbiol. (Tokyo) *9*, 253 (1963); J. Biochemistry (Tokyo) *51*, 89 (1962).

[68] *P. Ó Carra* and *C. Ó hEocha*, Phytochemistry *5*, 993 (1966).

ingest with their food (which includes red algae)[69]. *(11a)* is more readily obtainable than the phycobilins, since it is only loosely bound (presumably by salt-like bonds) to the protein in the secretion, and can thus be obtained free from protein under mild conditions with no secondary changes. Its structure was therefore established at an early stage[33,34]. Aplysioviolin *(11a)* is a monomethyl ester; the phycobilins obtained by methanolysis, on the other hand, are unesterified dicarboxylic acids.

For comparison purposes, all the pigments were converted into the dimethyl esters. The dimethyl esters from phycobiliviolin and aplysioviolin are identical according to their chromatographic behavior (mixed chromatograms in several developers), the electronic spectra of the free bases, the hydrochlorides, and the zinc complexes, and the reactions with alkali and acid[70,71]. The algal pigment is thus the dicarboxylic acid *(11)* whose monomethyl ester is aplysioviolin *(11a)*. This supports the name "phycobiliviolin" introduced here (instead of "purple pigment").

4.2. Chromate and Chromic Acid Degradation of the Phycobilins

Aplysioviolin and phycobiliviolin are decolorized by chromate under standard conditions (cf. Section 3.1) with a half life of 0.5 min; they thus undergo this reaction faster than any other bile pigments[40]. The structural agreement of these two pigments was further confirmed by a comparison of their degradation products. Chromic acid degradation of *(11)* at 20 °C yields methylvinylmaleimide *(16)*, ethylidenemethylsuccinimide *(25)*, and hematinimide *(17)*, while *(11a)* also gives the ester *(17a)*. On chromate degradation, both pigments give the pyrroledicarbaldehyde *(29a)* as well as the imides. These results agree with the structure *(11)* assumed for phycobiliviolin.

Phycoerythrobilin also gives the imides *(16)*, *(17)*, and *(25)* on chromic acid degradation, while chromate degradation also yields the dialdehyde *(29a)*. This means that the substituents in the β positions in this pigment are the same as in phycobiliviolin; since the two pigments are interconvertible, the substituents must occupy the same positions. The differences in the spectra are thus due to differences in the α positions of the pyrrole rings, which have not yet been investigated in detail.

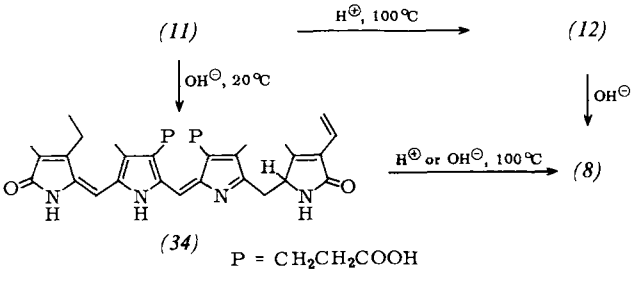
The pigments phycobiliverdin ("blue pigment") and phycocyanobilin obtainable from the phycocyanins give the imides *(15)*, *(17)*, and *(25)* as well as the pyrroledicarbaldehyde *(29a)* on chromic acid or chromate degradation. Thus the side chains in the β positions are again the same in both pigments. Since the first of these pigments ("blue pigment") is most like mesobiliverdin *(8)* in its spectral properties, it will be called phycobiliverdin. The structure *(12)* can be deduced from the degradation results and from the spectral behavior.

The structures *(11)* and *(12)* were proposed for the pigments obtained from the biliproteins with boiling methanol[72] in independent investigations on the basis of the mass and NMR spectra[73–76]. The dicarboxylic acid containing 2 hydrogens more than *(12)* at first supposed to be the native pigment[73] is possibly a product of disproportionation in the mass spectrometer[76].

4.3. Reactions of the Phycobilins with Alkali and Acid

The spectra of all phycobilins (and their chromoproteins) exhibit reversible bathochromic shifts in the alkaline range. The red bile pigments temporarily become blue, and the blue pigments turn colorless to light yellow at first, since the principal absorption band is displaced into the near infrared, and there is no longer a band in the visible region of the spectrum.

This shift can initially be reversed by neutralization of the solution but new pigments are formed (slowly in the cold, rapidly on heating) in alkaline solution. *(11)* first gives a pigment similar to mesobiliviolin, which has the structure *(34)* according to the results of the chromic acid degradation. It is converted by prolonged action of alkali into mesobiliverdin *(8)*, which is formed directly from *(12)*. Since the mesobiliverdin obtained by alkaline hydrolysis of the red chromoprotein had already been identified as the IXα isomer[64], it follows that all phycobilins have the IXα structure.



When *(11)* is heated with dilute hydrochloric acid, the principal product is *(12)*. In concentrated hydrochloric acid, on the other hand, the reaction leading to phycoerythrobilin[68] and further to a urobilin[77]

[69] *D. J. Chapman* and *D. L. Fox*, J. exp. Marine Biol. Ecology *4*, 71 (1969).

[70] *W. Rüdiger*, *P. Ó Carra*, and *C. Ó hEocha*, Nature (London) *215*, 1477 (1967).

[71] *W. Rüdiger* and *P. Ó Carra*, Europ. J. Biochem. *7*, 509 (1969).

[72] Called phycocyanobilin or phycoerythrobilin in [73–76].

[73] *H. L. Crespi*, *L. J. Boucher*, *G. D. Norman*, *J. J. Katz*, and *R. C. Dougherty*, J. Amer. chem. Soc. *89*, 3642 (1967).

[74] *W. J. Cole*, *D. J. Chapman*, and *H. W. Siegelman*, J. Amer. chem. Soc. *89*, 3643 (1967).

[75] *D. J. Chapman*, *W. J. Cole*, and *H. W. Siegelman*, J. Amer. chem. Soc. *89*, 5976 (1967).

[76] *H. L. Crespi*, *U. Smith*, and *J. J. Katz*, Biochemistry *7*, 2232 (1968).

[77] *W. J. Cole*, *C. Ó hEocha*, *A. Moscowitz*, and *W. R. Krueger*, Europ. J. Biochem. *3*, 202 (1967).

predominates. In contrast to the alkali reaction the ethylidene group is retained in all these reactions. The acid causes a prototropic rearrangement in which a vinyl group is converted into an ethyl group, with simultaneous conversion of a methylene bridge into a methine bridge. Rearrangements of this type are known in other bile pigments [78,79].

4.4. Linkage of the Phycobilins to the Protein

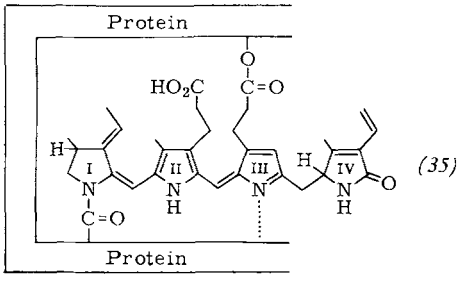
The chromic acid degradation of the native chromoproteins gives different results, depending on the conditions. This may be illustrated for C-phycocyanin. At 100 °C (hydrolytic degradation), the initially precipitated protein is hydrolyzed to peptides, which pass into solution; the same imides [*(15)*, *(17)*, and *(25)*] are obtained from the solution as from the free phycobilin *(12)*. If, on the other hand, the chromoprotein is degraded at 20 °C (non-hydrolytically), the protein precipitate remains intact; though the same quantity of *(15)* can be extracted from the suspension as on hydrolytic degradation, only half as much *(17)* is obtained, and no *(25)*. The missing imides [*(25)* and the second half of *(17)*] can be liberated by hydrolysis (without further oxidizing agent) from the separated and washed protein precipitate.

The same result is obtained with R-phycocyanin and in principle with R- and C-phycoerythrin, as well as with the chromopeptides obtainable from C-phycoerythrin with pancreatin, except that the red pigments give *(16)* instead of *(15)*.

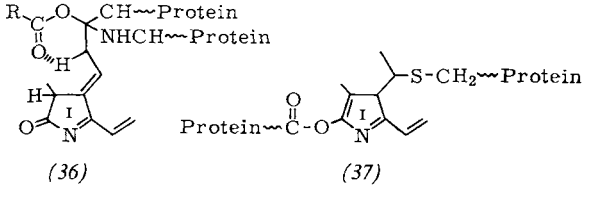
According to these degradation experiments, only two of the four pyrrole nuclei of the phycobilins are free in the native chromoprotein, whereas the other two must be covalently linked to the protein. It is not yet known which functional group of the protein is involved in this linkage. In any case, the terminal ring I [which yields the imide *(25)*] and one of the inner rings [from which *(17)* is formed] must be bound, while the terminal ring IV [which gives *(15)* or *(16)*] and the other inner ring are free. Which of the inner rings is free and which is bound has been established for phycoerythrin. The pyrroledicarbaldehyde *(29a)* is liberated on chromate degradation at 20 °C, while the imide *(17)* is liberated only on hydrolysis of the protein precipitate. Since the pyrroledicarbaldehyde is formed from ring II in bile pigments of the biliviolin type (cf. Section 3.1), this ring must be free, while the ring III, which yields the imide, is bound.

The pyrrole nitrogen of ring III is probably masked by a hydrogen bond in the native chromoprotein, this hydrogen bond being broken on denaturation. For example, the nitrogen atom is accessible for the formation of a zinc complex in the denatured chromoprotein, but not in the native substance [66,80]. The nitrogen cannot be involved in the covalent bonding of ring III; linkage *via* the propionic acid side chain is most likely, and is certainly not an amide linkage, as was formerly [81] assumed, but presumably an ester linkage (but one that is relatively stable to alkali) [65,66]. We have shown the probable existence of an *N*-acyl linkage (*e.g.* aspartoyl or glutamoyl) between ring I and the protein [71]; this gives *(35)* as a partial formula of the biliprotein phycoerythrin.

Possibilities discussed for the linkage between ring I and the protein in C-phycocyanin are *(36)* [76] and *(37)* [82], in which the ethylidene group is not present as such in the chromoprotein, but is formed only when the phycobilin is split off. A decision between these (and other) possibilities will probably become possible only after the amino acid sequence of the phycobiliproteins has been established.



(35)



(36) *(37)*

5. Further Results and Possibilities

Of the other results obtained by the methods described here (cf. Table 1), mention should be made of the discovery of biliverdin IXγ *(10)* [31], the first natural bile pigment that does not belong to the IXα series. In the investigation of its biosynthesis [83], as in the classic studies on the biosynthesis of porphyrin [43,84], the specific incorporation of radioactively labeled glycine into the pigment was detected by a definite degradation (in this case chromate degradation). Attention should also be drawn to the cases in which bile pigments are linked *covalently* to the protein. This has been so far found only for Crenilabrus blue in the animal kingdom [22,23] and for the phycobiliproteins and the gene regulator phytochrome in the plant kingdom [37,38].

Chromic acid degradation has played an important part in the elucidation of the structures of numerous

[78] *C. H. Gray* and *D. C. Nicholson*, J. chem. Soc. (London) *1958*, 3085.

[79] *C. H. Gray*, *A. Kulczycka*, and *D. C. Nicholson*, J. chem. Soc. (London) *1961*, 2268.

[80] *C. Ó hEocha* and *P. Ó Carra*, J. Amer. chem. Soc. *83*, 1091 (1961).

[81] Cf. [1], p. 147.

[82] *H. L. Crespi* and *U. H. Smith*, Phytochemistry 9, 205 (1970).

[83] *W. Rüdiger*, *W. Klose*, *M. Vuillaume*, and *M. Barbier*, Experientia *25*, 487 (1969).

[84] Cf. *D. Shemin*, Methods in Enzymol. *4*, 643 (1957).

pyrrole pigments [85]. Rapid progress may be expected in the investigation of new members of this class of compounds by the establishment of optimum degradation conditions for each type of pigment, operation on the micro scale, and combination of sensitive separation methods with modern analytical aids.

[85] A brief review of the most important works is given in [40].

My own investigations on the phycobilins were mainly carried out in collaboration with Dr. P. Ó Carra, Department of Biochemistry, University College, Galway (Eire). I am grateful to Professor C. Ó hEocha for his cooperation. Thanks are due to the Deutsche Forschungsgemeinschaft for generous support.

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Interferons

By Y. K. S. Murthy and Hans-Peter Anders [*]

Interferons are proteins which bring about a nonspecific and nonimmunological defence reaction against virus infections in vertebrates. Interferon formation is induced in vivo and in vitro by viruses and other agents, e.g. endotoxins, nucleic acids, synthetic anionic copolymers, and phytohemagglutinins. All attempts to produce pure interferons have so far been unsuccessful. Interferons can only exert an antiviral action when the cellular RNA and protein synthesis is intact.

1. Introduction

It has long been known that the formation of antibodies is not the only defence an organism has to protect itself against a virus infection. One of these nonimmunological defences is "viral interference", *i.e.* the adverse effect that various viruses can produce on the multiplication of another virus when the two are present in the same host.

In 1937 *Findlay* and *MacCallum* [1] showed that treatment with Rift Valley fever virus protected monkeys against subsequent challenge with the immunologically unrelated yellow fever virus. Shortly after infection of rabbit skin with vaccinia virus, *Ørskov* and *Andersen* [2] observed the appearance of a "local" antibody, although no antibodies could yet be demonstrated in the serum. In 1962 the authors discussed this observation as a possible interferon effect. *Lenette* and *Koprowski* [3] were able to demonstrate a slight antiviral effect in infected chick- and mouse-embryo cultures even after the viruses had been removed. *Matumoto et al.* [4] showed that mice that had been infected with a neurotropic Rift Valley fever virus were protected against a virulent pantropic variant of the same virus. (For reviews of viral interference see [5–7].)

In 1957 *Isaacs* and *Lindenmann* [8] succeeded in clearly differentiating the principle of viral interference from that of specific immunity. These authors treated the chorioallantoic membrane of chick embryos with inactivated influenza virus incapable of multiplication. After three hours at 37 °C pieces of membrane with adsorbed virus were added to a buffer solution and incubated for 24 hours. After removal of the tissue a substance having an antiviral action was found in the buffer solution, which the authors called "interferon" Subsequently, it has been found that interferons or similar substances are formed in the cells of many vertebrates in response to viral infection.

The effect of these interferons also extends to Bedsonia organisms, bacteria, protozoa, and some oncogenic viruses, *e.g.* leukemia viruses [9, 10]. Today it is generally accepted that interferons play an essential role in the formation of a host's nonspecific resistance to superinfection with a second virus. It is difficult to decide whether the effects of viral interference described before the discovery of interferons were due to interferon action or to other causes, but it is certain that

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[1] *G. M. Findlay* and *F. O. MacCallum*, J. Pathol. Bacteriol. *44*, 405 (1937).

[2] *J. Ørskov* and *E. K. Andersen*, Acta pathol. microbiol. scand., Suppl. *37*, 621 (1938).

[3] *E. H. Lenette* and *H. Koprowski*, J. exp. Medicine *83*, 195 (1946).

[4] *M. Matumoto, I. Nishi*, and *Y. Saburi*, C. R. Séances Soc. Biol. Filiales *153*, 1645 (1959).

[5] *W. Henle*, J. Immunology *64*, 203 (1950).

[6] *R. W. Schlesinger* in *T. M. Rivers* and *F. C. Horsfall*: Viral and Rickettsial Infections of Man. Pitman Publ., London 1959, p. 145ff.

[7] *R. Wagner*, Bacteriol. Reviews *24*, 151 (1960).

[8] *A. Isaacs* and *J. Lindenmann*, Proc. Roy. Soc. (London), Ser. B *147*, 258 (1957).

[9] *T. C. Merigan*, Symposium on Interferon, Lyons 1969.

[10] *E. F. Wheelock*, Symposium on Interferon, Lyons 1969.

there are other kinds of viral interference in addition to the interferon system [11–14]. (For the current position in interferon research see also [15–20].)

2. Biological Properties

One of the most interesting properties of interferons is the nonspecificity of their antiviral action. Interferon makes the host cell resistant to both RNA and DNA viruses, including some oncogenic viruses. In addition, its range of action also extends to bacteria, Bedsonia organisms, and protozoa. There are, however, considerable differences in the sensitivity of virus strains to interferon. *Ruiz-Gomez* and *Isaacs* [21] were able to show that 30 times the amount of interferon was necessary in chick embryo fibroblast cultures to inhibit Newcastle disease virus (NDV) [**] to the same degree as O'nyong-nyong virus. Other authors have also described differences in the sensitivity of viruses to interferons [22–24]. Such differences apparently also depend on the type of the host cell. Two strains of vesicular stomatitis virus (VSV), which are inhibited to different degrees in L cells (a stable mouse fibroblast cell line), show the same sensitivity in chick embryo cells [25].

It is very difficult to summarize the sensitivity of viruses to interferons, partly because of the contradictory results. The arbor viruses are among the most sensitive, whereas Newcastle disease, herpes, adeno, and Aujeszky's disease viruses appear to be relatively resistant. VSV has a moderate sensitivity. Most of the findings indicate that interferon sensitivity and the ability to induce interferon formation go in parallel. An interesting suggestion is that the virulence of viruses is closely connected with their interferon sensitivity and their ability to induce interferon formation [26, 27]. The interferon system is less effective against virulent than against nonvirulent strains.

Another important biological characteristic of interferons is shown by the observation that the inhibitory effect is much clearer if the cells used in the test come from homologous animal species. This "species specificity" was first observed by *Tyrell* [28] with interferon from calf and chick fibroblasts. Similar findings were made when chick and rabbit cells [29] or chick and duck cells were used [7, 30]. In all these cases the interferon had a weaker effect in heterologous tissue. Frequently no activity at all can be determined in such tissues. This "species specificity" of the antiviral effect – whether absolute or partial – is regarded as an important characteristic of the interferon system.

Recently, however, the general validity of this "species specificity" has been questioned. *Bucknall* [31] found that the interferon of *Macaca* monkeys exerted an antiviral activity in the cells of two other genera (*Cercopithecus* and *Erythrocebus*). Thus, this interferon not only did not show any "species specificity" but also no genus specificity. *Merigan* [32] observed a cross-reaction between human and rabbit interferons in cell cultures. *Bucknall* proposed that in future the "species specificity" of the antiviral effect should no longer be regarded as a typical interferon property.

The present account of important studies on interferon would be incomplete without any mention of the antigenicity of this substance. As interferons are proteins (see Section 4), attempts have been made to immunize animals with them, but the first experiments were unsuccessful [33–35].

Paucker et al. [36, 37] were the first to obtain an interferon antiserum. For this purpose guinea pigs and rabbits were injected intraperitoneally with highly purified interferon samples obtained from NDV-treated L cells. The treatment was repeated several times. An antiserum that inactivated up to 99 % of the interferon from L cells was thus obtained. Antibodies to mouse and chick interferon only neutralized the activity of the homologous preparations. The two interferons thus differed in their antigenic properties. *Paucker* considered it probable that all the earlier attempts to obtain an antiserum failed because too little interferon was given; interferon is obviously a substance with an extremely high biological activity, *i.e.* only relatively few interferon molecules are present

[11] *A. S. Huang* and *R. R. Wagner*, Virology *30*, 173 (1966).

[12] *P. I. Marcus* and *D. H. Carver*, J. Virol. (Baltimore) *1*, 334 (1967).

[13] *E. Zebovitz* and *A. Brown*, J. Virol. (Baltimore) *2*, 1283 (1968).

[14] *M. A. Bratt* and *H. Rubin*, Virology *35*, 395 (1968).

[15] *N. B. Finter*: Interferons. North Holland, Amsterdam 1966.

[16] *G. E. W. Wolstenholme* and *M. O'Connor*, Ciba Foundation, Symposium Interferon, J. A. Churchill Ltd., London 1968.

[17] *J. Vilcek*: Interferon, Springer, Heidelberg 1969.

[18] *M. S. Finkelstein* and *T. C. Merigan*, Calif. Med. *109*, 24 (1968).

[19] *M. R. Hilleman*, Clin. Pharmacol. Therapeutics *9*, 517 (1968).

[20] *R. Z. Lockart*, Progr. med. Virology *9*, 451 (1967).

[21] *J. Ruiz-Gomez* and *A. Isaacs*, Virology *19*, 8 (1963).

[**] Abbreviations: Newcastle disease virus = NDV; Vesicular stomatitis virus = VSV; Semliki Forest virus = SFV; Translation inhibitory protein = TIP

[22] *M. Ho* and *J. F. Enders*, Virology *9*, 446 (1959).

[23] *L. A. Glasgow* and *K. Habel*, J. exp. Medicine *115*, 503 (1962).

[24] *J. Vilcek*, Acta Virol. *6*, 144 (1962).

[25] *R. R. Wagner*, *A. H. Levy*, *R. M. Snyder*, *G. A. Ratcliff*, and *D. F. Hyatt*, J. Immunol. *91*, 112 (1963).

[26] *J. F. Enders*, Trans. Stud. Coll. Physicians Philadelphia *28*, 68 (1960).

[27] *R. F. Sellers*, *G. N. Mowat*, *J. H. Bennet*, and *D. A. Barr*, Arch. ges. Virusforsch. *23*, 12 (1968).

[28] *D. A. J. Tyrell*, Nature (London) *184*, 452 (1959).

[29] *A. Isaacs* and *M. A. Westwood*, Lancet *2*, 324 (1959).

[30] *M. Ho* and *J. F. Enders*, Virology *9*, 446 (1959).

[31] *R. A. Bucknall*, Nature (London) *216*, 1022 (1967).

[32] *T. C. Merigan*, Interferon Scientific Memoranda, Memo No. 146/1 (1969).

[33] *D. C. Burke* and *A. Isaacs*, Acta Virol. *4*, 215 (1960).

[34] *J. Lindenmann*, Z. Hyg. Infektionskrankh. *146*, 287 (1960).

[35] *A. Isaacs*, Advances Virus Res. *10*, 1 (1963).

[36] *K. Paucker* and *K. Cantell*, Virology *18*, 145 (1962).

[37] *K. Paucker*, J. Immunol. *94*, 371 (1965).

even in the highly active purified preparations (see Section 4).

An interesting and so far little-studied property of the interferon system is the occurrence of the refractory phase. *Cantell* and *Paucker* [38] established that the production of interferon ceased 24 hours after the treatment of L cells with inactivated NDV. No renewal of interferon production could be demonstrated after further treatment with NDV. *Ho* and *Kono* [39] and *Youngner* and *Stinebring* [40] made similar observations in experiments carried out *in vivo*. Rabbits were treated with Sindbis virus or endotoxin from *E. coli*, a very potent interferon inducer. When the treatment was repeated 24 hours later, no renewal of interferon production could be detected. In the serum of tolerant animals, *Ho et al.* [41] found a humoral factor which inactivated the interferon-inducing capacity of endotoxin.

3. Methods of Determining Interferons

All methods used to determine interferons are based on the fact that interferons inhibit virus multiplication. Of extreme importance in judging the results are the experimental conditions, such as the type of the host cell, the time of preincubation with interferon, the type and amount of the test virus, and the experimental temperature.

3.1. Reduction of Virus Hemagglutinin Titers

Many viruses, including influenza virus, can form hemagglutinins. The amount of hemagglutinin that can be measured is proportional to the quantity of the virus. Chorioallantoic membranes from chick embryos are incubated in an interferon-containing medium and are then infected with influenza virus. The decrease in the hemagglutinin titer parallels that in the interferon titer [8].

3.2. Decrease in Hemadsorption (Quantitative Hemadsorption Method)

The phenomenon of hemadsorption is based on the fact that many virus-infected cells can adsorb erythrocytes. The cells are incubated with the interferon preparation and infected, and erythrocytes are then added. After removing the unadsorbed erythrocytes, the adsorbed erythrocytes are lyzed; the hemoglobin released is measured spectrophotometrically. The method is simple and gives reliable results [42].

3.3. The Plaque Inhibition Method

The cells are incubated with the interferon sample and then infected with a definite amount of a plaque-forming virus. After adsorption of the virus the cells are covered with a layer of agar. The interferon titer is given as the reciprocal of the greatest dilution of the interferon sample that reduces the plaque count by 50 % compared with controls [43]. At the same time this shows that the interferon neither prevents virus adsorption nor inactivates extracellular viruses.

3.4. Indicator Test

Normal cells excrete acids into the incubation medium. Phenol red, a constituent of most cell culture media, thus changes to a yellow color. Infected cells do not excrete enough acid to produce a change in color, while interferon-treated cells behave in the same way as non-infected ones, *i.e.* the medium becomes yellow. *Paucker* [37] used this effect to develop a very reliable and sensitive method for the determination of interferons.

3.5. Reduction of the Cytopathic Effect

In certain tissues the multiplication of viruses leads to microscopically detectable cytopathic effects. The inhibition of these effects by pretreatment of the tissue with interferon preparations is also used for interferon determination.

3.6. Prevention of Incorporation of [^{14}C]-Thymidine into Virus DNA

Bodo [44] has described a biochemical method for the determination of interferons in which the decrease in the incorporation of [^{14}C]-thymidine into the acid-insoluble DNA fraction is taken as a measure of the amount of interferon (the cellular DNA was broken down with DNase in the presence of Triton X-100).

4. The Chemical and Physicochemical Properties of Interferons

Isaacs and *Lindenmann* [8] describe interferons as substances that are not dialyzable, not sedimented at 100000 × g, partly inactivated by trypsin, precipitated with a saturated ammonium sulfate solution, and not undergoing any loss of activity with DNase. They conclude from this that interferons or at least their essential components must consist of protein. Other research workers have confirmed this hypothesis [45]. Today, it is generally accepted that the operative part

[38] *K. Cantell* and *K. Paucker*, Virology *21*, 11 (1963).

[39] *M. Ho* and *Y. Kono*, J. clin. Invest. *44*, 1059 (1965).

[40] *J. S. Youngner* and *W. R. Stinebring*, Nature (London) *208*, 456 (1965).

[41] *M. Ho, K. Kono*, and *M. K. Breinig*, Proc. Soc. exp. Biol. Med. *119*, 1227 (1965).

[42] *N. B. Finter*, Virology *24*, 589 (1964).

[43] *R. R. Wagner*, Virology *13*, 323 (1961).

[44] *G. Bodo*, Interferon Scientific Memoranda, Memo No. 78 (1968).

[45] *K. H. Fantes*, see ref. [15], p. 119.

of an interferon consists of protein with a small carbohydrate component. It is considered certain that it does not contain any RNA or DNA.

The well-known methods of protein chemistry have been used in experiments to isolate interferons. It must be recalled that the only way of demonstrating an interferon is by biological tests – a fact that makes isolation very difficult. Two of the best-known methods of purification are briefly described in the following paragraphs.

Lampson et al.[46] purified interferon in the following way from hen's eggs infected with influenza A virus:

1. The virus and inactive protein were precipitated with 0.15 N $HClO_4$.

2. The interferon was precipitated at pH 6 with zinc acetate. After centrifuging, the sediment was dissolved in 0.2 N HCl, dialyzed against 0.9% NaCl solution, and re-precipitated with zinc acetate.

3. The precipitate was dissolved in 0.01 M phosphate buffer (pH 6), chromatographed on a carboxymethylcellulose column, and eluted using a 0.01 M phosphate buffer (pH 8) with 0.1 M NaCl.

4. The biologically active fractions were again treated with zinc acetate.

5. This was followed by another chromatographic separation on carboxymethylcellulose, and

6. precipitation with zinc acetate.

7. The operation was finished by zone electrophoresis at pH 8.9 on Pevikon.

The specific activity of the interferon purified in this way was 236000 units/mg protein[47].

A product with a still higher specific activity (1.6×10^6 units/mg protein) was obtained by *Fantes et al.*[48,49] using the following procedure:

1. Adsorption of interferon at pH 5 on Doucil (a synthetic sodium aluminum silicate) and elution at pH 7.5 with potassium thiocyanate.

2. Precipitation of the inactive protein at pH 2.

3. Precipitation of further inert protein with 5 volumes of methyl alcohol.

4. Precipitation of interferon by neutralization of the solution.

5. Precipitation of interferon in 0.01 M phosphate buffer (pH 7.5) and filtration through DEAE cellulose.

6. Chromatography of the filtrate at pH 5.9 on a carboxymethyl-Sephadex column. The interferon-containing fraction was eluted with an increasing pH gradient.

20000-fold concentration was obtained with this method of purification. The overall recovery of the activity was 7%.

The use of polyacrylamide gel electrophoresis resulted in a substantial advance in the field of interferon purification. On the one hand this showed that all the highly purified products still contain many impurities, and on the other hand that interferon itself is not homogeneous[45,50,51]. In polyacrylamide gel electrophoresis the biological activity of a highly purified product is distributed over a broad zone. The biologically active constituents of the interferon preparation of *Fantes et al.*[52] differed both in molecular weight and in isoelectric point. Other authors too have concluded that there may be no "interferon" as such; instead, there are probably several substances with interferon-like properties which appear simultaneously in the same animal in response to the same stimulus[53,54]. Thus, it seems to be certain that different types of cell from the same organism form different interferons[55,56]. Their molecular weight was between 13000 and 160000[17].

There is as yet no explanation for these facts. So far it is not clear whether these substances are preliminary stages of interferon formation, interferon produced by different cells, interferon with different carrier proteins, or something quite different.

Since the only possible conclusion is that none of the biologically active substances so far isolated and investigated was a pure interferon, it seems advisable to treat with reservation some of the values and properties so far determined *e.g.* the amino-acid composition.

On the other hand, certain characteristics can be accepted as generally valid. In all cases the interferons were neutral or weakly basic proteins or protein-containing compounds. Their stability over a wide pH-range is particularly worth mentioning. *Lampson et al.*[57] observed that highly purified chick interferon was stable at 23 °C for over an hour in the pH range 1–10. These results have been confirmed several times. Today the stability at pH 2 is regarded as an important characteristic of all interferons. Most interferons are relatively heat resistant. *Lampson et al.* found that purified chick interferon remained fully active for one hour at 66 °C. Some inactivation only occurred after heating at 76 °C for one hour. The biological activity of interferon is destroyed by proteolytic enzymes such as trypsin, chymotrypsin, and pepsin, but not by DNase, RNase, lipase, peptidase, and α-amylase.

It has already been mentioned that the general current opinion is that interferon or at least its active part consists of protein. A Japanese research team[58,59] has described an interferon-like compound, which was isolated from rabbit skin infected with vaccinia virus. This compound was reported to be a protein-free polysaccharide (molecular weight 10000), which

[46] *G. P. Lampson, A. A. Tytell, M. M. Nemes,* and *M. R. Hilleman,* Proc. Soc. exp. Biol. Med. *112,* 468 (1963).

[47] Interferon units are generally given as the reciprocals of the greatest dilution that protects cells against a virus attack under defined conditions.

[48] *K. H. Fantes,* Nature (London) *207,* 1298 (1965).

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[50] *T. C. Merigan, C. A. Winget,* and *C. B. Dixon,* J. molecular Biol. *13,* 679 (1965).

[51] *K. H. Fantes,* II. Int. Sympos. med. appl. Virol., Ft. Lauderdale.

[52] *K. H. Fantes* in *G. Rita*: The Interferons. Academic Press, New York 1968, p. 213.

[53] *R. R. Wagner* and *T. S. Smith,* see ref. [16], p. 95.

[54] *Y. H. Ke, M. Ho,* and *T. C. Merigan,* Nature (London) *211,* 541 (1966).

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[57] *G. P. Lampson, A. A. Tytell, M. M. Nemes,* and *M. R. Hilleman,* Proc. Soc. exp. Biol. Med. *121,* 441 (1965).

[58] *Y. Nagano, Y. Kojima, T. Haneishi,* and *M. Shirasaka,* Jap. J. exp. Med. *36,* 535 (1966).

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was only active *in vivo* and had no "species specificity". Whether this substance is the active part of interferon, which is combined with a species-specific protein in the animal body and thus forms a "normal" interferon molecule, or whether it is an interferon-inducing compound, has not so far been elucidated.

5. Mode of Action of Interferon

Isaacs et al.[60,61] observed an increased rate of glycolysis in interferon-treated cells. In addition, it was found that there was a decline in the direct oxidation of glucose *via* the pentose phosphate cycle and that less inorganic phosphate was incorporated. As the same metabolic changes are produced by chemical uncoupling of oxidative phosphorylation, *Isaacs et al.* came to the conclusion that interferon likewise acts as an agent of uncoupling oxidative phosphorylation and that this uncoupling occurs not in the mitochondria but in the cell nucleus. However, *Lampson et al.*[62] were able to show later that the described effects failed to appear when the experiments were carried out with highly purified interferon preparations. It now appears certain that the uncoupling of oxidative phosphorylation and other effects on the uninfected cells were produced by impurities[63].

The following processes must occur before a virus can multiply within a host cell: Adsorption of the virus onto the cell surface; penetration of the cell; and liberation of the viral nucleic acids by removal of the protein coat.

Interferon has no effect on the adsorption of viruses[64,65]. From the fact that the multiplication of infectious RNA isolated from viruses is inhibited by interferon, it was concluded that interferon has no effect on the penetration of intact virus or the liberation of viral nucleic acids[66,67].

This conclusion does not seem to be absolutely correct, at least for certain DNA viruses, as the recent findings of *Magee et al.*[68] indicate that interferon probably inhibits the uncoating process in vaccinia virus. Since it is known that the uncoating enzymes of some DNA viruses are virus proteins[69], this effect can be attributed to an inhibition of virus-specific protein synthesis. It has also been possible to exclude a direct inactivating action of interferon on the complete virus particle[70,71] as well as on viral RNA[72]. From this it can be concluded that the action of interferon must be based on an inhibition of the synthesis of virus-specific proteins or viral nucleic acids.

RNA viruses multiply in the following way:

1. The "early" cistrons of the parental RNA molecule (plus strand) encode directly as m-RNA for the synthesis of "early" enzymes such as the RNA-dependent polymerase.
2. Through the RNA-dependent RNA polymerase is formed the "replicative" form of the virus, *i.e.* a second RNA strand (minus strand) is synthesized on the parental plus strand which then acts again as a matrix for the synthesis of plus strands.
3. Translation of the "late" cistrons and thus synthesis of the viral coat protein.
4. Combination of viral RNA (plus strand) with coat protein to form the intact virus.

The synthesis of viral RNA is inhibited in interferon-treated cells[73–75]. This means that either the synthesis or the activity of RNA-dependent RNA polymerase is interrupted by interferon. *Sonnabend, Martin*, and *Mécs*[75] have shown that interferon has no effect on the activity of the RNA-polymerase of Semliki Forest virus (SFV) in a cell-free system.

Miner, Ray, and *Simon*[76] studied the effect exerted by a homogenate of interferon-treated L cells on Mengo virus RNA polymerase, and established that the activity of the polymerase was not decreased. The same authors, however, found that pretreatment of L cells with interferon clearly decreased their content of virus-specific RNA polymerase after a Mengo virus infection. *Sonnabend et al.* also demonstrated a decrease in the extractable amount of SFV RNA polymerase when they pretreated L cells with interferon. This means it is not the action but the synthesis of viral RNA polymerase that is inhibited.

Marcus and *Salb*[77] were able to show that although Sindbis virus RNA and the ribosomes of interferon-treated chick embryo cells form a polysome complex, no amino acids are incorporated. The action of interferon on the multiplication of RNA viruses thus obviously consists in an inhibition of the translation of virus-specific m-RNA, and consequently in inhibition of the synthesis of virus proteins.

The multiplication of DNA viruses take place according to the following series of events:

1. "Early" transcription of the viral DNA molecule with the formation of "early" viral m-RNA.
2. Translation of the "early" m-RNA into "early" proteins.

[60] *A. Isaacs*, Virology *10*, 144 (1960).

[61] *A. Isaacs, H. G. Klemperer*, and *G. Hitchcock*, Virology *13*, 191 (1961).

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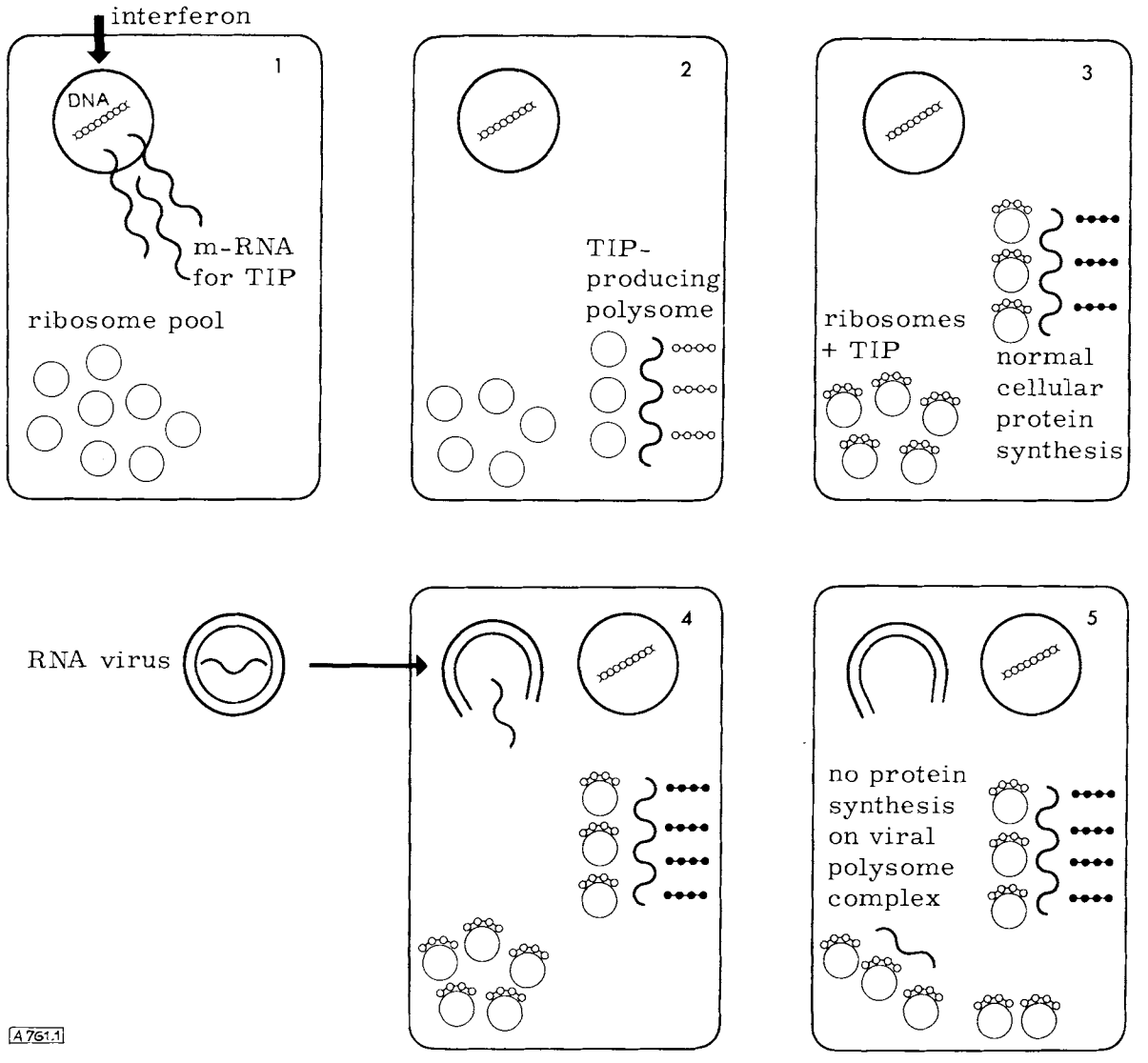


Figure 1. Mode of action of interferon according to *Marcus* and *Salb* [77] and *Hilleman* [19].

1. Interferon penetrates the uninfected cell and induces the synthesis of m-RNA for TIP. 2. With the help of this m-RNA the cell synthesizes TIP 3. TIP interacts with the ribosomes, but does not effect the cellular protein synthesis. 4. A virus penetrates the cell. 5. Although the viral RNA comes in contact with the TIP ribosome complex, no viral protein is synthesized.

3. Synthesis of viral DNA.

4. Formation of "late" m-RNA.

5. Translation of the "late" m-RNA into the viral coat proteins.

6. Combination of viral DNA and coat protein to form intact virus (maturation).

In several systems it has been possible to show that the synthesis of viral DNA is inhibited in interferon-treated cells [78,79].

Joklik and *Merigan* [80] showed that the synthesis of viral m-RNA is not affected by interferon in the L cells/vaccinia virus system. The virus infection produced a disintegration of the host's polyribosomes, which was followed by a formation of virus-specific polyribosomes with viral m-RNA. In the presence of interferon the formation of these polyribosomes fails to occur, with the result that no virus-specific proteins —and thus no DNA polymerase – are synthesized.

Looking for common factors in the inhibitory action of interferon on the multiplication of RNA and DNA viruses, it can be established that in both cases it is the "early" translation of virus-specific message, *i.e.* the formation of "early" virus-specific proteins, that is inhibited. Whether the inhibition is based on the prevention of reading of the m-RNA in the polyribosome, or whether the formation of the polyribosomes is suppressed, has not been finally resolved. It is even possible that both effects can occur. The problem of the site of action of interferon seems to be solved, but the mode of action at the molecular level remains an open question.

Taylor [81] established that actinomycin C, which is known to inhibit cellular DNA-dependent RNA synthesis, prevents the antiviral action of interferon. A similar effect is produced by many inhibitors of protein biosynthesis such as puromycin [82,83] and *p*-

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fluorophenylalanine [84]. The cellular RNA and protein synthesis must therefore be intact for the development of the antiviral action of interferon. It was concluded that interferon induces the formation of a second protein, which is the substance with the true antiviral effect ["antiviral protein", "translation inhibitory protein (TIP)"] [77,85].

Using the model proposed by *Jacob* and *Monod* to explain these processes, the development of the antiviral effect of interferon can be supposed to proceed largely in accord with Figure 1. There has been no lack of attempts to provide direct experimental proof of the existence of TIP. Using a double labeling method, *Vilcek et al.* [86,87] were able to demonstrate that the ribosomal protein fraction of interferon-treated cells showed a different distribution of activity in polyacrylamide electrophoresis from that of normal cells. The authors found one completely new band and an increased amino-acid incorporation in two other protein bands. The identification of one or more of these proteins as TIP has still not yet been accomplished.

Marcus and *Salb* [88] allowed trypsin to react under mild conditions with the ribosomes of interferon-treated cells. At 0 °C the ribosomes could form a polysome complex with Sindbis virus RNA, which rapidly disintegrated again and took up amino acids at 37 °C. *Marcus* and *Salb* regarded this as an indication of normal translation, since the corresponding complex with interferon-treated nontrypsinized ribosomes was not broken down and did not take up any amino acids.

Surprisingly, *Dianzani*, *Buckler*, and *Baron* [89] found that cycloheximide – another inhibitor of protein biosynthesis – did not neutralize the antiviral action of interferon. The authors considered that it was possible that the m-RNA for TIP is formed in the presence of the inhibitor and remains relatively stable, and that the period after removal of the cycloheximide and before addition of the virus is sufficient for enough TIP to be formed with this m-RNA.

Summing up, it may be said that there is yet no definite proof of the existence of one or more antiviral proteins whose synthesis is induced by interferon, but that the majority of the experimental findings supports this hypothesis. It should also be added that, if this theory is confirmed, the formation of m-RNA and the synthesis of TIP would be the only effects of interferon on normal, *i.e.* uninfected cells.

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[86] *M. H. Ng*, *J. Vilcek*, and *T. G. Rossman*, Bacteriol. Proc. *1969*, 147.

[87] *J. Vilcek*, *M. H. Ng*, and *T. G. Rossman* in *G. Rita*: The Interferons. Academic Press, New York 1968, p. 185.

[88] *P. I. Marcus* and *J. M. Salb* in *G. Rita*: The Interferons. Academic Press. New York 1968, p. 111.

[89] *F. Dianzani*, *C. E. Buckler*, and *S. Baron*, Proc. Soc. exp. Biol. Med. *130*, 519 (1969).

6. Interferon Inducers

As already mentioned, both intact and inactivated viruses, *i.e.* viruses not capable of multiplying, can induce the formation of interferon. This ability to induce interferon formation is apparently a feature of all viruses, no matter to what class they belong. It has been known for some years that other agents besides viruses can stimulate interferon formation. Such agents include bacteria, rickettsiae, phytohemagglutinins, Toxoplasma, Mycoplasma, protozoa, cycloheximide, as well as some anionic copolymers and nucleic acids.

6.1. Bacteria and Bacterial Endotoxins

Even before the discovery of interferon it was recognized that bacteria have an inhibitory effect on the growth of some viruses. In 1938 *Armstrong* [90] observed that certain myxovirus infections of mice are prevented by bacteria. *Horsfall* and *McCarty* [91] established that the multiplication of viruses in the lungs of mice infected with pneumonia virus was decreased 10–100 fold if the animals were also treated with a nonhemolytic Streptococcus MG′ strain.

Youngner and *Stinebring* [92] were the first to show that bacteria can act as interferon-inducers. These authors infected hens with a virulent strain of *Brucella abortus* and found an antiviral activity in the birds' serum. The substance responsible for this showed the same physicochemical and biological properties as interferon. They also found an interferon-like substance after treating mice with purified *E. coli* endotoxin [93]. Thus bacterial multiplication is not a prerequisite for the induction of interferon. Similar results were obtained by *Ho* [94] with an endotoxin which he administered to rabbits. *Hopps et al.* [95] were also able to isolate an interferon-like substance from chick embryo cells inoculated with *Rickettsia tsutsugamuchi*. There are indications that endotoxin treatment does not induce the synthesis of interferon but only the release of preformed molecules. Endotoxin-induced interferon appears earlier in the serum of treated rabbits than virus-induced interferon, and, in addition, its formation is not inhibited by actinomycin D [96].

6.2. Phytohemagglutinin

Phytohemagglutinin is a substance contained in an extract of *Phaseolus vulgaris*. *Wheelock* [97] established that this plant product has an antiviral effect in human

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[96] *Y. Khono* and *M. Ho*, Virology *25*, 162 (1965).

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leukocytes; the cytopathic effect of Sindbis virus was also decreased. Like interferon, the antiviral substance can be neither dialyzed nor sedimented.

6.3. Synthetic Anionic Copolymers

In 1966 *Regelson*[98] found that copolymers of maleic anhydride and divinyl ether (molecular weight 17000–450000) develop an antiviral activity after intraperitoneal administration to mice, and this appears in the serum 24 hours after the injection.

Merigan[99] was able to show that this antiviral substance had all the known properties of interferon. The same agent also inhibited virus-induced leukemia in mice, and in clinical trials it inhibited neoplasm formation in man[100]. An interferon-inducing effect could also be demonstrated with copolymers of maleic anhydride and vinyl methyl ether or vinyl acetate[101]. The corresponding styrene compounds were not such good inducers and were more toxic.

Some of these copolymers have been tested clinically. A maleic anhydride/divinyl ether copolymer with a molecular weight 17000 was tested in the USA as an antitumor drug. A definite disadvantage of this compound is that it is not broken down in the body but is stored in the reticulo-endothelial system[102]. So far there has been no success in inducing interferon formation *in vitro*. The exact mode of action of these polymers is not known. It has been argued that the antiviral action is based not only on the formation of interferon but also on a direct interaction with the cell due to the polyanionic structure of the molecule.

6.4. Nucleic Acids

In 1961 *Isaacs*[103] put forward the theory that the formation of interferon is a reaction of the cell to a "foreign" nucleic acid, in the same way that antibodies are formed by recognizing differences between foreign and the body's own proteins.

Rotem et al.[104] established that mouse liver RNA inhibits the growth of pox viruses in chicken cell cultures, exactly in the same way as chicken RNA inhibits it in mouse cell cultures. A much smaller inhibition occurred with the homologous RNA. *Isaacs*[105] continued these investigations and established that nucleic acids did not induce interferon formation in the homologous cells. The RNA could do this, however, after treatment with nitrous acid. *Isaacs* concluded that the RNA was so changed by deamination that it was taken for a foreign nucleic acid by the cells. Although some later findings supported this concept[106–108], *Isaacs*' theory did not find general recognition. In 1965 *Isaacs*[109] reported that he himself had also obtained "different results" in further studies.

The theory that the foreign nucleic acids induced interferon formation received further experimental support from *Hilleman*'s group. For some years this team had sought a potent interferon inducer that would be suitable for clinical use. *Hilleman* reported attempts to fractionate viruses into their constituent parts and to examine the individual fractions for their capacity to induce interferon formation[110]. These experiments were unsuccessful.

Braun and *Nakano* reported[111,112] that they had succeeded in stimulating antibody synthesis with some synthetic oligonucleotides. This prompted *Hilleman*'s group to test the interferon-inducing capacity of synthetic polynucleotides. These investigations were crowned with success: a few μg of a double-stranded complex of polyriboinosinic acid and polyribocytidylic acid (poly-I:C) induced interferon formation in mice[113]. This interferon protected the animals against a lethal dose of Columbia SK virus. A double-stranded complex of polyriboadenylic acid and polyribouridylic acid (poly-A:U) and a mixture of polyinosinic acid and cytidylcytidine (I + CpC) were also active, but to a lesser degree. No activity, however, was shown by single-stranded polynucleotides, and by some oligonucleotides, dinucleotides, nucleotides, and nucleosides. Interferon formation could also be demonstrated *in vitro* with poly-I:C.

These findings led to a search for other kinds of double-stranded RNA. *Hilleman* and his associates succeeded in isolating such a double-stranded RNA from helenine (an antiviral substance produced by *Penicillium funiculosum*)[114]. *Rytel*[115] was able to show that helenine can induce interferon formation *in vivo* and *in vitro*. The double-stranded RNA from helenine was also an excellent interferon inducer[116].

Subsequently it was established that the antiviral principle of statolon, an extract of *Penicillium staloniferum* is likewise a double-stranded ribonucleic

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[109] *A. Isaacs*, Aust. J. exp. Biol. med. Sci. *43*, 405 (1965).

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[113] *A. K. Field*, *A. A. Tytell*, *G. P. Lampson*, and *M. R. Hilleman*, Proc. nat. Acad. Sci. USA *58*, 1004 (1967).

[114] *R. E. Shope*, J. exp. Medicine *123*, 213 (1966).

[115] *M. W. Rytel*, *R. E. Shope*, and *E. D. Kilbourne*, J. exp. Medicine *123*, 577 (1966).

[116] *G. P. Lampson*, *A. A. Tytell*, *A. K. Field*, *M. M. Nemes*, and *M. R. Hilleman*, Proc. nat. Acad. Sci. USA *58*, 782 (1967).

acid [117]. Another source of naturally occurring RNA is the replicative form of RNA viruses. The replicative form of the MS2 bacteriophage was isolated and shown to be an interferon inducer even in very small amounts [118]. A similar result was obtained with purified reovirus RNA [119]. Reovirus is one of the few viruses whose nucleic acid core consists of double-stranded RNA.

It is interesting to note that the ability of poly-I:C to induce interferon formation can be increased about 100-fold by the addition of DEAE-dextran [120]. This raises the question why double-stranded ribonucleic acids are some of the most powerful interferon inducers. The possibility of these nucleic acids conveying genetic information can be ruled out, since double-stranded homopolynucleotides such as poly-I:C cannot do this.

Two explanations have been suggested. *Hilleman* believes that the appearance of the double-stranded replicative form, one of the first steps in the multiplication of RNA viruses, is normally the starting signal for interferon synthesis. When double-stranded RNA is supplied, the cell reacts as if virus multiplication were occurring, and interferon synthesis begins. The weak point in this theory is that RNA viruses incapable of multiplication and also DNA viruses are good interferon inducers, although, according to present knowledge, there is no double-stranded RNA in either of these cases.

The surprising finding reported by *Colby* and *Duesberg* [121] is of special interest in this connection. These authors observed that chick embryo cells infected with vaccinia virus (a DNA virus) contained 10 times as much double-stranded RNA as did noninfected cells. According to the concepts generally accepted today concerning DNA virus multiplication, there is as yet no evidence of the presence of double-stranded RNA after vaccinia virus infection. Likewise, there is no explanation for the existence of double-stranded RNA in noninfected cells. However, it is also worth mentioning that *Montagnier* [122] was able to demonstrate double-stranded RNA in normal rat liver cells.

The second explanation for the good inducer properties of double-stranded RNA is the principle of "foreign" nucleic acid put forward by *Isaacs*. A well-known characteristic of double-stranded RNA is its relative stability in the presence of RNase; this gives it a greater chance of reaching the cell than all the other types of nucleic acids, which are very quickly broken down by nucleases.

[117] *L. F. Ellis* and *W. J. Kleinschmidt*, Nature (London) *215*, 215 (1967).

[118] *A. A. Tytell, G. P. Lampson, A. K. Field*, and *M. R. Hilleman*, Proc. nat. Acad. Sci. USA *58*, 1719 (1967).

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7. Future Prospects

There has been no lack of ideas and experiments on the use of the interferon system for the control of virus diseases. Its broad antiviral spectrum of activity, its lack of toxicity, and its low antigenicity apparently make interferon especially suitable for this purpose. The virus diseases, for which only a limited number of serologically different types of viral agents are responsible and which in addition lead to prolonged immunity, are today largely kept in check by vaccination. This is the case with measles, pox virus diseases, yellow fever, poliomyelitis, *etc.* In addition to this, virus chemotherapy has been introduced with the use of iododeoxyuridine, adamantamine, and methylisatin-β-thiosemicarbazone in the treatment of herpes, influenza, and pox virus infections, respectively.

The hope that interferon could help in the effective control of virus diseases was recently strengthened when *Hilleman* reported in 1967 that some double-stranded ribonucleic acids were extremely potent interferon inducers. *Park* and *Baron* [123] as well as *Pollikoff* [124] were also able to establish that interferon is suitable for both prophylactic and therapeutic treatment. The above authors observed that rabbits recovered from herpetic conjunctivitis much quicker and better after treatment with poly-I:C than the control animals. This therapeutic effect was observed both with local and systemic administration. *Guerra et al.* [125] described the poly-I:C treatment of 22 patients suffering from herpetic keratitis. A good therapeutic effect was obtained in 17 cases.

The great difficulties which stand in the way of clinical use of interferon inducers are, in the first place, the already mentioned refractory phase and, secondly, the considerable toxicity of most of the inducers known at present.

The clinical application of interferon itself, *i.e.* exogenous interferon, is problematic, since it is very difficult to prepare sufficient quantities of human interferon.

Thirteen years have passed since the discovery of interferon by *Isaacs* and *Lindenmann*, and much new information has been acquired during this time. The process of interferon induction on the molecular level, and the mode of action of interferon are still obscure in many respects. Another task for the future is the further purification of interferon, so that its chemical composition can be investigated. Recently, *Vilcek* [126] discussed an interesting possibility: "Further studies may perhaps lead to the discovery of non-interferon inducers of TIP. Or would such agents be called interferons?"

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German version. Angew. Chem. *82*, 489 (1970)
Translated by Express Translation Service, London

[123] *J. H. Park* and *S. Baron*, Science (Washington) *162*, 811 (1968).

[124] *R. Pollikoff, P. Cannavale, P. Dixon*, and *A. Dipuppo*, Bacteriol. Proc. *1969*, 150.

[125] *R. Guerra, R. Frezzotti, R. Bonanni, F. Dianzani*, and *G. Rita*, II. Conf. Antiviral Substances New York, June 1969.

[126] *J. Vilcek*, see ref. [17], p. 111.

Disorder in Solids (Ionic Crystals and Metals)

By Jens Nölting[*]

Important properties of crystalline solids are due to deviations from the ideal crystal structure. Lattice defects can be divided into structural defects (grain boundaries, dislocations, impurities) and intrinsic defects. The present article deals mainly with the problems and possibilities for the determination of intrinsic disorder. This disorder, which varies reversibly with temperature, plays an important role in many solid-state processes, such as diffusion, ionic conduction, and chemical reactions in the solid phase.

After an introduction to the usual physical and chemical descriptions of the state of disorder, the principal methods of investigation are discussed. Special emphasis is placed on methods of determining disorder data from "anomalous" specific heats.

1. General

1.1. Introduction

Ideally ordered crystalline solids, characterized by an absolutely regular and perfect arrangement of their atoms in a crystal lattice, do not occur in nature. Crystal growth itself depends on the presence of structural defects (at least one dislocation with a screw component). However, even a single crystal with a very small number of dislocations has lattice defects on the atomic scale, which increase in number with rising temperature, and which are known as intrinsic defects. They are characterized by their occurrence in a reversible, temperature-dependent equilibrium. The number of defects increases with rising temperature, and decreases again when the temperature is lowered; to each temperature there corresponds a precisely defined concentration of defects. Apart from the properties of the crystal, therefore, the temperature alone determines the concentration of such lattice defects.

These defects are all of the type known as point defects. The regions of non-ideality in the lattice are confined to one lattice point and its immediate surroundings. An example of a typical and commonly occurring point defect is a missing lattice atom; this is called a vacancy. Another type of point defect is an interstitial atom, which is an atom inserted in a normally unoccupied site in the lattice. In comparison with a regularly occupied lattice site, a defect always involves an increase in the energy requirement by an amount necessary to produce the defect[**]. The type of defect in a lattice is largely determined by the lattice geometry. Vacancies are nearly always favored in structures with close packing of atoms (*e.g.* face-centered atomic lattices), whereas more open structures (*e.g.* body-centered atomic lattices) may also allow interstitial atoms. In ionic crystals, on the other hand, either type of defect may be favored, depending on the relation between the sizes of the ions. In this case the condition of electroneutrality plays a special role. Each defect in an ionic lattice means the absence of one charge or the presence of an additional charge in comparison with the perfect lattice. At equilibrium, the state of disorder must be such that the sum of the charges of all the defects is zero.

Foreign atoms incorporated into the lattice in small numbers are also point defects in our scheme. They play an important role in disorder equilibria, since they can cause a marked difference in the state of disorder from that in the pure substance. Deviations from the stoichiometric composition, which are possible for many ionic compounds, also cause changes in the state of disorder. Thus a deficit of one type of ion means either vacancies in the lattice of these ions or the insertion of interstitial ions of the other type. The presence of foreign atoms and nonstoichiometry are often referred to collectively as chemical disorder, which is characterized by introduction of disorder with a change in the composition of the crystal. These additional defects are independent of temperature, but they influence the (temperature-dependent) equilibrium of the intrinsic disorder.

1.2. Statistics of the Disorder in Thermal Equilibrium

The reason for the presence of intrinsic defects in the crystal lattice of a pure solid of stoichiometric composition is the temperature-dependent vibration of the lattice atoms about the rest positions of their ideal lattice points[*]. The normal vibrations correspond to a Boltzmann energy distribution. At a finite temperature, there are always combinations of the individual normal vibrations that allow the deflection of a

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[**] It is naturally assumed here that the lattice is in thermodynamic equilibrium *i.e.* that its structural units have in fact assumed the arrangement that gives the minimum free energy for the temperature in question. This is always assumed to be so in the following discussion. It is shown in Section 1.2 that the free energy minimum is reached only when a certain number of defects are present (at a finite temperature).

[*] According to quantum theory, the lattice atoms cannot be definitely located even at absolute zero, since they have a finite zero-point energy.

lattice atom in a favorable direction to become so large that it can escape from the potential trough of its lattice point and reach other positions in the lattice (*e.g.* a neighboring interstitial site). The important question of the equilibrium defect concentration at a given temperature can be answered with the aid of statistical thermodynamics[1]. We begin with the requirement that the free energy of the disordered crystal at equilibrium must be a minimum. This minimum condition then gives the definite concentrations of the various types of defects.

It is clear even without explicit calculation that the completely ordered state cannot correspond to the minimum free energy $A = E - TS$[*] since the entropy S is a minimum in this state. As defects appear, S increases very rapidly at first, so that the increase in TS exceeds the increase in the internal energy E. The free energy minimum, *i.e.* equilibrium, is reached only when so many defects are present that the increases in the two terms are exactly equal. For low defect concentrations (<1 %), a simple expression for the entropy can be given with the aid of the Boltzmann formula $S = k \ln W$. The probability W is proportional to the number of distinguishable ways in which the state can be achieved with a certain number of defects in the lattice. Besides this "configuration entropy", other entropy changes in the vicinity of a defect are taken into account by an extra additive term.

1.3. Disorder Models

Let us first consider a crystal lattice that contains only one type of particle, such as the atomic lattice of a pure metal. Two possible types of defect are shown in Figures 1 and 2. In the Schottky type, atoms have migrated from the interior of the crystal to the surface, leaving behind a corresponding number of vacancies. However, the atoms generating the vacancies may also remain in interstitial sites in the interior of the crystal lattice (Frenkel type). A third possibility would be the migration of surface atoms to interstitial sites in the interior (anti-Schottky disorder); however, this type is less likely because of the unfavorable energy requirements.

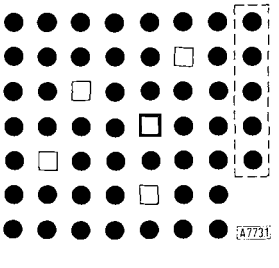


Fig. 1 (left). Atomic lattice with Schottky disorder.

Some atoms have left their lattice sites and migrated to the surface of the crystal. *One* disorder center (vacancy) is formed per misplaced lattice atom.

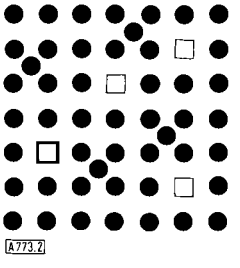


Fig. 2 (right). Atomic lattice with Frenkel disorder.

Some atoms have left their lattice sites and occupied interstitial sites in the interior of the crystal. *Two* disorder centers (vacancy and interstitial atom) are formed per misplaced lattice atom.

[1] *C. Wagner* and *W. Schottky*, Z. physik. Chem., Abt. B *11*, 163 (1930); *C. Wagner*, *ibid.*, Bodenstein-Festband, 177 (1931); Abt. B *22*, 181 (1933).

[*] We should really use the Gibbs function $G = E - TS + pV$ instead of the Helmholtz function A, but since all the cases discussed here relate to normal pressure, the term pV may be neglected for solids.

Basically the same types of defects occur in ionic crystals. Figure 3 shows Frenkel disorder of the cations[*] in the silver bromide lattice. The Br^- lattice shows negligible disorder in comparison with the Ag^+ lattice. On the basis of energy considerations, *Jost*[2] and *Schottky* found that Schottky disorder should be favored in alkali metal halides, and this has been confirmed experimentally (Figure 4).

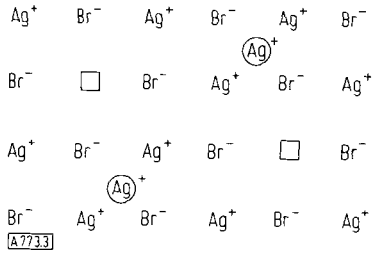


Fig. 3. Frenkel disorder in the Ag ion lattice of AgBr.

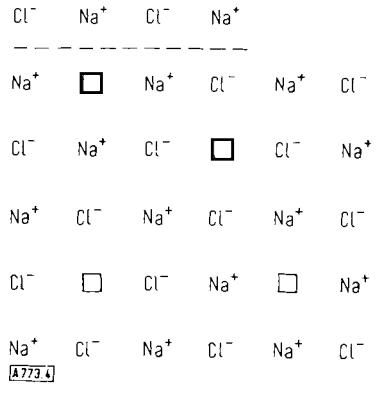


Fig. 4. Schottky disorder in the NaCl lattice.

The anion lattice and the cation lattice contain the same number of vacancies. *Two* vacancies are formed per defective NaCl unit. The missing NaCl unit is situated on the surface of the crystal.

1.4. Disorder Equilibria

The concept of the disorder equilibrium has a special significance in the case of compounds, particularly ionic crystals. The view of chemical equilibrium familiar to the chemist can be applied without difficulty to the state of disorder. The crystal is regarded as a reactive system in which the "reacting species" are regularly occupied, vacant, and incorrectly occupied lattice positions. These species can be interconverted in accordance with a certain reaction scheme and a "reaction equilibrium" will be set up between them. The equilibrium is characterized by the minimum free energy that the system then assumes.

[*] Frenkel disorder in the anion lattice, which is much less common, is known as anti-Frenkel disorder (example: SrF_2).

[2] *W. Jost*, J. chem. Physics *1*, 466 (1933); Physik. Z. *36*, 757 (1935); *W. Jost* and *G. Nehlep*, Z. physik. Chem., Abt. B *32*, 1 (1936).

Let us consider the case of Frenkel disorder, where vacancies and interstitial atoms are present in equal numbers. The reaction scheme can be written as follows:

$$\left.\begin{array}{l}\text{occupied lattice site A}\\ +\ \text{vacant interstitial site A}'\end{array}\right\} \rightleftharpoons \left\{\begin{array}{l}\text{vacant lattice site A } (\square)\\ +\ \text{occupied interstitial}\\ \text{site A } (\circ)\end{array}\right.$$

(the "energy of reaction" is E_f)

and the corresponding mass action expression, where c_A, $c_{A'}$, $c_\square$, and $c_\circ$ are the concentrations of occupied lattice sites, vacant interstitial sites, vacant lattice sites, and occupied interstitial sites respectively, is

$$\frac{c_\square \times c_\circ}{c_A \times c_{A'}} = K_f = \exp(S_f/R) \times \exp(-E_f/RT) \qquad (1)$$

The mass action constant K_f is a pure function of temperature, and is expressed in the usual manner as an exponential function with the free "energy of reaction" $E_f - TS_f$. S_f is the increase in entropy due to disturbance of the lattice in the vicinity of the defect.

In the pure, stoichiometric substance, the defects (vacancies and interstitial atoms) occur in equal numbers. Thus $c_\square = c_\circ$. If S_f and E_f are independent of temperature, for low defect concentrations ($c_\square \ll c_A$) and $c_A = c_{A'}$, we can deduce the degree of disorder γ from eq. (1)

$$\gamma = c_\square/c_A = c_\circ/c_A = \gamma_0 \exp(-E_f/2\,RT) \qquad (2)$$

As in chemical reactions, the equilibrium (1) can be displaced by addition of another component. For example, if pure silver bromide is doped with cadmium ions (Fig. 5), one additional vacancy must be produced in the cation lattice for each Cd^{2+} introduced, or else an interstitial cation must disappear from the equilibrium, in order to preserve electroneutrality. Since the product of the concentrations of vacancies and of interstitial lattice cations is constant according to eq. (1), the concentration of interstitial cations decreases to a degree that varies with the amount of Cd^{2+} added.

In the case of ionic compounds that can exhibit pronounced deviations from the stoichiometric composition (examples: Cu_2O, ZnO, TiO_2, FeS, Ag_2S),

Ag^+	Br^-	Ag^+	Br^-	Ag^+	Br^-
Br^-	$\square$	Br^-	$\square$	Br^-	Ag^+
Ag^+	Br^-	Ag^+	Br^-	$\underline{Cd}^{2+}$	Br^-
Br^-	$\underline{Cd}^{2+}$	Br^-	Ag^+	Br^-	Ag^+
Ag^+	Br^-	$\square$	Br^-	$\underline{Cd}^{2+}$	Br^-
Br^-	Ag^+	Br^-	Ag^+	Br^-	Ag^+

A773.5

Fig. 5. AgBr lattice with added $CdBr_2$.

Each Cd^{2+} ion incorporated in an Ag^+ lattice site requires an additional vacancy in the cation lattice. Interstitial ions are largely suppressed.

the number of defects can also vary widely. A metal deficit usually leads mainly to cation vacancies; with a deficit of non-metal, anion vacancies can occur as well as interstitial cations (example: TiO).

2. Processes in the Solid State Due to Lattice Defects

2.1. Diffusion

Though the degree of disorder γ of solids even in the vicinity of the melting point is usually only of the order of 10^{-3}, it has a decisive influence on mass transport within the lattice since only the defect centers can move in the lattice; a direct transposition of neighboring lattice atoms is unlikely on energy grounds.

The following transposition mechanisms involving disorder centers are important and have been verified experimentally:

1. Exchange of a vacancy with a neighboring lattice atom (vacancy migration).
2. Migration of an interstitial atom to a neighboring (equivalent) interstitial site (interstitial migration).
3. Displacement of a normal lattice atom to an interstitial site by a neighboring interstitial atom (*Wagner*'s displacement mechanism [11]).

All these elementary steps require a particular "threshold energy" U, which corresponds to the position of the saddle point between the initial and final states of the migrating particle. For the migrating step, therefore, an arbitrarily chosen particle requires the threshold energy U in addition to the disorder energy E_f. In the description of mass transport by a diffusion coefficient, therefore, we find an exponential expression of the form

$$D = D_0 \exp\left(-\frac{E_f + U}{RT}\right) \qquad (3)$$

for a monatomic substance with Schottky disorder, and a similar expression for an ionic compound A^+B^- [*].

$$D = D_0 \exp\left(-\frac{E_f/2 + U}{RT}\right) \qquad (4)$$

The energy relations for a lattice site and a neighboring interstitial site are shown schematically in Figure 6.

The factor D_0 in the diffusion coefficient involves the vibration frequency and the distance through which the defect jumps, as well as some quantity depending on the geometry of the lattice.

[*] $E_f/2$ occurs if two defects are formed per misplaced lattice atom, as is the case in Schottky or Frenkel disorder in an ionic compound A^+B^-. The simple expression (4) is sufficiently accurate only if the threshold energies U_1 and U_2 of the two defect centers are not very different. If $U_1 \gg U_2$, *e.g.* eq. (3) with $U = U_2$ is valid; if U_1 and U_2 are of the same order of magnitude, but differ appreciably, eq. (4) is replaced by an exponential expression containing two terms with different values of D_0 and U.

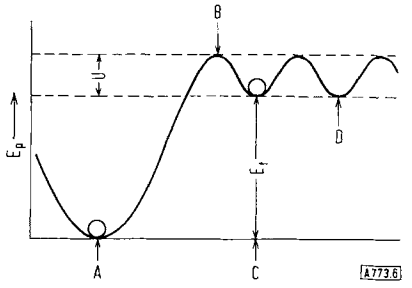


Fig. 6. Potential energy diagram of a particle in various lattice positions.

A: Occupied normal lattice site; B: Saddle point for transition into interstitial site; C: Occupied interstitial site; D: Vacant interstitial site.

Diffusion plays a decisive role in many solid state reactions, such as tarnishing and scaling processes. The rate-determining step is often not the reaction at the interface but the diffusion of the reactants through the solid layer formed. Thus the parabolic oxidation law discovered empirically by *Tammann* [3]

$$(\Delta\xi)^2 = 2\,k't \qquad (5)$$

($\Delta\xi$ = thickness of oxide layer, t = oxidation time, k' = tarnishing constant)

is readily explained if the diffusion of ions and electrons through the reaction layer is assumed to be rate-determining [4].

2.2. Ionic Conductivity

The random diffusion of atoms due to disorder proceeds by essentially the same mechanism in ionic crystals and in metals; in ionic crystals a preferred flow of ions can be superimposed on this random motion by application of an external electric field. The defect centers (vacancies, interstitial ions) move with or against the electric field, depending on their charge in relation to the neutral crystal.

The ionic conductivity can thus be described by an expression similar to that found for diffusion:

$$\sigma = \sigma_0 \exp\left(-\frac{E_f/2 + U}{RT}\right) \qquad (6)$$

This expression is valid if only one type of defect is present and the threshold energies for the defect centers are not very different.

Since diffusion and ionic conduction involve the same transport mechanism, a definite relation must exist between the two. This relation is given by the Nernst-Einstein equation

$$D = \frac{kT}{n\,(z \times e)^2}\,\sigma \qquad (7)$$

(k = Boltzmann's constant, T = absolute temperature; e = electronic charge; z = valency of ions; n = concentration of ions).

However, this equation is valid only if all the defect centers that contribute to diffusion also contribute to conduction. Thus there must be no neutral defect associations, which would diffuse, but would not exhibit a preferred migration direction in an electric field. Moreover, σ naturally must not contain any electronic conduction component. For very accurate comparisons of diffusion and conductivity, a "correlation factor" must be introduced into eq. (7) to take into account the differences in the migration of the defect centers and of the labeled ions observed in the diffusion experiment. The correlation factor has characteristic values for the various migration mechanisms. The correlation factor found by comparison of very accurate diffusion and conductivity measurements can thus serve as an indication of the nature of the defect migration mechanism [5].

2.3. Disorder in Nonstoichiometric Compounds

So far we have been dealing mainly with pure substances whose components are present in exactly the correct stoichiometric ratio; any atomic disorder in such cases must be thermal intrinsic disorder. Though the problems of substances with nonstoichiometric compositions can only be touched on lightly here, the principal aspects in connection with disorder cannot be completely ignored.

The disorder equilibria of binary nonstoichiometric ionic compounds depends not only on the temperature but also on the partial pressure of one of the components in the external gas phase; this pressure fixes the equilibrium ratio of metal to non-metal in the compound. Corresponding to the deviation from the stoichiometric composition, an equivalent number of ionic and electronic defects are produced, and these largely determine the properties of the compound. Owing to the very much greater mobility of electrons, substances of this nature are always predominantly electronic conductors. With an excess of metal, conduction is by electrons (n-type conduction), while with an excess of the non-metal, conduction is by defect electrons (p-type conduction).

Information about the equilibrium of disorder is provided above all by measurements of the conductivity as a function of the temperature and of the external gas phase. Many investigations of this nature have been carried out. They have made an important contribution to the elucidation of the complicated problems of tarnishing and scaling processes, particularly in the oxidation of metals [6, 7].

The characteristics of heterogeneous catalysts are undoubtedly also largely determined by the electronic properties due to disorder. This will probably also receive considerable attention in future fundamental

[3] *G. Tammann*, Z. anorg. allg. Chem. *111*, 78 (1920).

[4] *C. Wagner*, Z. physik. Chem., Abt. B *21*, 25 (1932); *32*, 447 (1936).

[5] *K. Compaan* and *Y. Haven*, Trans. Faraday Soc. *52*, 786 (1956); *54*, 1498 (1958).

[6] *C. Wagner*: Atom Movements. Amer. Soc. Metals, Cleveland, Ohio 1951, p. 153ff.

[7] *K. Hauffe*: Oxidation of Metals. Plenum Press, New York 1965.

research. Apart from the possibility of controlling chemical reactions, the processes involved in heterogeneous catalysis are of great interest in themselves. However, the problem is very complex, since in addition to the disorder phenomena, which are now relatively well known, many other factors such as chemisorption, electronic charge reversal processes, and boundary layer phenomena must also be considered [8].

3. Methods of Determining Disorder Data

3.1. Diffusion and Ionic Conductivity

The experimental methods most commonly used for testing disorder models and for the quantitative determination of disorder data are conductivity and diffusion measurements. The conductivity measurements must be supplemented by transport number measurements in order to separate the cationic, anionic, and electronic components of conductivity.

According to *Tubandt* [9], this can usually be done by measurements on several tablets of the material in question between two suitable electrodes (Fig. 7). After the passage of a certain quantity of electricity, which is measured with a coulometer, the transport numbers of the ions can be determined from the changes in the weights of the cathode and anode cylinders. If the ion equivalents transported are less than that indicated by the coulometer, the difference is due to an electronic conduction component. However, the simple arrangement shown in Figure 7 is often inadequate; it is frequently necessary to interpose "protective electrolytes" (*e.g.* AgI, $BaCl_2$), which prevent the growth of metal filaments and the liberation of components as a result of electronic conduction.

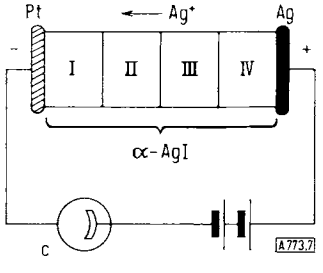


Fig. 7. *Tubandt*'s arrangement for the measurement of transport numbers in solids.

In the investigation of AgI, silver ions flow from the Ag anode to the Pt cathode. The quantity of electricity passed is determined with the coulometer C.

A similar arrangement is normally used to measure the total conductivity, but only a single tablet is placed between the electrodes in this case. For a sample of medium conductivity, one need only measure the current as a function of the voltage across the electrodes. For higher conductivities, the potential drop along the sample should be measured with probes and a compensating apparatus; this avoids the inclusion of contact resistances at the electrodes in the measurement. An arrangement of this type is shown in Figure 8. Alternating current is frequently also used (an AC bridge with an oscillograph as a zero indicator) to eliminate polarization processes at the electrodes.

[8] *K. Hauffe*, Angew. Chem. *67*, 189 (1955); *68*, 776 (1956).

[9] *C. Tubandt* in *W. Wien* and *F. Harms*: Handbuch der Experimentalphysik. Akademische Verlagsgesellschaft, Leipzig 1932, Vol. XII/1, p. 383.

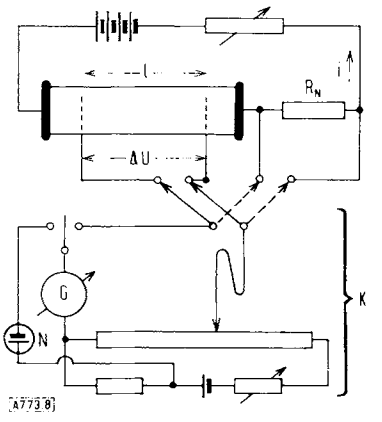


Fig. 8. Arrangement for conductivity measurement with probes.

Using the compensating apparatus, one measures: (a) the current i flowing through the sample as the potential drop across the standard resistance R_N; (b) the potential drop Δu over the length l of the specimen. The specific conductivity of the specimen is given by $\sigma = li/q\Delta u$ (q = cross section of specimen).

If eq. (6) is valid, the usual plot of the conductivity in an Arrhenius diagram (log σ against $1/T$) gives a straight line, the slope of which can be used to find the apparent [*] activation energy $[(E_f/2) + U]$ for the migration of the defect centers.

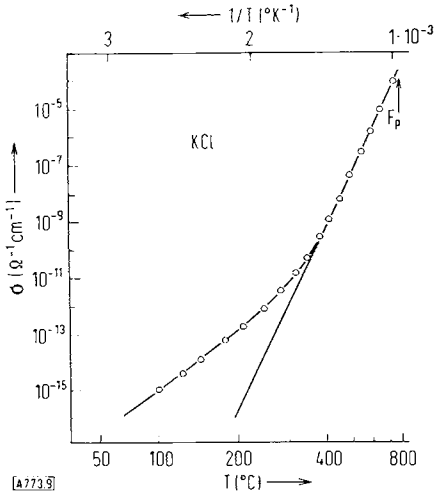


Fig. 9. Temperature dependence of the electrical conductivity of an ionic conductor, with KCl as example.

The intrinsic conduction range is seen above 400 °C. Below 200 °C the conductivity is determined by extraneous Ca^{2+} ions; the KCl specimen, which was purified by zone melting, had a Ca^{2+} content of 10^{-8}—10^{-9} (after [10]).

Figure 9 shows a typical diagram for an ionic conductor [10]. A particularly striking feature is the sharp change from the steeper linear section at high temperatures to a much shallower curve at low temperatures; this point separates the region of intrinsic conduction, in which the determining factor is the thermal

[*] The descriptions "apparent" and "formal" as applied to the activation energy refer to the fact that we are not usually concerned with a single elementary step of migration associated with an activation step that can be described precisely. Thus in ionic crystals, several transport processes usually take place simultaneously (*e.g.* vacancy migration and interstitial migration); the apparent activation energy found experimentally is then merely a formal expression obtained as the average of various processes. This correct designation is particularly important in reaction kinetics.

[10] *H. Gründig*, Z. Physik *158*, 577 (1960).

disorder [the apparent activation energy here is found from eq. (6)], from the region of impurity-dependent conduction in which the thermal disorder is so slight that the defects due to impurities predominate. The number of induced defects of the latter type is independent of the temperature, and the temperature dependence of the conductivity in this region depends only on the threshold energy U. It is therefore possible to find U alone, and hence also E_f. The purer the sample, the lower is the temperature at which the discontinuity in the conductivity curve appears. This temperature can be displaced within certain limits by specified additions of cations having a different valency. At the temperature of the discontinuity, the concentration of bivalent ions is roughly equal to the concentration of thermal defects. All disorder data can in principle be found from conductivity measurements on anomalous solid solutions [*], as has been shown by *Koch* and *Wagner* [11].

Self-diffusion measurements offer another method of obtaining information about the state of disorder. They fit in well with conductivity measurements, since the self-diffusion coefficient and the conductivity are related by the Nernst-Einstein equation [eq. (7)]. Since radioactive isotopes of most elements have become available, self-diffusion measurements essentially can be carried out without difficulty, but the experimental outlay is greater than for conductivity measurements.

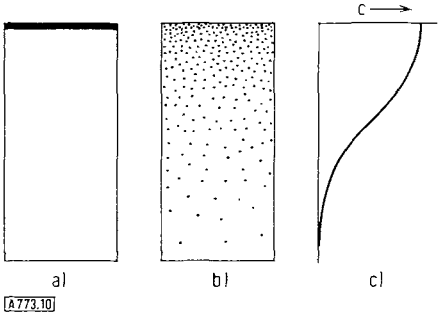


Fig. 10. Frequently used form of diffusion specimen for measurement with radioactive isotopes.

a: Before diffusion; a thin layer containing radioactive atoms is situated on the face of the specimen.

b: After diffusion; the radioactive atoms are distributed throughout the specimen.

c: Concentration profile of the radioactive atoms along the specimen.

The specimen normally used is as shown in section in Figure 10a. Radioactive isotopes of the atoms under investigation are applied to the polished face in the thinnest possible layer. Diffusion at high temperatures leads to distribution of the radioactive atoms in the interior of the specimen. If the dilution of the labeled atoms is sufficiently high, the diffusion coefficient is concentration independent and can be readily determined from the concentration profile. The most reliable method of finding the concentration profile (cf. Fig. 10c) is to cut the specimen into thin sections parallel to the surface. The activities of the various layers provide a relative measure of the concentration of radioactive atoms that have diffused in at the corresponding distance from the surface.

[*] This is the most usual term. *Wagner* refers to solid solutions in which additives with different valencies are incorporated into normal lattice sites as heterotypical mixed phases.

[11] *E. Koch* and *C. Wagner*, Z. physik. Chem., Abt. B *38*, 295 (1937).

It is sometimes very difficult to cut specimens of ionic crystals into such sections. In this case the absorption of the radiation of the tracer atoms that have diffused in is normally utilized. If the radioactivity above the surface is measured with a counter tube, a decrease in radiation is observed after diffusion as a result of absorption of the radiation of diffused atoms in layers nearer to the surface. If the linear absorption coefficient for the radiation in the medium in question is known, the diffusion coefficient can be calculated from the drop in intensity of the radiation.

Some methods involving the use of radioactive isotopes for diffusion measurements [12] are suitable for special problems, and particularly for the measurement of very small diffusion coefficients (between 10^{-14} and 10^{-19} cm^2/s). It is necessary to use diffusion measurements in such cases, since the partial conductivity of an ionic component is then less than $10^{-8}\,\Omega^{-1}$ cm^{-1}. Diffusion measurements are particularly important for metals, since there is no alternative method that allows the direct measurement of mass transport in the lattice, as there is in the case of ionic crystals.

3.2. Cubic Expansion Determined from Macroscopic and X-Ray Measurements

The accurate determination of the expansion of a lattice by X-ray diffraction gives smaller values than macroscopic measurement if appreciable Schottky disorder is present in the temperature range in question. In this case atoms migrate from the interior of the crystal to the surface as the temperature is raised (see Fig. 1), with the result that the expansion of the lattice is accompanied by an additional macroscopic increase in volume.

Disorder data have been obtained for some metals with the aid of this behavior. Figure 11 shows the result of such measurements on gold [13]. Table 1 shows some values obtained by this method and/or from the increase in the electrical resistance for quenched metal specimens as a result of "frozen-in" defects.

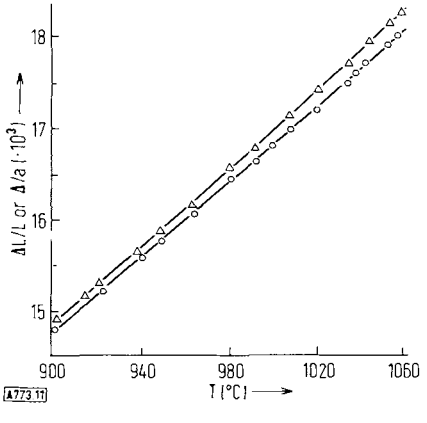


Fig. 11. Different linear expansions in gold.

△: $\Delta L/L$ = linear expansion found by macroscopic measurements.

○: $\Delta a/a$ = lattice expansion found by X-ray measurements.

The Schottky disorder that occurs preferentially in metals leads to an additional macroscopic expansion (after [13]).

[12] *R. Lindner*, Acta chem. scand. *5*, 735 (1951).

[13] *R. O. Simmons* and *R. W. Balluffi*, Physic. Rev. *125*, 862 (1962).

Owing to the low defect concentrations and the correspondingly small measurement effects, the accuracy of the measurements must be very high. For these reasons, measurements have so far been carried out only on a few metals with favorable mechanical and metallurgical properties.

In the case of ionic crystals, this method offers a possibility of distinguishing between Frenkel and Schottky disorder. Frenkel disorder does not lead to an additional macroscopic increase in volume since the atoms from the vacancies remain inside the crystal; this produces only a slight expansion of the lattice, which is practically undetectable at low degrees of disorder.

Table 1. Disorder data for some metals.

	Energy of disorder E_f (kcal/mole)	Degree of disorder at m.p. $\gamma_{m.p.} \times 10^3$	Ref.	Method
Au	21.7 ± 2	0.72 ± 0.06	[13]	[b]
Al	17.6 ± 1.6	0.90 ± 0.06	[14, 15]	[a, b]
Ag	25.1 ± 2.3	0.17 ± 0.05	[16]	[b]
Pt	35 ± 1	—	[17]	[a]
Cu	27 ± 2.5	0.20 ± 0.05	[18]	[b]

[a] From electrical resistance measurements.
[b] From density measurements.

4. Influence of Disorder on the Temperature Dependence of the Specific Heat

4.1. Specific Heats of Solids

The increase in the intrinsic disorder in the crystal lattice with rising temperature means that more energy is required, and this in turn increases the heat content of the crystal. The specific heat must therefore contain a component due to the change in disorder with temperature.

Before estimating the magnitude of this effect and deriving quantitative expressions for it on the basis of the disorder models, let us recall some basic facts about the specific heats of solids.

According to Dulong and Petit's law, the specific heats of most solid elements in the vicinity of normal temperatures are roughly equal to $3R$, where R is the molar gas constant. By extension of this rule we find that the molecular heats of many solid compounds can be calculated by summation of the atomic heats of the elements present (Kopp's law). Thus a diatomic solid compound would have a molar heat of $2 \times 3R$, and the values for polyatomic compounds, provided that they are not too complicated, should roughly be multiples of 6 kcal/mole °K $\approx$ 25 J/mole °K.

[14] *W. Desorbo* and *D. Turnbull*, Acta metallurg. *7*, 83 (1959).
[15] *R. O. Simmons* and *R. W. Balluffi*, Physic. Rev. *117*, 52, 62 (1960).
[16] *R. O. Simmons* and *R. W. Balluffi*, Physic. Rev. *119*, 600 (1960).
[17] *F. J. Bradshaw* and *S. Pearson*, Philos. Mag. *1*, 812 (1956); *B. G. Lazarev* and *O. N. Ovcharenko*, Ž. eksper. teoret. Fiz. *36*, 42 (1959).
[18] *R. O. Simmons* and *R. W. Balluffi*, Physic. Rev. *129*, 1533 (1963).

Above normal temperature, the specific heat slowly increases with rising temperature. This can be explained by slight anharmonicities of the lattice vibrations, and in the case of metals by a small contribution from the quasi-free electrons. The important point here is that both components lead to an approximately *linear* increase with rising temperature.

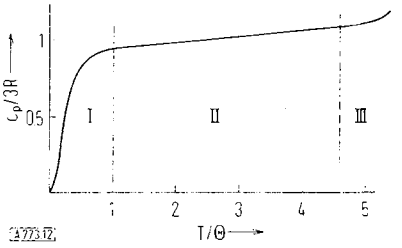


Fig. 12. Typical course of the specific heat of a solid.
Region I: Lattice vibrations not fully excited.
Region II: The lattice vibrations are fully excited; slight temperature dependence of c_p.
Region III: Stronger temperature dependence as a result of anharmonicities of the lattice vibrations.

Figure 12 shows a typical plot of the specific heat of a monatomic substance against temperature in units of the characteristic Debye temperature. We are interested here in the portion II above the Debye temperature, which corresponds to the range of validity of Dulong and Petit's law in the extended form mentioned above. In region III, the increase with rising temperature is faster than linear; this is due to a stronger influence of the anharmonicity of the lattice vibrations, and possibly to a greater contribution from the electrons at higher temperatures.

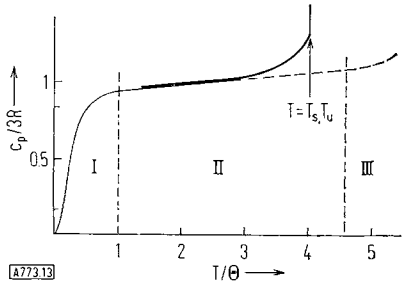


Fig. 13. Temperature dependence of the specific heat before melting and transition points.

Figure 13 illustrates the situation in which a melting point or transition point occurs in region II. It has been found that pronounced disorder is produced in the crystal even in a temperature range below this point, as can be seen from a marked increase in c_p some 100–150 °C before the transition point. The form of this increase can be predicted with the aid of the disorder models. It must be approximately exponential, since the degree of disorder also increases roughly exponentially according to eq. (2).

4.2. Estimation of the Component Due to Disorder

To illustrate the estimation of the additional specific heat due to disorder, let us consider the metal aluminum. Aluminum crystallizes in a simple close-packed, face-centered cubic atomic lattice, for which the degree

of disorder is not expected to be very large. It is known from a comparison of the densities as found by macroscopic and X-ray measurements (Table 1) that only about every thousandth lattice site in solid aluminum is unoccupied in the immediate vicinity of the melting point; approximately 20 kcal must be supplied in order to produce one gram atom of such defects.

Thus if one gram atom of aluminum is heated from a low temperature, where the disorder is still negligible, to a temperature very close to the melting point, an energy of $\gamma_{m.p.} \times E_f \approx 10^{-3} \times 20 \times 10^3 \approx 20$ cal must be supplied to the lattice for the disorder in addition to the heat of vibration. Owing to the exponential increase in the disorder with rising temperature, therefore, we obtain an additional specific heat of $\approx$1 cal/mole · °K in the vicinity of the melting point; this corresponds to more than 15% of the normal specific heat of aluminum.

Jost [19] deduced some considerable time ago for silver bromide that the effect can be very much greater for other solid substances whose structures are still relatively simple. Since conductivity measurements had given a degree of disorder of $\approx$2% and the disorder energy had been found to be 20 kcal/mole [11], the total heat effect at the melting point should be $\approx$400 cal/mole. Experiments have in fact given additional heats of this order of magnitude (cf. Section 4.5).

4.3. Experimental

Heat effects of this type are best measured with a continuous-operation adiabatic calorimeter (Isoperibol type); it should give high accuracy over the widest possible temperature range, since we require accurate determination not only of the additional heat effect at high temperatures, but also of the linear portion of the specific heat curve at low temperatures. A suitable apparatus is shown schematically in Figure 14.

The apparatus [20] used by our team in the investigations described in Section 4.5 has now been improved to such a degree that all adjustments and the recording of the measured values (temperature-time function) within a single run are carried out automatically. An individual series of measurements is reproducible to within ±0.2%. Comparisons with measurements carried out on aluminum by the National Bureau of Standards (USA) showed an agreement to within ±0.3% over the entire temperature range from −70 to 650 °C.

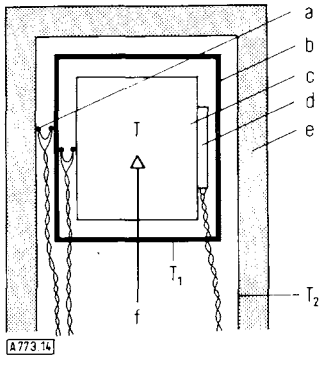


Fig. 14. Scheme of an adiabatic calorimeter.

a: Differential thermocouples; b: Adiabatic jacket; c: Sample container (cf. [21]); d: Pt resistance thermometer; e: Outer jacket and insulation; f: Heat input $u \times j$ = const.).

Adiabatic condition $T = T_1$; control condition $T_1 > T_2$. Energy is supplied continuously (under control) to the sample inside (constant heat supply) in such a way that its temperature rises steadily. The adiabatic jacket undergoes the same temperature rise and prevents heat exchange with the environment.

4.4. Evaluation of the Heat Effects

For a simple evaluation of this anomalous temperature dependence of the specific heats of solids, it is assumed that the deviation of the c_p values from linearity, as found at low temperatures, is due only to disorder in the lattice. The additional specific heat Δc_p can thus be obtained by taking the difference between the experimental curve and the linear extrapolation of the specific heat from the low temperature range. At low degrees of disorder ($\gamma < 10^{-2}$), the contributions of the individual defects are additive. For a temperature-independent disorder energy E_f, the total additional quantity of heat per mole that must be supplied for disorder up to the temperature T is

$$Q = E_f \times \gamma(T) = E_f \times \gamma_0 \exp(-E_f/RT)\ [*] \qquad (8)$$

The additional specific heat is obtained by differentiation of this expression with respect to temperature

$$\Delta c_p = \frac{dQ}{dT} = \frac{E_f^2 \gamma_0}{RT^2} \exp(-E_f/RT) \qquad (9)$$

or

$$\ln(\Delta c_p T^2) = \text{const.} - \frac{E_f}{RT} \qquad (10)$$

A plot of $\ln(\Delta c_p \cdot T^2)$ against $1/T$ should therefore give a straight line, from whose slope the disorder energy E_f can be obtained.

According to eq. (8), the degree of disorder is

$$\gamma(T) = Q(T)/E_f = \frac{1}{E_f} \int_0^T \Delta c_p \, dT' \qquad (11)$$

$Q(T)$ is usually found by graphical integration of the area between the measured c_p curve and the linear extrapolation.

4.5. Results of Measurements

Figure 15 shows the temperature dependence of the specific heat of silver bromide, for which the disorder effect was detected first [22, 23]. As expected, the curve shows a very pronounced, quasi-exponential increase, which begins 200 °C below the melting point. The total

[19] *W. Jost*: Diffusion in Solids, Liquids, Gases (Third Printing with Addendum), Academic Press, New York 1960, p. 95.

[20] *J. Nölting*, Ber. Bunsenges. physik. Chem. *67*, 172 (1963).

[21] *J. Nölting*, Ber. Bunsenges. physik. Chem. *68*, 932 (1964).

[*] This is valid for Schottky disorder in a monatomic substance. Frenkel disorder in a monatomic substance and in ionic crystals of the form A^+B^- requires the insertion of the factor 1/2 in the exponent [see eq. (2)].

[22] *R. W. Christy* and *A. W. Lawson*, J. chem. Physics *19*, 517 (1951).

[23] *W. Jost* and *P. Kubaschewski*, Z. physik. Chem. N. F. *60*, 69 (1968).

anomalous heat effect is 776 cal/mole. This leads to the astonishing conclusion that 9% of the total heat content of AgBr at the melting point is due to Frenkel defects in the cation lattice. The disorder component of the specific heat at the melting point is almost 50%. Figure 16 shows a plot in accordance with eq. (10), which gives a straight line to a good approximation. The disorder data are given in Table 2, which also contains comparison values obtained by other methods However, the agreement is not expected to be particularly good in the extreme case of AgBr, since the simple idea of independent defects is undoubtedly only approximately valid at degrees of disorder $\gamma > 10^{-2}$ [*]

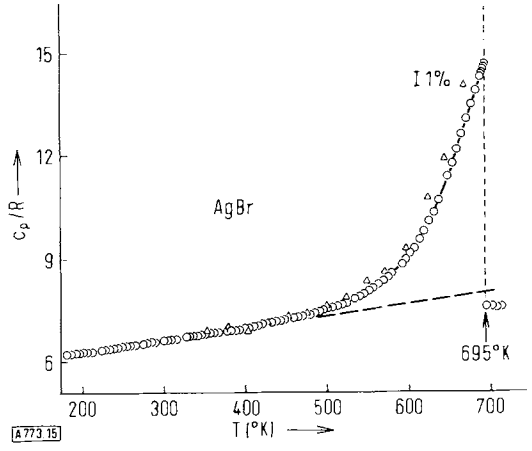


Fig. 15. Specific heat of AgBr.
△: Values according to [22]. ○: Values according to [23].

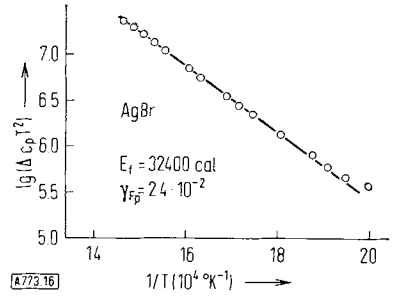


Fig. 16. Determination of the disorder energy E_f of the Frenkel disorder in AgBr from additional specific heats.

Figure 17 shows the results of measurements on AgI [24]. A distinct, though not very pronounced, ascent is found for the β phase (up to 147 °C). This can again be attributed to Frenkel disorder in the cation lattice (see Table 2). According to X-ray structure analysis [25] and conductivity measurements [26], the disorder in the cation lattice of α-AgI (147–558 °C) is practically complete; the disorder consequently cannot

[*] At a 1% degree of disorder, the average distance between a vacancy and an interstitial ion is only about three times the distance between cations in the lattice. Associations of defects, which can have a strong influence on the ionic conductivity in particular, must therefore be expected.

[24] *J. Nölting* and *D. Rein*, Z. physik. Chem. N. F. *66*, 150 (1969).

[25] *L. W. Strock*, Z. physik. Chem., Abt. B *25*, 441 (1934).

[26] *C. Tubandt* and *E. Lorenz*, Z. physik. Chem., Abt. A *87*, 513, 543 (1914).

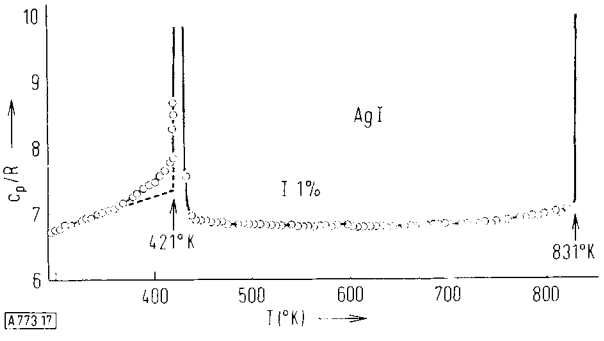


Fig. 17. Specific heat of AgI.

increase with rising temperature, and no additional specific heats appear. The slight fall of the curve can be attributed to residual short-range order in the cation lattice, the breakdown of which requires further small quantities of energy. According to self-diffusion measurements [27], the disorder in the anion lattice is very slight, and the absence or near-absence of disorder anomalies of the iodide ions at the melting point of AgI is quite understandable.

Further examples of pronounced anomalies in ionic crystals are shown in Figures 18 to 20 [23,28]. In addition to the characteristic increases in c_p in the low-temperature phases, which are very pronounced for CuI and CuBr, unusual downward trends are also observed. It can be seen that these occur only in phases that are almost completely disordered. One might therefore attribute it to a short-range order effect like that in α-AgI; however, the descent with temperature is about an order of magnitude too fast for this, as can be deduced from the theories of order-disorder transitions for metal alloys [28]. An attempt to explain it by the transition of a vibration into a quasi-free translation of the cation in the disordered lattice, corresponding to the treatment of the inhibited rotator [29], can also provide only a qualitative explanation of such a variation of the specific heat. For quantitative interpretations, it is necessary to take into account the

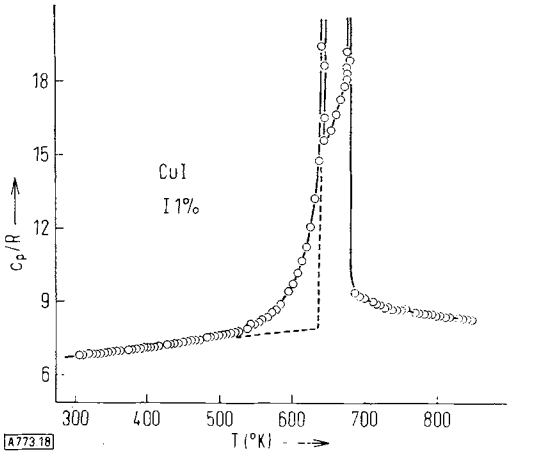


Fig. 18. Specific heat of CuI.

[27] *J. Nölting*, Z. physik. Chem. N. F. *19*, 118 (1959).

[28] *J. Nölting*, *J. Troe*, and *D. Rein*, Nachr. Akad. Wiss. Göttingen, II. math.-physik. Kl. *1969*, 31

[29] *K. S. Pitzer* and *W. D. Gwinn*, J. chem. Physics *10*, 428 (1942).

difference $c_p - c_v$ between the measured and the calculated values (on the basis of the formula $c_p - c_v = \alpha^2 TV/\varkappa$); measurements of the coefficients of linear expansion α and of the compressibilities $\varkappa$ of the substances mentioned are now in progress [30].

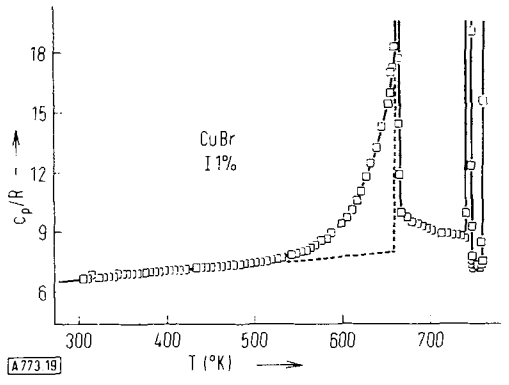


Fig. 19. Specific heat of CuBr.

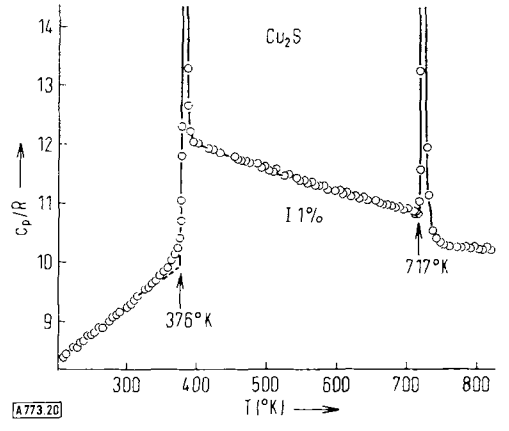


Fig. 20. Specific heat of Cu_2S.

The disorder data for alkali metal halides are particularly interesting. For example, Figures 21 and 22 show the results of c_p measurements on NaCl and NaBr [31]. The disorder data obtained from these assuming Schottky disorder are shown in Table 2. Comparison data from conductivity measurements agree well with these results. On the other hand, the degrees of disorder found in this way are higher by a factor of about 10 than the few known estimates [32, 33]. In connection with the results of measurements on metals, we must ask ourselves whether it is necessary to modify the simple evaluation method hitherto used for the anomalous specific heats.

It is very difficult to determine the intrinsic disorder for metals. Though the apparent activation energy ($E_f + U$) can be determined by diffusion measurements, U cannot be determined separately by a simple method similar to that used for ionic crystals. The only methods available are those based on density comparison and

[30] *C. D. Gericke*, Diplomarbeit, Universität Göttingen 1969.

[31] *W. Kramer*, Dissertation, Universität Göttingen 1968.

[32] *A. Seeger* in *S. Flügge*: Handbuch der Physik. Springer, Berlin 1955, Vol. 7/1, p. 385ff.

[33] *R. W. Dreyfus* and *A. S. Nowick*, J. appl. Physics *33*, 473 (1962).

Table 2. Disorder data for ionic crystals and metals.

	Stable up to (°K)	Disorder energy [a] E_f (kcal/mole)	Apparent activation energy [b] (kcal/mole)	$\gamma_{m.p.}$ [c] $\times 10^3$	Ref. [d]
AgBr	695	32.4 ± 0.3	18.5	24	[34]
β-AgI	421	26 ± 2	16	0.88	[35, 36]
γ-CuI	642	46 ± 4	35	9	[26]
γ-CuBr	659	49 ± 5	35	13	[37]
β-Ag_2S	450	33 ± 1	21	0.5	[38]
γ-Cu_2S	376	31 ± 1	—	0.2	—
NaCl	1075	46 ± 2	46—49 [e]	3.2	[39, 40]
NaBr	1014	40.5 ± 2	39 [e]	4.1	[41, 42]
In	430	9.8 ± 0.5	18	0.53	[43]
Sn	505	10.5 ± 0.4	∥ 24.3 ⊥ 25.0	1.3	[44]
Pb	601	9.0 ± 0.6	22—24	2.3	[45, 46]
Zn	693	14 ± 2	∥ 22 ⊥ 24	2.3	[47]
Sb	904	26 ± 2	∥ 47 ⊥ 44	1.2	[48]
Al	933	18.2 ± 1	32—34	2.2 (1.0)	[49, 50]

[a] Calculated from specific heats. [b] From ionic conductivity and diffusion. [c] Degree of disorder immediately before the melting or transition point (see Column 2), calculated from specific heats. [d] References to Column 4. [e] Disorder energy.

on the increase in electrical resistance (cf. Section 3.2), which are not without complications.

Disorder data for metals can be obtained from anomalous specific heats. Some examples are shown in Figures 23 to 25. It can be seen from the diagrams, however, that the anomalous effect is about one order of magnitude smaller than for ionic crystals. The additional specific heats are only a few per cent of the total c_p. The measurements must therefore be accurate to within 1 promille if the additional component is to be determined to within a few per cent. It is also doubtful whether the extrapolation of the linear part is sufficiently accurate. We have found that the energy of disorder found for aluminum by the usual evaluation

[34] *J. Teltow*, Ann. Physik *5*, 63, 71 (1949).

[35] *K. E. Zimen*, *G. Johannson*, and *M. Hillert*, J. chem. Soc. (London) *1949*, 392.

[36] *K. Weiss*, *W. Jost*, and *H. J. Oel*, Z. physik. Chem. N. F. *15*, 429 (1958).

[37] *J. Geiler*, Dissertation, Universität Halle 1928.

[38] *H. Reinhold* and *H. Möhring*, Z. physik. Chem., Abt. B *28*, 178 (1935).

[39] *H. W. Etzel* and *R. J. Maurer*, J. chem. Physics *18*, 1003 (1950).

[40] *R. W. Dreyfus* and *A. S. Nowick*, J. appl. Physics *33*, 473 (1962).

[41] *D. Mapother*, *H. N. Crooks*, and *R. J. Maurer*, J. chem. Physics *18*, 1231 (1950).

[42] *H. W. Schwamp* and *E. Katz*, Physic. Rev. *94*, 828 (1954).

[43] *R. E. Eckert* and *H. G. Drickamer*, J. chem. Physics *20*, 13 (1952).

[44] *D. Lazarus*, Solid State Physics *10*, 116 (1960).

[45] *N. H. Nachtrieb* and *G. S. Handler*, J. chem. Physics *23*, 1569 (1955).

[46] *D. Frenzel*, Z. physik. Chem. N. F. *51*, 67 (1966).

[47] *G. A. Shirn*, *E. S. Wadja*, and *H. B. Huntington*, Acta metallurg. *1*, 513 (1953).

[48] *H. B. Huntington*, *P. B. Gate*, and *J. H. Rosolkowsky*, J. appl. Physics *35*, 3027 (1964).

[49] *T. G. Stoebe*, *R. D. Gulliver II*, *T. O. Ogurtani*, and *R. A. Huggins*, Acta metallurg. *13*, 701 (1965).

[50] *T. S. Lundy* and *J. F. Murdock*, J. appl. Physics *33*, 1671 (1962).

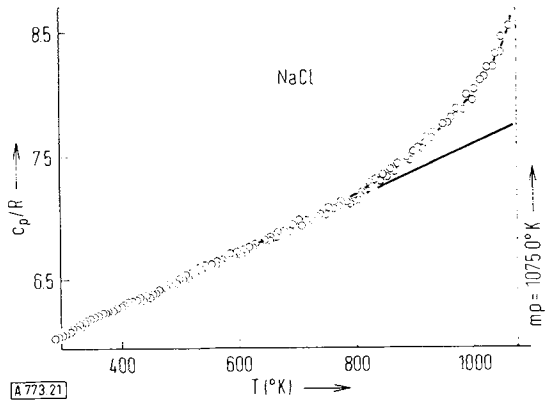


Fig. 21. Specific heat of NaCl.

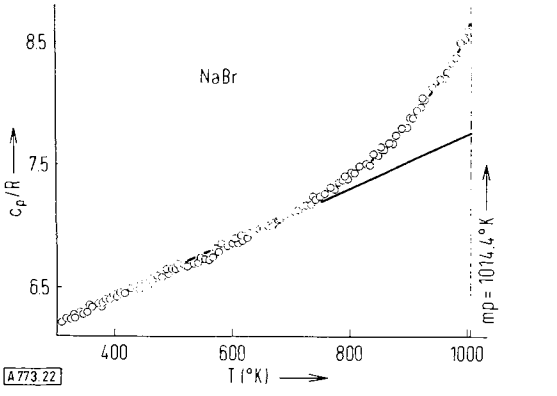


Fig. 22. Specific heat of NaBr.

agrees well with values obtained by other methods [15], whereas the degree of disorder is too large by a factor of 2. This deviation may be due to stronger anharmonicities of the lattice vibrations in the vicinity of the melting point. This difficulty may be overcome by conversion of the measured c_p values into c_v values. The specific heat at constant volume c_v should contain only very small components due to the anharmonicities of the lattice vibrations. This conversion and the corresponding evaluation [*] for aluminum gave agreement with the values reported by *Simmons* and *Baluffi* even in the degree of disorder (Table 2; in parentheses). The same evaluation method also seems to be called for in the case of the alkali metal halides. Unfortunately, however, the necessary coefficients of linear expansion and of compressibility are only very rarely known with sufficient accuracy for temperatures up to the melting point.

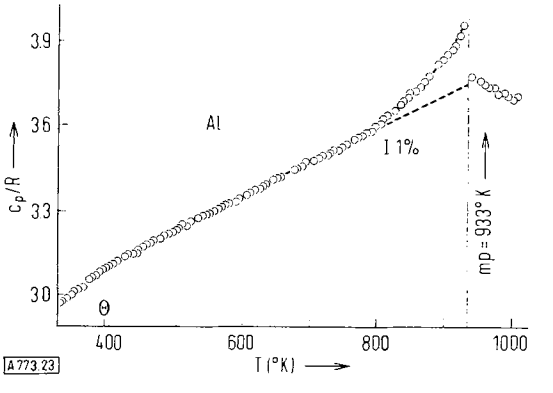


Fig. 23. Specific heat of Al.

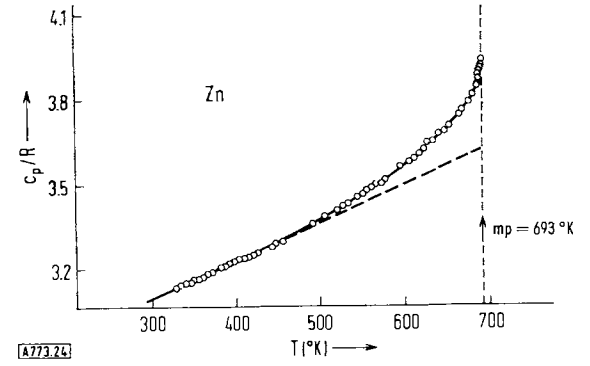


Fig. 24. Specific heat of Zn.

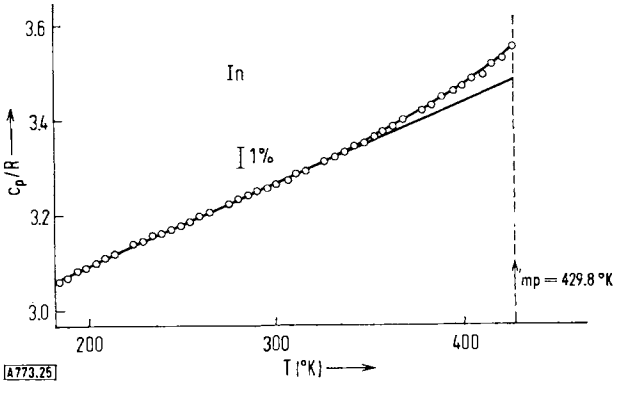


Fig. 25. Specific heat of In.

4.6. Outlook

In addition to the disorder properties, the temperature dependence of the specific heats of solids provides further important information which will not be discussed here. Apart from the surprising negative temperature coefficients, for which no conclusive explanation has yet been found, valuable information can be obtained from $c_p(T)$ measurements particularly on solid solutions. Phases in which temperature-dependent states of order occur exhibit a characteristic behavior. This has been known for a long time in the λ transitions of some metal alloys [52]. However, entropy considerations sometimes also provide a further insight into structural peculiarities in the case of ionic crystals [53]. Though thermal analysis is favored as a fairly economical method for the construction of phase diagrams, direct measurement of the specific heat may be prefer-

[*] In the conversion of c_p into c_v here it should be remembered that the macroscopic expansion coefficient contains the volume component of the Schottky disorder. To ensure that the defect component is retained in c_v, therefore, the expansion found from X-ray measurements must be used in the conversion formula [51].

[51] *W. Kramer* and *J. Nölting*, to be published.

[52] *F. C. Nix* and *W. Schockley*, Rev. mod. Physics *10*, 1 (1938).

[53] *J. Nölting*, Ber. Bunsenges. physik. Chem. *68*, 944 (1964).

able in complicated cases. For solid solutions, the absolute value of c_p and its variation with temperature often yield definite information about the nature of the phase present or of a phase transition.

Another group of problems surrounds the processes involved in delayed transitions. Here, particularly in connection with phenomena at critical phase separation points in the solid phase, we find difficult but extremely interesting applications of high-temperature calorimetry.

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Polarity of Covalent Bonds

By Martin Klessinger [*]

The concept of "partial ionic character" has proved exceedingly valuable and fruitful as a qualitative description of the electronic structure of molecules; however, the theoretical ideas underlying the empirical relations for the determination of the ionic character of a bond do not bear critical examination. Even Mulliken's population analysis fails in many cases as a means of interpreting quantum-chemical calculations. On the other hand, a graphical representation of the spatial charge density distribution allows an intuitive interpretation even of complicated calculations, and (possibly in combination with an analysis of the forces acting on the atomic nuclei) yields very much farther-reaching information on the polarity of a bond than can be expressed by the values of some parameters on the basis of excessively simplified models.

"*I believe the chemical bond is not so simple as some people seem to think.*" *R. S. Mulliken* [1].

1. Introduction

A bond between two atoms A and B is described as polar if the distribution of the valence electrons shared by these two atoms is unsymmetrical, so that the centers of the negative electronic charge and of the positive nuclear charge do not coincide. Any bond between non-equivalent atoms is therefore more or less polar; nonpolar bonds occur only between identical atoms in identical environments, examples being the bonds in homonuclear diatomic molecules such as H_2 or N_2 and the C–C bond in ethane.

The concept of bond polarity is of great practical value for the qualitative understanding of the properties and reactions of chemical compounds. Thus the inductive effect exerted by a bond on its environment depends on its polarity, as does the reactivity or the mode of reaction of the bond.

It would be very useful if one could determine the polarity of a bond quantitatively, and so place any bond between the limiting cases of an ideal covalent bond with a symmetrical charge distribution and an ideal ionic bond with complete charge transfer. Numerous empirical equations have been established in order to attain this goal, and some of these will be described shortly. This will be followed by a brief discussion of the theoretical basis of the concept of bond polarity and a description of more recent results and views based on extensive quantum-chemical calculations. For the sake of simplicity, only diatomic molecules will be dealt with in Sections 2 to 5. It will finally be shown how the results obtained for diatomic molecules can be applied to polyatomic molecules.

2. Empirical Rules for the Determination of Bond Polarity

2.1. Partial Ionic Character

Pauling [2,3] introduced the concept of partial ionic character as a measure of the polarity of a bond. The partial ionic character I_{AB} of a two-electron bond A–B shows how much negative charge (in % of the charge of an electron) was transferred from one atom to the other as a result of bonding. For an ideal ionic bond, therefore, $I_{AB} = 100\%$, while for an ideal covalent bond with a symmetrical charge distribution, $I_{AB} = 0\%$. The partial ionic character cannot be

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[1] Cited by *C. A. Coulson*, Rev. mod. Physics *32*, 177 (1960).

[2] *L. Pauling*, J. Amer. chem. Soc. *53*, 1367 (1931).

[3] *L. Pauling*: The Nature of the Chemical Bond. Cornell University Press, Ithaca, N.Y., 1939.

found experimentally, since even if charge distributions could be determined as accurately as one wished, it would still be necessary to make a more or less arbitrary division of the charge of a molecule into the components belonging to the individual atoms in order to be able to determine the partial ionic character. The ionic character of a bond must therefore be expressed by other quantities, which are better defined.

2.2. Bond Moments

Polar bonds have a dipole moment. It seems reasonable to correlate this bond moment with the partial ionic character. *Pauling* [3] determined the partial ionic characters of the hydrogen halides from the observed dipole moments μ and the internuclear distances R on the basis of the following argument. For a positive point charge and a negative point charge δe separated by a distance R, $\mu = \delta e \cdot R$; consequently, $100\,\mu/eR$ should give the charge transfer as a percentage of the charge e of an electron. From the experimental data for the dipole moments and internuclear distances (cf. Table 1), an ionic character of 17% is found in this way for HCl, 11% for HBr, and 5% for HI; *Pauling* estimated a value of 60% for the ionic character of HF.

The value of the partial ionic character found in this way must, however, seem questionable, since on the one hand the "theoretical" bond moment $\mu = eR$ (100% ionic character) is not reached even for an ideal ionic bond, owing to the mutual polarization of the charge distributions [4], and on the other the charge transfer is not the only factor that contributes to the bond moment. The dipole moment of a bond can be formally broken down into four components:

$$\mu = \mu_e + \mu_{at} + \mu_{hom} + \mu_{pol} \qquad (1)$$

The first term $\mu_e = \delta e \cdot R$ is the component of the dipole moment that results from the transfer of the charge δe from one atom to the other, and which alone is a measure of the polarity or partial ionic character of the bond. μ_{at} is the atomic dipole moment, which results from the asymmetry of the charge distribution in hybrid orbitals (Fig. 1a). μ_{hom} is the homopolar dipole moment due to the difference in the sizes of the orbitals (Fig. 1b), and μ_{pol} is due to the mutual polarization of the charge distributions as mentioned earlier. In practice, the individual contributions to the overall

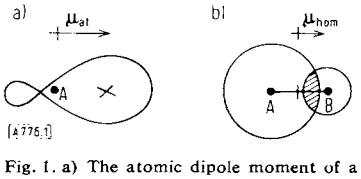


Fig. 1. a) The atomic dipole moment of a hybrid orbital. The atomic nucleus A is the center of positive charge and x is the center of negative charge.

b) The homopolar dipole moment. The accumulation of charge in the bond occurs in the shaded overlap region, which is not symmetrical with respect to the center of the line joining the nuclei.

dipole moment can only be isolated by calculation, and it is found that they often have different signs [5].

The following example illustrates how unsuitable the dipole moment of a bond is as a measure of its polarity. Since the C atom is more strongly electron attracting than the H atom, one should expect a transfer of charge δe from H to C in a C—H bond of methane; $\mu_e \approx 1$D when $\delta e = 0.2\,e$. The atomic moment can be estimated to be $\mu_{at} \approx 2$D [5], and is opposed to the moment μ_e due to the charge displacement. Despite the polarity C^-H^+, therefore, each bond of methane is found to have a bond moment whose direction is given by $\overset{+}{C}\!-\!\overset{-}{H}$, *i.e.* despite the charge transfer from H to C, the carbon forms the positive end of the dipole. These arguments are confirmed by quantum-chemical calculations for methane. The calculated values are $\delta e = 0.096\,e$ and $\mu_{CH} = 1.77$ D [6].

2.3. Nuclear Quadrupole Coupling Constants [7]

The nuclear quadrupole coupling constant eQq is the product of the quadrupole moment eQ of an atomic nucleus and the field gradient q, which gives the deviation of the potential V from spherical symmetry at the position of the nucleus. s electrons and complete inner shells have spherical charge distributions, and d and f electrons have practically no effect on the charge density in the vicinity of the nucleus; any asymmetry of the potential at the position of the nucleus is therefore mainly due to incompletely occupied p orbitals [8], so that to a good approximation, q is a measure of the occupancy of the p orbitals of an atom, and can thus be used for the estimation of the partial ionic character [8,9].

For the free Cl atom with one unoccupied p orbital, $eQq = -110$ MHz, while for the Cl^- ion with its spherically symmetrical charge distribution, $eQq = 0$. From the measured value $eQq = -75$ MHz [10] found for the Cl atom in CH_3–Cl, therefore, it follows that instead of one free p orbital as in the Cl atom, there is the fraction $(eQq)_{CH_3-Cl}/(eQq)_{Cl} = 0.68$ of an unoccupied p orbital.

$(eQq)_{AB}/(eQq)_B$ values for some diatomic molecules AB are given in Table 1. These values may be interpreted either in the sense that $[1-(eQq)_{AB}/(eQq)_B]$ electrons have been transferred from the atom A to the atom B in the molecule AB, or as indicating that the unoccupied orbital on the atom B is not a pure p orbital but a hybrid orbital with $100 \cdot [1-(eQq)_{AB}/(eQq)_B]$ % s character. Both the ionic character of a bond and the hybridization influence the value of the coupling constant, but both quantities cannot be determined from one measured value [11]. Information

[4] *E. S. Rittner*, J. chem. Physics *19*, 1030 (1951).

[5] *C. A. Coulson*: Valence, 2nd Edit., Oxford University Press, London 1961, p. 218.

[6] *M. Klessinger*, unpublished.

[7] See reviews by *J. W. Orville-Thomas*, Quart. Rev. (chem. Soc., London) *11*, 162 (1957), and *E. Scrocco*, Advances Chem. Physics *5*, 319 (1963).

[8] *C. H. Townes* and *B. P. Dailey*, J. chem. Physics *17*, 782 (1949).

[9] *W. Gordy*, Discussions Faraday Soc. *19*, 14 (1955).

[10] *W. Gordy*, J. chem. Physics *19*, 792 (1951).

[11] *K. Ito, D. Nakamura, Y. Kurita, K. Ito*, and *M. Kubo*, J. Amer. chem. Soc. *83*, 4526 (1961).

Table 1. Electronegativity and ionic character of diatomic molecules A—B.

	R (Å)	μ (D)	μ/eR	$\Delta\chi_P$	$\Delta\chi_M$	I_{AB} [eq. (2)]		I_{AB} [eq. (3)]		$(eQq)_{AB}/(eQq)_B$	I_{AB}(G)	I_{AB}(DT)
HF	0.917	1.91	0.43	1.66	1.69	50	(51)	36	(37)	—	—	—
HCl	1.274	1.03	0.17	0.98	0.74	21	(13)	19	(14)	—	—	—
HBr	1.414	0.79	0.11	0.73	0.41	12	(4)	14	(7)	0.69 [a]	31 [a]	19 [a]
HI	1.604	0.38	0.05	0.21	0.31	1	(2)	4	(5)	0.79 [b]	21 [b]	7 [b]
FCl	1.628	0.88	0.11	0.75	0.95	13	(20)	14	(18)	1.33	—	26
BrCl	2.138	0.57	0.06	0.29	0.33	2	(3)	5	(6)	0.94	6	6
ICl	2.32	0.65	0.06	0.42	0.43	4	(5)	7	(8)	0.75	25	12
LiF	1.51	6.28 [c]	0.87	2.12	3.06	67	(90)	50	(82)	—	—	—
KCl	2.666	10.06	0.85	1.56	2.18	46	(69)	33	(52)	0	100	100

R = internuclear distance (after [12]); μ = dipole moment (after [13]); $\Delta\chi_P$ and $\Delta\chi_M$ = differences $|\chi_A-\chi_B|$ in the Pauling and Mulliken electronegativities (after [14]); I_{AB} = ionic character, calculated from $\Delta\chi_P$ and from $\Delta\chi_M$ (values in parentheses); $(eQq)_{AB}/(eQq)_B$ = nuclear coupling constants (after [15]); I_{AB}(G) = ionic character after *Gordy* [10]. I_{AB}(DT) = ionic character after *Dailey* and *Townes* [15].
[a] Based on DBr; [b] based on DI; [c] after [17].

about the ionic character is consequently obtainable only if one can make plausible assumptions about the hybridization.

2.4. Electronegativity [18]

According to *Pauling* [3,19], the electronegativity χ_A is the ability of the atom A to attract electrons towards it in a molecule. It seems reasonable on the basis of this definition to assume the existence of a relation between the ionic character I_{AB} of a bond and the electronegativity difference $|\chi_A - \chi_B|$. *Pauling* [3] gave the relation

$$I_{AB} = 100\left[1-e^{-\frac{1}{4}(\chi_A-\chi_B)^2}\right] \quad (2)$$

while another formula was given by *Hannay* and *Smyth* [20]:

$$I_{AB} = 16\,|\chi_A-\chi_B| + 3.5\,|\chi_A-\chi_B|^2; \quad (3)$$

The latter is claimed to be more suitable for large values of $|\chi_A - \chi_B|$. *Gordy* [10,16] proposed a linear relation

$$I_{AB} = 50\,|\chi_A-\chi_B|, \quad (I_{AB} = 100 \text{ for } |\chi_A-\chi_B| \geqq 2) \quad (4)$$

whereas *Dailey* and *Townes* [15] reported an S-shaped relation between the partial ionic character and the electronegativity difference. These various relations are illustrated in Figure 2.

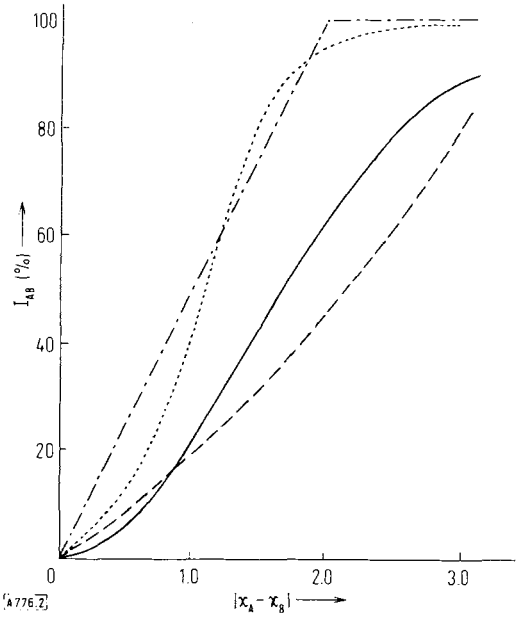


Fig. 2. Graphical representation of the relation between ionic character and electronegativity difference:
——— after *Pauling* [3], - - - - after *Hannay* and *Smyth* [20], — · — · — after *Gordy* [10, 16], · · · · after *Dailey* and *Townes* [15].

Equations (2) and (3) were derived on the basis of the values found for the partial ionic characters of the hydrogen halides from the dipole moments [21]. The ionic character values used by *Gordy* and by *Dailey* and *Townes*, on the other hand, were obtained from nuclear quadrupole coupling constants, but the hybridization was taken into account differently.

The four relations mentioned are clearly affected by all the inaccuracies that are associated with the determination of the polarity of a bond from the bond moments or the nuclear quadrupole coupling constants. Moreover, the electronegativity itself is not a measurable physical quantity which can be rigorously defined, but is an empirical quantity in certain greatly simplified models of the chemical bond. It is therefore pointless to try to determine electronegativity differences with great accuracy.

In Table 1, the differences in the electronegativity values determined by *Pauling* [3] from bond energies

[12] *L. E. Sutton*: Tables of Interatomic Distances, Special Publications No. *11* (1958), *18* (1965). The Chemical Society, London.

[13] *J. W. Smith*: Electric Dipole Moments. Butterworth, London 1955.

[14] *J. Hinze*, Fortschr. chem. Forsch. *9*, 448 (1968).

[15] *B. P. Dailey* and *C. H. Townes*, J. chem. Physics *23*, 118 (1955).

[16] *W. Gordy*, J. chem. Physics *22*, 1470 (1954).

[17] *R. F. W. Bader* and *W. H. Henneker*, J. Amer. chem. Soc. *87*, 3063 (1967).

[18] For a review cf. [14].

[19] *L. Pauling*, J. Amer. chem. Soc. *54*, 3570 (1932).

[20] *N. B. Hannay* and *C. P. Smyth*, J. Amer. chem. Soc. *68*, 171 (1946).

[21] *Hannay* and *Smyth* based their equation on the dipole moment of HF, which was determined by them for the first time, and which corresponds to an ionic character $I_{HF} = 43\%$, whereas the value estimated by *Pauling* was $I_{HF} = 60\%$.

are given for some diatomic molecules under $\Delta\chi_P$, while $\Delta\chi_M$ are the differences in the absolute electronegativity values defined according to *Mulliken*[22] by the ionization potential I_A and the electron affinity E_A of the valence state as follows:

$$\chi_A = {}^1/_2 (I_A + E_A) \tag{5}$$

Columns 6 and 8 of Table 1 contain the values of the partial ionic character calculated from eq. (2), eq. (3), and eq. (4). It is clear from the data in this table and from earlier remarks that the concept of the partial ionic character (as it was defined here as an empirical quantity) can certainly be useful for qualitative treatments, but that the quantitative data found in many textbooks for ionic character (Be–F 79 %, Be–O 63 %, *etc.*) are probably of no great significance.

3. Theoretical Principles of the Determination of the Partial Ionic Character

3.1. VB Method

The concept of partial ionic character is closely linked historically with the VB (valence bond) expression for the wave function Ψ of a diatomic molecule A–B, which can be written in the form[23]

$$\Psi = C_1 \{\varphi_A(1)\varphi_B(2) + \varphi_B(1)\varphi_A(2)\} + C_2\varphi_A(1)\varphi_A(2) + C_3\varphi_B(1)\varphi_B(2) \tag{6}$$

where the constants C_1, C_2, and C_3 are determined according to the variation principle by minimizing the energy calculated using the wave function Ψ. The first term in eq. (6), the Heitler-London function[24], is described as the covalent part of the wave function, and expresses the situation that one of the two indistinguishable electrons 1 and 2 is situated on the atom A and the other on the atom B, and that they can be described by the atomic orbitals (AOs) φ_A and φ_B of these atoms. The second and third terms take into account the case in which both electrons are situated on the atom A or on the atom B, and so characterize the ionic component of the wave function.

If A is more strongly electron-attracting than B, the probability of finding both electrons on the atom B will be very small, so that the third term in eq. (6) may be neglected, and the wave function can be written in the form

$$\Psi = \psi_{cov} + \lambda\psi_{ion} \tag{7}$$

λ is then regarded as a measure of the polarity of the bond, and $100\,\lambda^2/(1+\lambda^2)$ as the definition of the percentage ionic character[2].

Clear as this theoretical model appears at first sight, however, its physical significance is doubtful[25,26]. To see this, one must remember that all physical states, as eigenstates of a Hamiltonian operator, are described by orthogonal wave functions. The covalent and ionic components ψ_{cov} and ψ_{ion} in eq. (7), on the other hand, are not orthogonal to each other, but are linearly dependent[27]. Thus ψ_{cov} and ψ_{ion} do not describe physically realizable states; they can be broken down in any number of ways into mutually orthogonal components, but it cannot be decided in the model used here which of these breakdowns is physically meaningful.

The linear dependence of ψ_{cov} and ψ_{ion} is best demonstrated geometrically for the extensively studied example of the H_2 molecule. A normalized[28] wave function ψ can be represented as a unit vector in function space. The scalar product of two such vectors ψ_1 and ψ_2 is given by $\int\psi_1^*\psi_2 d\tau = S_{12} = \cos\theta$, where θ is the angle between ψ_1 and ψ_2; if ψ_1 and ψ_2 are orthogonal, this means that $S_{12} = 0$ and $\theta = 90°$. The normalized wave functions for the covalent and ionic components of the bond in the H_2 molecule are

$$\psi_{cov} = \frac{1}{\sqrt{2\,(1+S^2)}}\,[\varphi_A(1)\varphi_B(2) + \varphi_B(1)\varphi_A(2)]$$

and (8)

$$\psi_{ion} = \frac{1}{\sqrt{2\,(1+S^2)}}\,[\varphi_A(1)\varphi_A(2) + \varphi_B(1)\varphi_B(2)]$$

since C_2 and C_3 in eq. (6) must be equal on symmetry grounds. $S = \int\varphi_A^*(1)\varphi_B(1)dv_1$ is the overlap integral of the AOs φ_A and φ_B, and

$$\int\psi_{cov}\psi_{ion}d\tau = \frac{2S}{1+S^2} \tag{9}$$

For the equilibrium distance, this corresponds roughly to an angle $\theta = 20°$. These relations are shown graphically in Figure 3, where the x axis corresponds to the correct wave function for the ground state of the H_2 molecule, which is purely covalent by definition, whereas the y axis defines the orthogonal, purely ionic state[29]. It can be seen from this

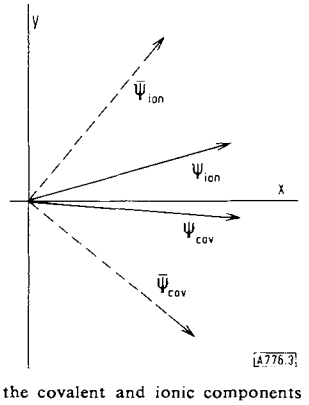


Fig. 3. Vector representation of the covalent and ionic components ψ_{cov} and ψ_{ion} (nonorthogonal AOs φ_A and φ_B in eq. (8)) and $\bar{\psi}_{cov}$ and $\bar{\psi}_{ion}$ (orthogonal AOs $\bar{\varphi}_A$ and $\bar{\varphi}_B$ in eq. (8)) of the wave function for the H_2 molecule (after [27]).

[22] *R. S. Mulliken*, J. chem. Physics *2*, 782 (1934); *3*, 573 (1935).

[23] *S. Weinbaum*, J. chem. Physics *1*, 593 (1933).

[24] *H. Heitler* and *F. London*, Z. Physik *44*, 455 (1927).

[25] *R. McWeeny*, Proc. Roy. Soc. (London) *A 223*, 63 (1954).

[26] *H. Shull*, J. appl. Physics Suppl. *33*, 290 (1962).

[27] *J. C. Slater*, J. chem. Physics *19*, 220 (1951).

[28] A wave function ψ is said to be normalized if $\int\psi^*\psi\,d\tau = 1$, where $\int d\tau$ denotes the integration over the entire definition range of all variables.

[29] Only these two states can be obtained as the solution of the Schrödinger equation if a wave function with a covalent and an ionic component is used.

vector representation that while ψ_{cov} is a good approximation for the covalent ground state, ψ_{ion} is far from describing the ionic state.

One might assume that the intuitive model could be rescued if φ_A and φ_B in eq. (8) were replaced by orthogonal AOs $\bar{\varphi}_A$ and $\bar{\varphi}_B$, since S is then automatically zero, and $\bar{\psi}_{cov}$ and $\bar{\psi}_{ion}$ are orthogonal. However, $\bar{\psi}_{cov}$ describes a state that is shown by the calculation to be not bonding [27], and which is in no way suitable for the definition of the partial ionic character (cf. Fig. 3) [25].

3.2. Population Analysis

The polarity of a bond would be known if the electronic charges on the individual atoms could be determined. The spinless one-electron density function $P(1)$, which describes the electron distribution in a molecule, thus seems a more suitable starting point for a discussion of bond polarity than the very special VB expression chosen by *Pauling*. Irrespective of the quantum-chemical approximation, $P(1)$ is defined for any N-electron wave function $\Psi(1, \ldots N)$ by [25, 30]

$$P(1) = N \int |\Psi(1,\ldots N)|^2 ds_1 d\tau_2 \ldots d\tau_N \qquad (10)$$

$\int ds_1$ is the integration over the spin coordinates of electron 1, and $\int d\tau_2 \ldots d\tau_N$ is the integration over the (space and spin) coordinates of all the other electrons.

$P(1)dv_1$ is the probability of finding an electron with any spin, and irrespective of the positions and spins of the other electrons, in the volume element dv_1. Integration of $P(1)$ over a volume enclosing the atom A gives the number $\bar{N}_A$ of electrons in the vicinity of A. The number of electrons transferred from the vicinity of A to the vicinity of B is then equal to $1/2|\bar{N}_A - \bar{N}_B|$, so that the partial ionic character of a bond A–B is given by $I_{AB} = 50 \cdot |\bar{N}_A - \bar{N}_B|$. The methodical difficulty now lies entirely in defining the "vicinity of A".

The definition of the vicinity of an atom is the purpose of the population analysis introduced by *Mulliken* [31], which is based on the following idea. In nearly all quantum-chemical calculations one starts from a basis of atomic orbitals φ_μ, *i.e.* the total wave function of a molecule is expanded in terms of functions that are centered on the individual atoms, and which therefore differ appreciably from zero only in the neighborhood of an atom. The calculation of $P(1)$ then involves squared terms $|\varphi_\mu(1)|^2$ and mixed terms $\varphi_\mu^*(1)\varphi_\nu(1)$, which are known on suitable normalization as orbital and overlap densities [32]

$$\rho_\mu(1) = |\varphi_\mu(1)|^2 \quad \text{und} \quad \rho_{\mu\nu}(1) = \varphi_\mu(1)\varphi_\nu(1)/S_{\mu\nu} \qquad (11)$$

where $S_{\mu\nu} = \int \varphi_\mu^*(1)\varphi_\nu(1)dv_1$ is the overlap integral of the AOs φ_μ and φ_ν.

$\rho_\mu(1)$ describes the electron distribution in the orbital φ_μ (*i.e.* in the neighborhood of the atom A if φ_μ is centered on A), and $\rho_{\mu\nu}(2)$ describes the electron distribution in the region where φ_μ and φ_ν are both different from zero (*i.e.* between the atoms A and B if φ_μ is centered on A and φ_ν on B).

With the aid of these orbital and overlap densities, $P(1)$ can be written in the form

$$P(1) = \sum_\mu q_\mu \rho_\mu(1) + 1/2 \sum_{\substack{\mu\,\nu \\ (\mu \neq \nu)}} \sum q_{\mu\nu}\rho_{\mu\nu}(1) \qquad (12)$$

where, owing to the normalization of $\rho_\mu(1)$ and $\rho_{\mu\nu}(1)$, it follows from

$$N = \int P(1)dv_1 = \sum_\mu q_\mu \int \rho_\mu(1)dv_1 + 1/2 \sum_{\mu \neq \nu} \sum q_{\mu\nu} \int \rho_{\mu\nu}(1)dv_1$$

that

$$\sum_\mu q_\mu + 1/2 \sum_{\mu \neq \nu} \sum q_{\mu\nu} = \sum_\mu (q_\mu + 1/2 \sum_{\nu \neq \mu} q_{\mu\nu}) = N \qquad (13)$$

q_μ and $q_{\mu\nu}$ being the orbital and overlap charges (populations). If a formal charge p_μ of the orbital φ_μ is defined by

$$p_\mu = q_\mu + 1/2 \sum_{\nu \neq \mu} q_{\mu\nu} \qquad (14)$$

then $\sum_\mu p_\mu = N$, *i.e.* the sum of the formal charges is equal to the total number of electrons in the molecule [33]. Summation of the formal charges of all the AOs φ_μ centered on the atom A gives the formal atomic charge

$$p_A = \sum_{\mu(A)} p_\mu \qquad (15)$$

which allows the division of the overall charge density into components belonging to the individual atoms. The charge transferred from the atom A to the atom B is then equal to $1/2|p_A - p_B|$, and the partial ionic character is given by $I_{AB} = 50\,|p_A - p_B|$.

As an example, let us consider a molecule AB with the AOs φ_A and φ_B (μ = A or B). Let us calculate the density function $P(1)$, the orbital and overlap charges q_A, q_B, and q_{AB}, and the formal atomic charges p_A and p_B for a Heitler-London function

$$\psi(1,2) = 1/\sqrt{2(1+S^2)}\,\{\varphi_A(1)\varphi_B(2) + \varphi_B(1)\varphi_A(2)\}$$

and for a simple MO function

$$\Phi(1,2) = \{c_A\varphi_A(1) + c_B\varphi_B(1)\}\{c_A\varphi_A(2) + c_B\varphi_B(2)\}:$$

VB function:

$$P(1) = N\int\psi^2(1,2)dv_2$$

$$= \frac{2}{2(1+S^2)}\,[\int\varphi_A^2(1)\varphi_B^2(2)dv_2 + 2\int\varphi_A(1)\varphi_B(1)\varphi_B(2)\varphi_A(2)dv_2 + \int\varphi_B^2(1)\varphi_A^2(2)dv_2]$$

$$= \frac{1}{1+S^2}\,[\varphi_A^2(1) + 2S\varphi_A(1)\varphi_B(1) + \varphi_B^2(1)]$$

i. e. $q_A = q_B = \frac{1}{1+S^2}$, $q_{AB} = \frac{2S^2}{1+S^2}$ and

$$p_A = p_B = \frac{1}{1+S^2} + \frac{S^2}{1+S^2} = 1;$$

[30] *R. McWeeny*, Rev. mod. Physics *32*, 335 (1960).

[31] *R. S. Mulliken*, J. chem. Physics *23*, 1833 (1955).

[32] *R. McWeeny*, J. chem. Physics *19*, 1614 (1951).

[33] *Ruedenberg* [34] refers to the components q_μ and $1/2\sum q_{\mu\nu}$ in eq. (14) as the "valence inactive fraction" and the "valence active fraction", respectively, of the formal charge, since a chemical bond is produced by an accumulation of charge between the atoms.

[34] *K. Ruedenberg*, Rev. mod. Physics *34*, 326 (1962).

MO function:

$$P(1) = N\int\Phi^2(1,2)dv_2$$
$$= 2\int[c_A^2\varphi_A^2(1) + 2c_Ac_B\varphi_A(1)\varphi_B(1) + c_B^2\varphi_B^2(1)] \times$$
$$[c_A^2\varphi_A^2(2) + 2c_Ac_B\varphi_A(2)\varphi_B(2) + c_B^2\varphi_B^2(2)]dv_2$$
$$= 2\,[c_A^2\varphi_A^2(1) + 2c_Ac_B\varphi_A(1)\varphi_B(1) + c_B^2\varphi_B^2(1)]$$

i. e. $q_A = 2c_A^2$, $q_B = 2c_B^2$, $q_{AB} = 4\,Sc_Ac_B$ and

$$p_A = 2[c_A^2 + Sc_Ac_B],\ p_B = 2[c_B^2 + Sc_Ac_B]$$

For homonuclear diatomic molecules, $c_A = c_B = 1/\sqrt{2(1+S^2)}$ and it follows that $p_A = p_B = 1$, in agreement with the result of the VB calculation and the definition of the partial ionic character, which must be zero in this case.

In general, eq. (15) assumes the form

$$p_A = \sum_i \eta_i \sum_{\mu(A)} [c_{\mu i}^2 + \sum_\nu c_{\mu i}c_{\nu i}S_{\mu\nu}] \qquad (16)$$

in the LCAO–MO method [31], the sum over i extending over all MOs $\Phi_i = \sum_\mu c_{\mu i}\varphi_\mu$ with the occupation number η_i ($\eta_i = 2$, 1, or 0). Eq. (16) is the definition of *Mulliken*'s "gross atomic population", which is therefore identical with the formal charge that is defined rather more generally in equations (14) and (15). ($q_A = \sum_i \eta_i \sum_{\mu(A)} c_{\mu i}^2$ is referred to by *Mulliken* as the "net atomic population").

A relation can also be qualitatively derived within the MO method between the ionic character as defined by the formal charges and the electronegativity [35], but despite this apparently closed relation between formal charge, ionic character, and electronegativity difference, the definition of the partial ionic character on the basis of the population analysis is not yet entirely satisfactory. The results of the population analysis can depend very strongly on the choice of the AOs; physically meaningful results can be expected only if a sufficient number of AOs is used for each atom, corresponding to its electronic structure, and also only if AOs that can describe the polarization of the atomic charge distribution on molecule formation are used. Such a basis is described by *Mulliken* [36] as a formally balanced basis set [37].

The difficulty of deciding whether a basis is formally balanced is shown by the example of two very extended calculations for the HF molecule [39,40], both of which give almost the exact Hartree-Fock energy ($E = -100.0575$ and $E = -100.0571$ a.u.) and practically the same electron density function $P(1)$. However, the population analysis leads to the very different values $p_H = 0.52$ and $p_H = 0.77$ for the formal charge density on the H atom [41]. It must be concluded that a formally unbalanced basis of atomic orbitals was used in one calculation (or in both).

Thus the overall electron density in the molecule can in principle be broken down into the components belonging to the various atoms by *Mulliken*'s population analysis. However, the practical use of this method requires that a check be made in every case, *e.g.* by increasing the number of basis AOs in steps, to ensure that the basis is in fact formally balanced.

4. Graphical Representation of the Electron Distribution

4.1. The One-Electron Density Function $P(1)$

Whereas the result of the population analysis can depend on the choice of the AOs, the density function $P(1)$ is independent of this provided that sufficiently high accuracy of the calculation (the "Hartree-Fock approximation") has been achieved [42]. It seems reasonable, therefore, to use the density function $P(1)$ directly for the characterization of a bond, instead of trying to use it to derive simple numerical values such as the formal charge.

Figure 4 shows the density functions $P(1)$ for first row diatomic hydrides AH in the form of contour diagrams. These and the following diagrams were calculated by *Bader et al.* [44–46] and are based on molecular Hartree-Fock calculations by *Cade et al.* [47]; the accuracy of the diagrams is therefore sufficient to show all the essential features of the chemical bond.

The extent r_A and r_H of the density function $P(1)$ on the atoms A and H along the molecular axis away from the bond (measured to the last contour line shown here, which corresponds to $0.002\ e/a_0^3 \approx 0.01\ e/Å^3$; cf. Fig. 6) can be read off from Figure 4.

The differences Δr_A and Δr_H between these quantities for the molecules and for the isolated atoms are shown in Figure 5 for the diatomic hydrides of the first and second rows (the density diagrams of the hydrides of the second row [46] are so

[35] Cf. *e.g.* [14].

[36] *R. S. Mulliken*, J. chem. Physics *36*, 3428 (1962).

[37] The wave function of a molecule can be expanded in terms of any complete set of basis functions, *i.e.* also in terms of AOs that are all centered on the same atom A. One-center expansions of this kind have been successfully carried out for molecules with a heavy central atom, such as CH_4 or NH_3 [38]; results of any desired accuracy can in principle be obtained in this way for physical quantities such as energy and dipole moment, and also for the density function $P(1)$. The population analysis, on the other hand, gives the formal charge $p_A = N$ for the atom A and $p_R = 0$ for all other atoms R. According to *Mulliken*, therefore, a one-center expansion is a physically balanced but formally unbalanced basis.

[38] *D. M. Bishop*, Advances Quantum Chemistry *3*, 25 (1967).

[39] *E. Clementi*, J. chem. Physics *36*, 33 (1962).

[40] *R. K. Nesbet*, J. chem. Physics *36*, 1518 (1962).

[41] *C. W. Kern* and *M. Karplus*, J. chem. Physics *40*, 1374 (1964).

[42] Not only does this emerge from the example of the two Hartree-Fock calculations for the HF molecule (Section 3.2), but it can also be shown in general [41] that the Hartree-Fock density function differs from the true density function at most in terms of the second order of smallness. *Bader* and *Chandra* [43] have also shown explicity for the H_2 and Li_2 molecules how small the changes in $P(1)$ are when one goes beyond the Hartree-Fock approximation.

[43] *R. F. W. Bader* and *A. K. Chandra*, Canad. J. Chem. *46*, 953 (1968).

[44] *R. F. W. Bader*, *W. H. Henneker*, and *P. E. Cade*, J. chem. Physics *46*, 3341 (1967).

[45] *R. F. W. Bader*, *I. Keaveny*, and *P. E. Cade*, J. chem. Physics *47*, 3381 (1967).

[46] *P. E. Cade*, *R. F. W. Bader*, *W. H. Henneker*, and *I. Keaveny*, J. chem. Physics *50*, 5313 (1969).

[47] *P. E. Cade*, *K. D. Sales*, and *A. C. Wahl*, J. chem. Physics *44*, 1973 (1966); *P. E. Cade* and *W. M. Huo*, *ibid. 47*, 614, 634 (1967).

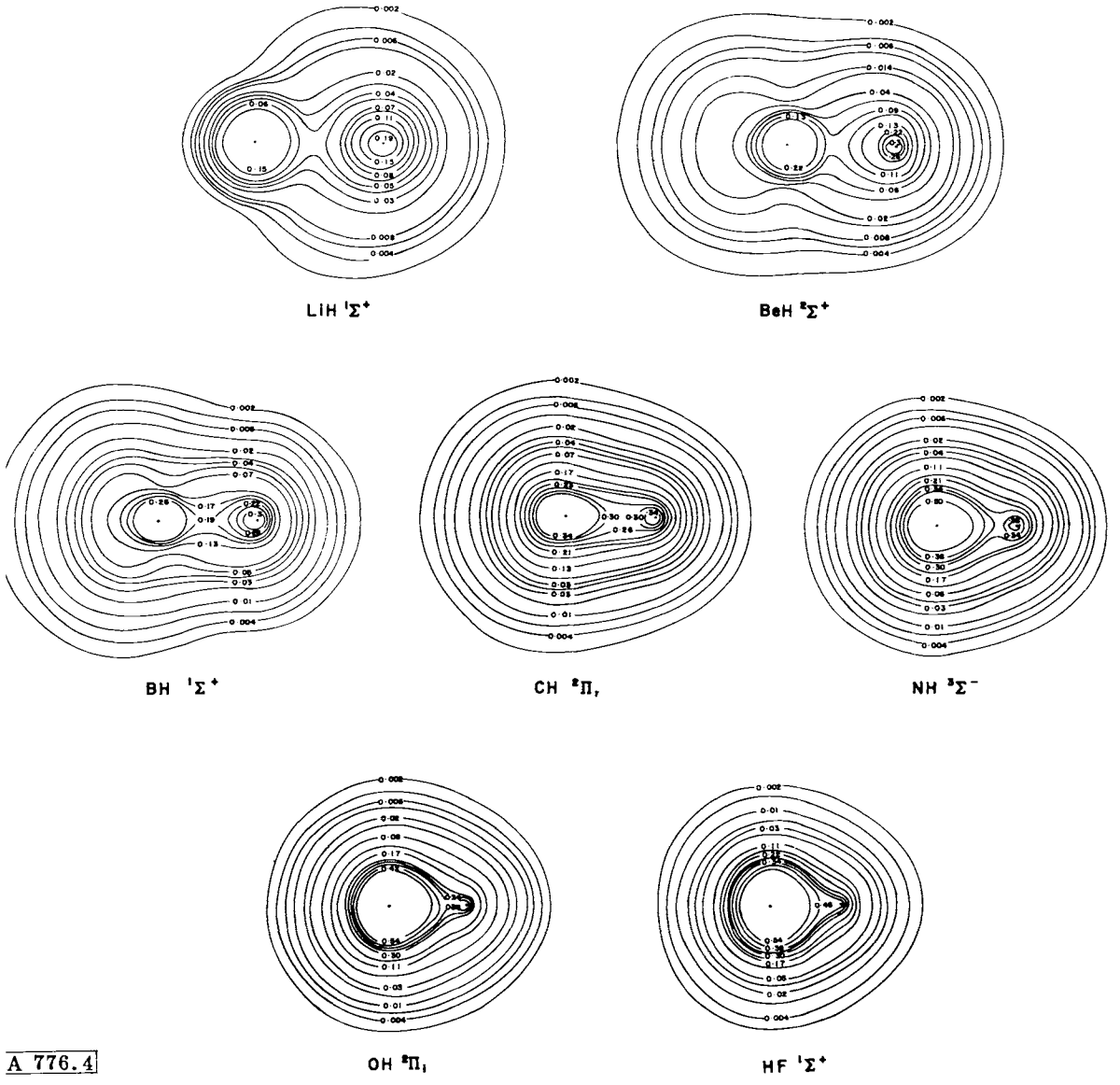


Fig. 4. Contour diagrams of the density functions $P(1)$ for the diatomic hydrides AH of the first row (after [45]; nucleus A is always on the left in these and later diagrams).

similar to those of the hydrides of the first row that they need not be reproduced here). In both series the r_A and r_H values as well as the Δr_A and Δr_H values decrease with increasing atomic number of A, *i.e.* the charge density is increasingly concentrated on the atomic nuclei. LiH and NaH at the beginning of the series appear to be exceptions as far as the charge on the Li or Na nucleus is concerned; this can be readily explained by the fact that Li and Na have only one valence electron, which is evidently transferred to the H atom in the hydride.

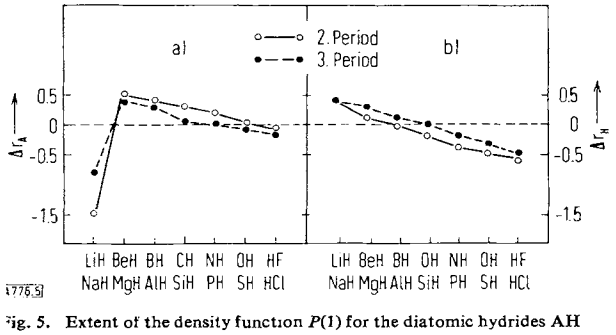


Fig. 5. Extent of the density function $P(1)$ for the diatomic hydrides AH of the first and second rows. a) Difference Δr_A between r_A in the molecule AH and in the isolated atom A, b) difference Δr_H between r_H in the molecule AH and in the isolated H atom [in Bohr radii a_0 ($1a_0$ = 0.52917 Å)] (after [46]).

The charge transfer from Li or Na to H is also seen in the "nonbonded charges" $\tilde{p}_A$ and $\tilde{p}_H$, where $\tilde{p}_A$ and $\tilde{p}_H$ are the fractions of the charge that are situated in the shaded region of the atom A and of the atom H respectively in Figure 6; $\tilde{p}_A$ for an isolated atom A is thus exactly equal to half of the nuclear charge Z_A.

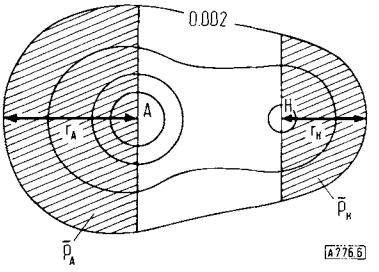


Fig. 6. Definition of the extent r_A and r_H of the density function $P(1)$ and of the nonbonded charge $\tilde{p}_A$ and $\tilde{p}_H$.

It can be seen from Figure 7 that the decrease $\Delta\tilde{p}_A$ in the nonbonded charge $\tilde{p}_A$ as compared with the isolated atom is approximately 0.5 *e* for LiH and NaH, as would be expected for an ideal ionic bond. $\Delta\tilde{p}_A$ is also negative for BeH and MgH; for the other hydrides of the first and second rows,

$\Delta\tilde{p}_A$ is positive, $\tilde{p}_A$ being almost constantly 0.22 and 0.1 *e*, respectively, higher than in the free atom. The difference $\Delta\tilde{p}_H$ between the nonbondet charge on the proton in the molecule and on the isolated H atom decreases from positive values for LiH and NaH to negative values for HF and HCl.

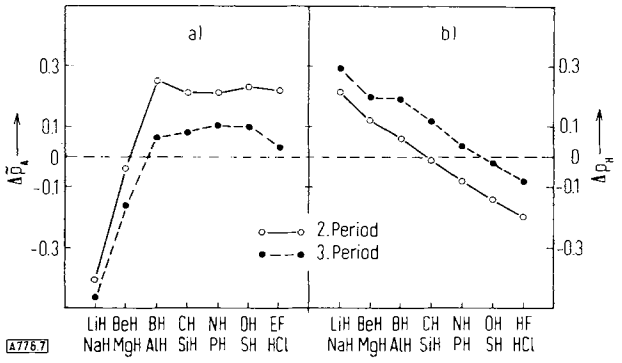


Fig. 7. Nonbonded charge for the diatomic hydrides of the first and second rows: a) Difference $\Delta\tilde{p}_A$ between $\tilde{p}_A$ in the molecule AH and in the isolated atom A, b) difference $\Delta\tilde{p}_H$ between $\tilde{p}_H$ in the molecule AH and in the isolated H atom [in electronic charge units *e*] (after [46]).

Both the extent of the density function and the nonbonded charges indicate that charge is transferred from the heavy atom to H in LiH and NaH, whereas charge transfer in the opposite direction, *i.e.* from the proton to the heavy atom, occurs to an increasing degree in the series BeH to HF; this is confirmed by the decrease in the number of contour lines that surround only the proton. The charge transfers are only slight in SiH to HCl.

4.2. Density Difference Diagrams

The density diagrams shown in Figure 4 give a good picture of the overall charge distribution in the molecule, but many details are not shown with sufficient prominence. A very much more detailed picture of the charge rearrangement associated with molecule formation is obtained by subtracting the density functions $P_R(1)$ of the isolated atoms R at the same internuclear distance from the density function $P(1)$ of the molecule [48]. Density difference diagrams of this type, *i.e.* contour diagrams of the function $\Delta P(1) = P(1) - \sum_R P_R(1)$, are shown in Figure 8 together with the profile of the charge density difference $\Delta P(1)$ for LiF and N_2 as typical examples of molecules having an ionic and a homonuclear covalent bond [44]. The difference in appearance of these diagrams for the two extreme types of bonds is obvious.

Any chemical bond, whether covalent or ionic, results from a charge accumulation between the atomic nuclei that is sufficient to counterbalance the forces of repulsion between the nuclei. In the purely covalent bond, the electrostatic equilibrium results from the removal of charge from the atoms and its symmetrical concentration between the nuclei; at the same time the charge remaining on the atoms experiences a strong polarization directed away from the bond (Fig. 8). In the ionic bond, on the other hand, the electrostatic equilibrium is achieved by a highly unsymmetrical rearrangement of the charge. The increase in charge is mainly concentrated on one nucleus, *i.e.* the zero contour of the region of increased charge encloses only one nucleus; polarization of the charge also occurs in the direction opposite to that of the charge transfer (cf. Section 5.2).

Figure 9 shows the density difference diagrams for the diatomic hydrides AH of the first row [45], which are substantially the same as the corresponding diagrams for the hydrides of the second row [46].

The diagrams for LiH and NaH, which differ markedly from those of the other molecules, are very similar to the corresponding diagram for LiF, and so point to ionic bonding of the type Li^+H^- and Na^+H^-. The characteristics of covalent bonding predominate in the series BeH to HF and MgH to HCl, though differences from the diagram of the first member of the series become increasingly noticeable, particularly in the hydrides of the first row. The main increase in charge still occurs between the nuclei; whereas it practically includes both nuclei in BH, it is clearly concentrated on the heavy atom in HF, corresponding to a polarity F^-H^+. At the same time an increasingly pronounced decrease in charge on the side of the proton away from the bond is observed in the series BH to HF. The ionic character of the A—H bond thus increases steadily from BH to HF. BeH as well as MgH and AlH occupy intermediate positions between the ionic bond in LiH and NaH and the covalent bond in BH and in SiH, PH, SH, and HCl, which is difficult to characterize.

5. The Hellmann-Feynman Theorem and the Forces Acting on the Atomic Nuclei

It can be seen from the density difference diagrams that in the discussion of the polarity of a bond, the size of the spatial regions of increased or decreased charge is equally important as the number of electrons on the individual atoms. Both the quantity of charge and its precise distribution are taken into account in the determination of the forces that hold the atomic nuclei of a molecule together.

5.1. The Hellmann-Feynman Theorem

According to the Hellmann-Feynman theorem [49,50], for two atoms A and B separated by a distance R, the force $F_A(R)$ acting on the nucleus A, which has a nuclear charge Z_A, is equal to the force calculated by classical electrostatics from the electron density distribution $P(1)$ and the point charge Z_B on the nucleus B:

$$F_A(R) = \frac{Z_A}{R^2}\left[Z_B - R^2 \int \frac{P(1)\cos\theta_A}{r_A^2}\, dv_1\right] \qquad (17)$$

r_A is the distance from the electron 1 to the nucleus A, and θ_A is the angle between the line joining the nuclei

[48] *M. Roux, S. Besnainou,* and *R. Daudel,* J. Chim. Phys. *54,* 218 (1956); *M. Roux, M. Cornille,* and *L. Burnelle,* J. chem. Physics *37,* 933 (1962).

[49] *H. Hellmann*: Einführung in die Quantenchemie. Deuticke, Leipzig and Wien, 1937; *R. P. Feynman,* Physic. Rev. *56,* 340 (1939).

[50] Cf. *A. C. Hurley* in *P. O. Löwdin* and *B. Pullman*: Molecular Orbitals in Chemistry, Physics and Biology. Academic Press, New York 1964, p. 161.

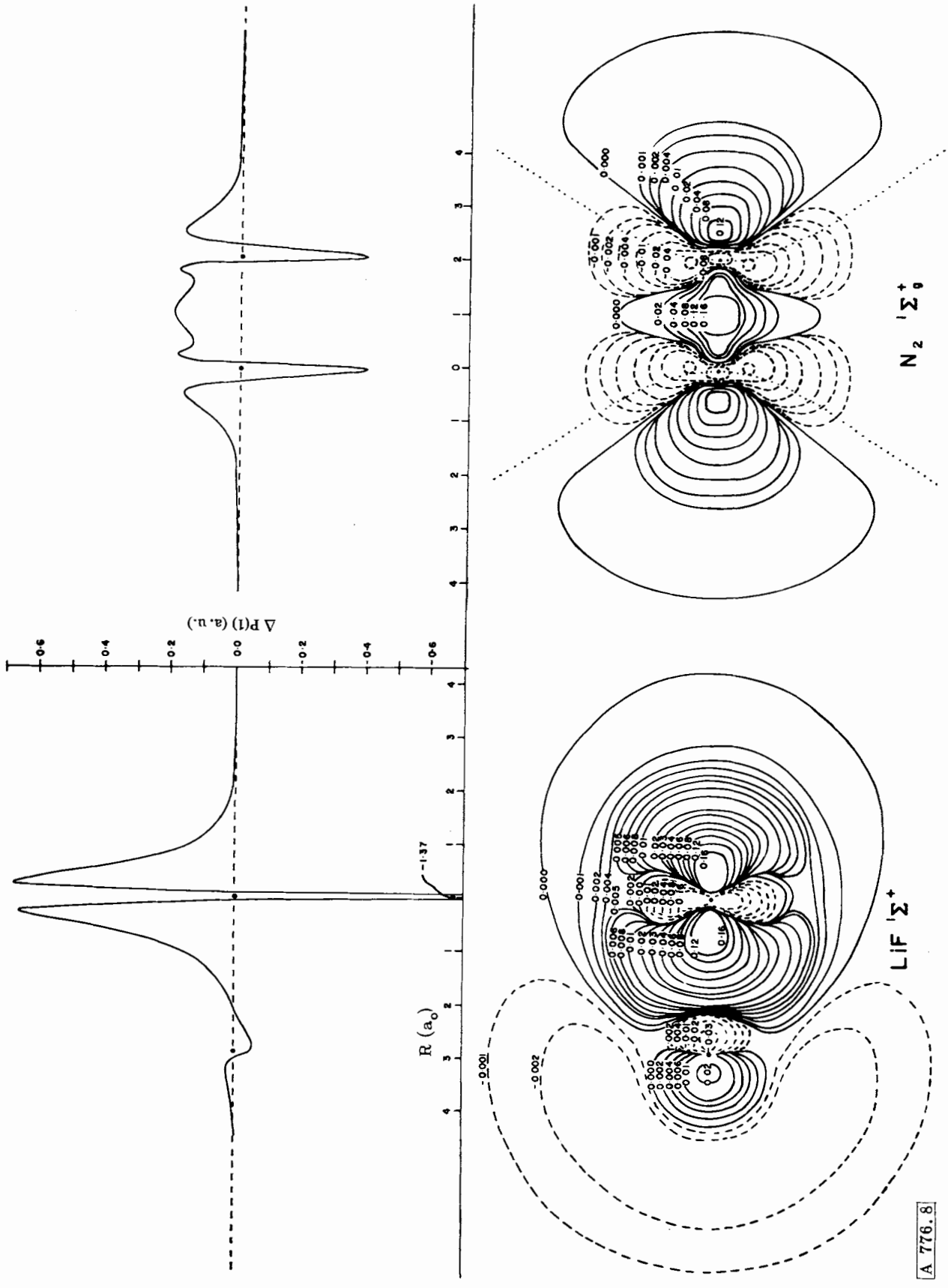


Fig. 8. Contour diagrams and profile of the density difference function $\Delta P(1)$ for LiF and N_2 as examples of an ionic and a covalent bond (after [44]).

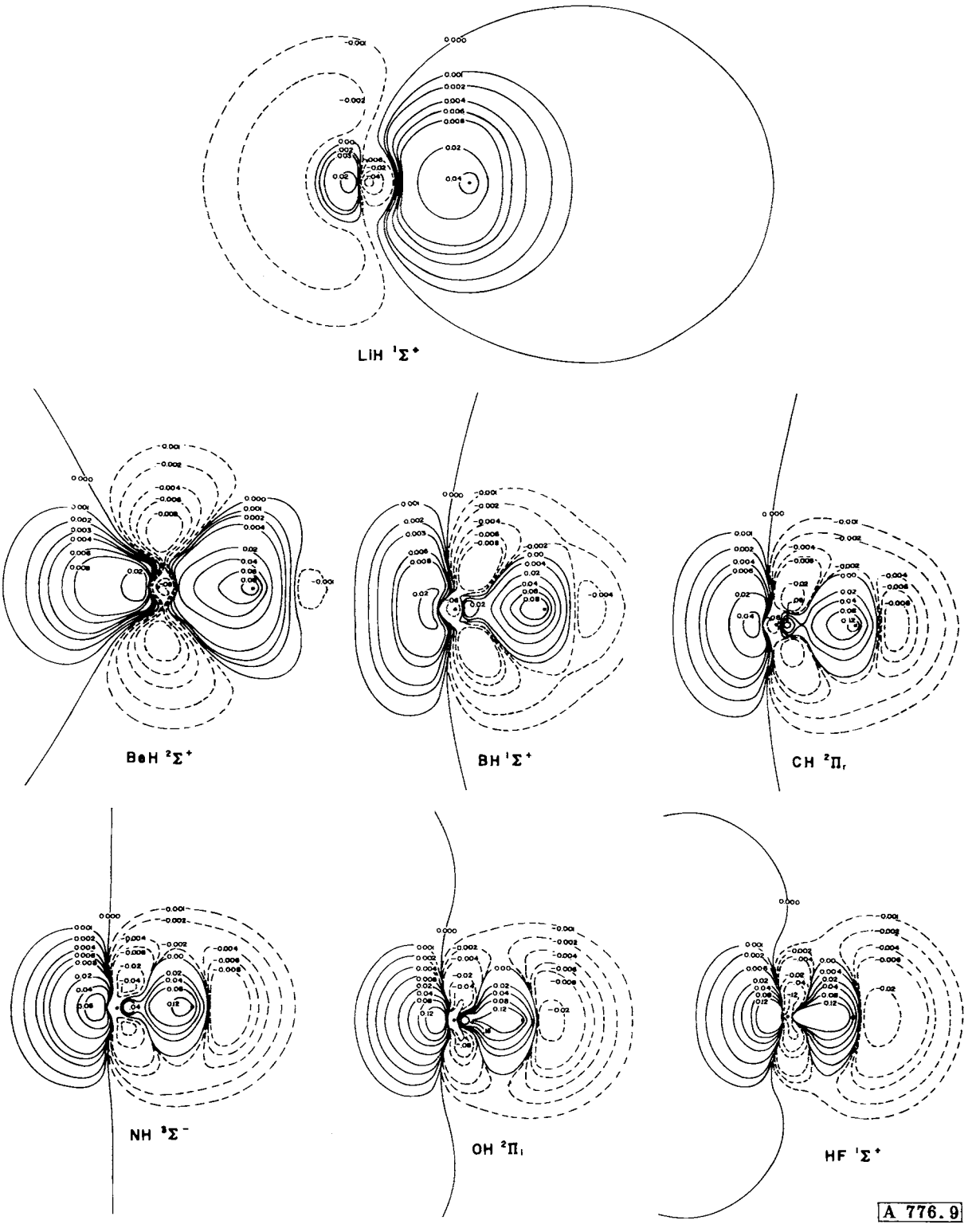


Fig. 9. Density difference diagrams for the diatomic hydrides AH of the first row (after [45]).

and the direction of r_A. By introduction of the abbreviation

$$f_A = R^2 \int \frac{P(1)\cos\theta_A}{r_A^2}\, dv_1 \qquad (18)$$

the force acting on the atom A can be written in the form [51]

$$F_A(R) = \frac{Z_A}{R^2}\,[Z_B - f_A] \qquad (19)$$

f_A/R^2 is the electrostatic force exerted by the charge density $P(1)$ on each unit of nuclear charge of the nucleus A. f_A has the dimensions of a charge, and is numerically equal to the point charge q_B on the nucleus B that would exert the same electrostatic force on A. f_A may therefore be described as the charge equivalent of the force acting on A.

[51] *R. W. F. Bader* and *G. A. Jones*, Canad. J. Chem. *39*, 1253 (1961).

For a diatomic molecule AB, the relation

$$F_A(R) = -F_B(R) \tag{20}$$

is valid for any internuclear distance R, *i.e.* the forces acting on the nuclei A and B are equal and opposite. The forces vanish for $R = \infty$ and for the equilibrium distance R_e, so that according to eq. (19) we have

$$f_A = Z_B;\ f_B = Z_A \quad (\text{for } R = R_e \text{ and } R = R_\infty) \tag{21}$$

5.2. Breakdown of the Charge Equivalents

If one assumes that a basis of AOs φ_μ were used in the calculation of $P(1)$, one obtains three additive contributions to f_A (and similarly to f_B) for a diatomic molecule A–B, corresponding to the breakdown of the charge density in accordance with eq. (12) [44]:

1. the atomic contribution $f_A^{(AA)}$, which is due to the charge density $\sum_{\mu(A)} q_\mu \rho_\mu(1)$ on the atom A,
2. the overlap contribution $f_A^{(AB)}$, which is due to the overlap density $^1/_2 \sum_{\mu \neq \nu} \sum q_{\mu\nu} \rho_{\mu\nu}(1)$, and
3. the screening contribution $f_A^{(BB)}$, which is due to the charge density $\sum_{\mu(B)} q_\mu \rho_\mu(1)$ on the atom B, and which indicates how many units of positive charge of the nucleus B are screened by this charge distribution [52].

A comparison of the atomic, overlap, and screening contributions of the charge equivalents for a molecule at the equilibrium distance R_e with the limiting values for the separated atoms ($R \rightarrow \infty$) shows clearly the changes in the charge distribution that are responsible for molecule formulation. The forces acting on the atomic nuclei and the charge rearrangement as illustrated by the $\Delta P(1)$ diagram are mutually complementary characterizations of a bond.

For the separated atoms ($R = \infty$) of a molecule A–B, the atomic contributions $f_A^{(AA)}$ and $f_B^{(BB)}$ and the overlap contributions $f_A^{(AB)}$ and $f_B^{(AB)}$ are zero, while the screening contributions are given by $f_A^{(BB)} = Z_B$ and $f_B^{(AA)} = Z_A$; the electric field of the electron distribution of an isolated neutral atom must therefore exactly balance the field of the nucleus.

In a covalent bond, both atomic nuclei are incompletely screened, and the resulting mutual repulsion of the nuclei is balanced by the forces due to the accumulation of charge between the nuclei. For the N_2 molecule, as an example of a pure covalent bond, the values obtained are as follows [44]. The screening contribution $f_A^{(BB)} = 5.136$ is considerably smaller than the nuclear charge number $Z_N = 7$, but the repulsion of the incompletely screened nuclei is more than compensated by the overlap contribution $f_A^{(AB)} = 3.853$. The atomic contribution ($f_A^{(AA)} = -1.943$) must therefore be negative, corresponding to polarization of the charge away from the bond, to satisfy $f_A \equiv f_A^{(AA)} + f_A^{(AB)} + f_A^{(BB)} = Z_B$ in accordance with eq. (21) [53] (cf. the $\Delta P(1)$ diagram in Fig. 8).

For an ideal ionic bond A^+B^-, the overlap contributions $f_A^{(AB)}$ and $f_B^{(AB)}$ should disappear, while the screening contributions of the anion and of the cation should be $f_A^{(BB)} = Z_B + 1$ and $f_B^{(AA)} = Z_A - 1$, owing to the charge transfer. To satisfy $f_A = Z_B$ and $f_B = Z_A$, therefore $f_A^{(AA)} = -1$ and $f_B^{(BB)} = +1$, *i.e.* the increased screening of the anion exerts an attraction on the nucleus of the cation, which is compensated by polarization of the charge on the cation away from the bond; conversely, the repulsion of the nucleus of the anion by the incompletely screened nucleus of the cation is compensated by polarization of the charge on the anion into the bond (cf. the $\Delta P(1)$ diagram in Fig. 8).

The f values to be expected on the basis of these arguments for a pure ionic bond in LiF are given in the first line of Table 2, while the values in the second line are found by calculation. It can be seen from the density difference diagram for LiF (Fig. 8) that the increase in charge in the region between the atoms is completely localized on the F atom.

Table 2. Contributions of the charge equivalents of the forces acting on the nuclei for LiF LiH, and NaH (after [44–46]).

AB	Forces acting on the cation A $f_A^{(AA)}$	$f_A^{(AB)}$	$f_A^{(BB)}$	Forces acting on the anion B $f_B^{(BB)}$	$f_B^{(AB)}$	$f_B^{(AA)}$	
LiF	−1.0	0.0	10.0 (=Z_F+1)	1.0	0.0	2.0 (=Z_{Li}−1)	[a]
	−0.710	0.346	9.511	0.068	0.985	2.041	[b]
	−0.71	—	9.86	1.05	—	2.04	[c]
LiH	−1.0	0.0	2.0 (=Z_H+1)	1.0	0.0	2.0 (=Z_{Li}−1)	[a]
	−0.616	0.732	0.890	0.225	0.573	2.226	[b]
	−0.62	—	1.62	0.80	—	2.23	[c]
NaH	−1.0	0.0	2.0 (=Z_H+1)	1.0	0.0	10.0 (=Z_{Na}−1)	[a]
	−0.392	0.105	1.354	0.528	0.410	10.059	[b]
	−0.39	—	1.46	0.94	—	10.06	[c]

[a] Ideal ionic bond. [b] Calculated; breakdown according to eq. (12). [c] Calculated; breakdown according to $\Delta P(1)$.

[52] $\sum_{\mu(A)}$ as in eq. (15) means that the summation is to be carried out over the μ that relate to AOs φ_μ centered on the atom A.

[53] The deviation from zero of the force F_A acting on the atomic nuclei A is a measure of how well a given wave function satisfies the Hellmann-Feynman theorem. Since the Hellmann-Feynman theorem is valid not only for the exact wave function but also for the Hartree-Fock function [50], the accuracy with which a given wave function satisfies the Hartree-Fock approximation can be established on the basis of the f_A and f_B values.

If this is taken into account by adding the overlap contributions $f_{Li}^{(LiF)}$ and $f_{F}^{(LiF)}$ to the contributions $f_{Li}^{(FF)}$ and $f_{F}^{(FF)}$ due to the charge density on the F atom, we obtain the f values given in the third line of Table 2, in very good agreement with the model of the pure ionic bond.

5.3. Diatomic Hydrides of the First and Second Rows

The f values and their individual contributions are given in Table 3 for the diatomic hydrides AH of the first and second rows [45,46].

The incomplete screening of the nucleus A (cf. the column $Z_A - f_H^{(AA)}$ in Table 3) is more pronounced in the second row than in the first; thus the unscreened nuclear charge of the F atom in HF is 0.88 charge unit, as compared with 2.05 for the Cl atom in HCl. Screening of the proton is also stronger in the hydrides of the second row than in those of the first; the effective charge on the proton in NaH, MgH, and AlH is increased by 0.35, 0.17, and 0.09 unit respectively.

Table 3. Contributions of the charge equivalents of the forces acting on the nuclei for the diatomic hydrides of the first and second rows (after [45, 46]).

AH	$f_H^{(HH)}$	$f_H^{(AH)}$	$f_H^{(AA)}$	$Z_A - f_H^{(AA)}$	F_H [a]	$f_A^{(AA)}$	$f_A^{(HA)}$	$f_A^{(HH)}$	$Z_H - f_A^{(HH)}$	F_A [a]
LiH	0.225	0.573	2.226	0.774	−0.003	−0.616	0.732	0.890	0.110	−0.002
BeH	0.279	0.925	2.808	1.192	−0.002	−0.762	1.044	0.701	0.299	−0.010
BH	0.283	1.097	3.664	1.336	−0.008	−0.912	1.350	0.596	0.404	−0.031
CH	0.177	1.007	4.880	1.120	−0.014	−0.584	1.283	0.341	0.659	−0.053
NH	0.133	0.940	5.999	1.001	−0.019	−0.496	1.275	0.259	0.741	−0.069
OH	0.109	0.897	7.076	0.924	−0.024	−0.424	1.254	0.201	0.799	−0.074
HF	0.093	0.864	8.124	0.876	−0.026	−0.369	1.233	0.161	0.839	−0.075
NaH	0.528	0.410	10.059	0.941	+0.0002	−0.392	0.105	1.354	−0.354	−0.0582
MgH	0.615	0.858	10.574	1.426	−0.0043	−0.407	0.286	1.168	−0.168	−0.0451
AlH	0.617	1.006	11.426	1.574	−0.0050	−0.430	0.257	1.090	−0.090	+1.1005
SiH	0.614	1.227	12.214	1.786	−0.0067	−0.433	0.378	0.942	0.058	+0.1903
PH	0.562	1.388	13.156	1.844	−0.0144	−0.406	0.528	0.773	0.227	+0.2204
SH	0.540	1.529	14.029	1.971	−0.0151	−0.390	0.659	0.642	0.358	+0.2090
HCl	0.502	1.613	14.949	2.051	−0.0108	−0.337	0.742	0.537	0.463	+0.1833

[a] Forces in a.u., $e^2/a_0^2 = 8.2378 \times 10^{-3}$ dyne.

The overlap contributions in the first row increase at first, pass through a maximum for BH, and then decrease again to HF. For the hydrides of the second row, the overlap contributions increase continuously from NaH to HCl, and unlike in the first row, the overlap density here does not exert a greater force on the proton than on the nucleus A.

BH and CH are typical examples of molecules with a covalent bond. Both nuclei are incompletely screened, and the overlap contributions of the forces acting on the two nuclei are large and approximately equal. The bond becomes increasingly polar from NH to HF, and the nucleus A increasingly determines the overall charge distribution. In the second row, on the other hand, the influence of the nucleus A on the charge distribution does not predominate, and distinctly polar bonds such as those in OH and HF are not observed; the molecules SiH to HCl all exhibit the characteristics of typical covalent bonds. In these molecules, however, the distribution of the valence electrons is much more strongly determined by the proton than in CH and BH.

The individual contributions of the f_A and f_H values for LiH and NaH, on the other hand, exhibit the characteristics seen in the case of the LiF molecule for an ionic bond. If one considers that on the basis of the density difference diagram, the increase in charge in the region between the nuclei in LiH and NaH is completely localized on the proton, one obtains the values given in the sixth and ninth lines of Table 2 for the atomic and screening contributions of f_A and f_H, which are not very different from the values to be expected for an ideal ionic bond [54]. The forces exerted on the proton by the Li and Na atoms correspond to a point charge distribution $Li^{+0.8}$ $H^{-0.8}$ and $Na^{+0.9}$ $H^{-0.9}$, which are close to the ionic limiting value found *e.g.* in $Li^{+1}F^{-1}$. Since the charge distribution on the anion is very diffuse while that on the cation is very compact (in comparison with the neutral atom in both cases), a molecular charge distribution appears more or less ionic according to whether it describes the electric field acting on the anion or that acting on the cation. Thus according to Table 3, the forces acting on the Li and Na nuclei in LiF, LiH, and NaH correspond to a point charge distribution $Li^{+0.9}F^{-0.9}$, $Li^{+0.6}H^{-0.6}$, and $Na^{+0.5}H^{-0.5}$. NaH is now less ionic than LiH, the reason being that the increase in charge on the proton is more diffuse in NaH than in LiH.

The values found from the dipole moments for the ionic character of the molecules LiH and HF are $I_{LiH} = 77\%$ and $I_{HF} = 39\%$, while those obtained from the electronegativity differences are $I_{LiH} = 26\%$ and $I_{HF} = 59\%$. The same arguments that have shown that the bond in LiH is essentially ionic while that in HF is essentially covalent also show why the dipole moment and the electronegativity difference lead to different results for the ionic character [55]. The overlap contributions $f_{Li}^{(LiH)}$ and $f_{H}^{(LiH)}$ in LiH differ less than the corresponding quantities in HF, and on this basis

[54] It is interesting to compare the bonding in LiH and in HF, which comes closest to the ionic limiting case A^-H^+. If as in the case of LiH the overlap component of the force acting on the cation is added to the corresponding screening contribution for HF, the resulting value (8.988) is smaller than the nuclear charge $Z_F = 9$, whereas one would expect $Z_F + 1 = 10$ for an ionic bond. While the bond in LiH may be described as ionic with a small covalent component, therefore, the bonds in the series NH, OH, and HF must be regarded as covalent with increasing ionic character.

[55] *R. W. F. Bader* and *W. H. Henneker*, J. Amer. chem. Soc. *88*, 280 (1960).

one would expect a stronger ionic character in HF than in LiH. Unlike in HF, however, the atomic contributions in LiH (as expected for an ionic bond) point to polarization of the charge in the direction opposite to that of the charge transfer, so that the dipole moment gives a very much stronger ionic character for LiH than the electronegativity difference.

It is clear from these last examples why all attempts to characterize the ionic character of a bond by a number or a percentage must be unsuccessful. The type of chemical bond is determined by the total molecular charge distribution, which cannot be described by a simple number.

6. Polyatomic Molecules

Some brief indication should now be given of how far the results described in the last few sections are applicable to polyatomic molecules, since it is clear that the concept of the polarity of a bond can be chemically useful only if its applicability is not restricted to diatomic molecules.

Density and density difference diagrams can be calculated for polyatomic molecules, but their interpretation involves new difficulties. If one wishes to discuss *e.g.* the properties of the bonds A–B and B–C of a triatomic molecule A–B–C, one must decide which of the two bonds was responsible for the characteristic charge rearrangement on the central atom. This will frequently not be immediately possible. (Similar arguments apply to the forces acting on the individual atomic nuclei.)

Before any discussion of the properties of individual bonds in a polyatomic molecule can be possible, therefore, the quantum-mechanical many-electron problem must be broken down into a series of two-electron problems. This allows a separate treatment of any bond, the influence of the inner electrons and of the electrons of other bonds being taken into account by an effective potential for the bonding electrons.

These ideas are in agreement with a suggestion by *Hurley*, *Lennard-Jones*, and *Pople*[56] that the wave function $\Psi(1, \ldots N)$ of a polyatomic molecule should be written as an antisymmetric product of localized two-electron functions $\Phi_R(1,2)$:

$$\Psi(1, \ldots N) = \mathcal{A}\,[\Phi_A(1,2)\Phi_B(3,4) \ldots \Phi_R(N-1, N)] \qquad (22)$$

This expression is the basis of the self-consistent group function (SCGF) method[57], which also enables many-electron groups to be taken into account, and which satisfies all the requirements for a discussion of the polarity of the bonds of polyatomic molecules in the manner described here for diatomic molecules.

SCGF calculations have so far been carried out only with a minimal basis of atomic orbitals, but even these calculations show that interesting results may be expected from a systematic analysis of the polarity of bonds in polyatomic molecules[58]. Thus a population analysis shows that the polarity of the CH bond in substituted methanes CH_3–X depends in a characteristic manner on the nature of the group X[59], or that in multiple bonds, the charge transfer in the σ-bond takes place in the direction to be expected from the electronegativity difference, whereas a smaller charge transfer in the opposite direction may occurs in the π-bonds[60].

Other methods for the interpretation of the charge distribution of a polyatomic molecule are based on the construction of orbitals localized in the bonds from a delocalized total wave function of the molecule[61]. However, these localized orbitals cannot be obtained without arbitrary additional assumptions, and different localization procedures sometimes yield different results.

7. Conclusion

Coulson[62] said in 1951: "It might humorously be said that there is a kind of uncertainty relation about our knowledge of molecular structure: the more closely we try to describe the molecule, the less clearcut becomes our description of its constituent bonds." However, it appears that studies of the type described here will be able to cast doubt on the validity of this "uncertainty relation", since as sufficiently accurate calculations are carried out on more and larger molecules, we shall also learn to read the information contained in the charge distribution that characterizes a molecule. The decisive factor that makes this possible is that the density function $P(1)$ is defined quite generally and independently of the quantum-chemical approximation used. The results of even the most complicated quantum-chemical calculations can therefore be represented graphically by density diagrams, which contain much farther-reaching, chemically important information than one can express by values of a few parameters on the basis of excessively simplified models.

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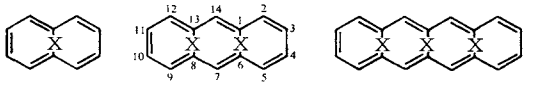
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anti-1,6:8,13-Bismethano[14]annulene[1]

By *Emanuel Vogel*, *Ulrich Haberland*, and *Harald Günther*[*]

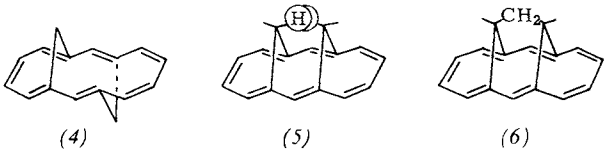
The synthesis and aromaticity of 1,6-methano[10]annulene [*(1)*, X = CH_2][2] and of its analogs with a hetero atom bridge [*(1)*, X = O or NH] suggested the existence of a homologous series of bridged annulenes *(1)*, *(2)*, *(3)*, *etc.*, whose members are formally derived from naphthalene, anthracene, naphthacene, *etc.*, by insertion of the bridges X into the bonds common to two rings and which, like the parent hydrocarbons, contain $(4n + 2)$ π-electrons. The "device of bridging" thus allows the well-known acene series to be converted into a series of $[4n + 2]$annulenes.



(1) *(2)* *(3)*

The presence of more than one bridge implies that there will be a *syn*- and an *anti*-form for the [14]annulenes *(2)* and three forms (*syn-syn*-, *syn-anti*-, and *anti-anti*-) for the [18]-annulenes *(3)*. Since the Hückel rule can be considered valid up to the 22 π-electron system[3], it depends essentially on the geometry of the annulene ring whether the aromaticity established for *(1)* extends to the higher homologs.

Inspection of Dreiding and space-filling models of the bridged [14]- *(2)* and [18]-annulenes *(3)* leads to the following conclusions: 1. In the *syn*-configuration of the [14]annulenes the annulene ring can assume an approximately planar conformation provided that no steric interaction occurs between the bridges. 2. In the *anti*-configuration of the [14]annulenes the $2p_z$ orbitals of the C_3 segments consisting of neighboring bridgehead atoms and the C atom (of the annulene ring) between them are considerably skewed with respect to one another. 3. For the *syn-syn*-configuration of the [18]annulenes the steric conditions resemble those in the *syn*-configuration of the [14]annulenes. 4. Extension of the annulene ring from 10 to 14 or 18 C atoms eases the restraint on the bridge angle and allows the ring for the *syn*- and *syn-syn*-configurations of the bridged [14]- and [18]-annulenes to approach planarity more closely than *(1)*.

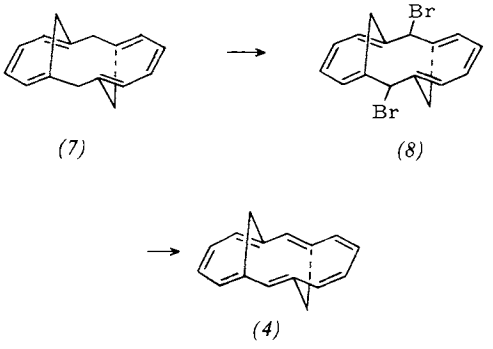


(4) *(5)* *(6)*

These conclusions have recently been substantiated for the *syn*-[14]annulenes (in absence of appreciable steric interference of the bridges) by preparation of the carmine-red *syn*-1,6 : 8,13-bisoxido[14]annulene[4].

We have now synthesized the *anti*-1,6 : 8,13-bismethano[14]-annulene *(4)*, and its properties also verify our ideas regarding the *anti*-configurations of the [14]annulenes. *syn*-1,6 : 8,13-Bismethano[14]annulene *(5)*, on the other hand, has so far defied all attempts at synthesis. It seems questionable whether *(5)* would possess aromatic character since the inner H atoms of the bridge will most probably force the annulene ring to be bent. If, however, these hydrogen atoms are replaced by a CH_2 group one obtains 1,6 : 8,13-propanediylidene[14]-annulene *(6)*[5, 2d] in which the annulene ring is approximately planar, as in *syn*-1,6 : 8,13-bisoxido[14]annulene; *(6)* is thus to be regarded as the actual *syn*-analog of *(4)*.

Synthesis of *(4)* was accomplished by reaction of 7,14-dihydro-*anti*-1,6 : 8,13-bismethano[14]annulene *(7)*[6] with 2 moles of *N*-bromosuccinimide and treatment of the resulting dibromide *(8)* (presumably a mixture of *cis-trans*-isomers) with sodium iodide in acetone under nitrogen. The hydrocarbon *(4)* produced forms lemon-yellow crystals of m.p. 41—42 °C [yield 58%, based on *(7)*] and, in striking contrast to *syn*-1,6 : 8,13-bisoxido[14]annulene and 1,6 : 8,13-propanediylidene[14]annulene, has a sensitivity to oxygen reminiscent of polyenes such as vitamin A, though it can be stored for months under nitrogen.



(7) *(8)*

(4)

The [14]annulene structure of the hydrocarbon and the nature of its π-electron system follow unambiguously from the NMR spectral findings:

In the room-temperature NMR spectrum (Fig. 1) the annulene protons are observed as two singlets at τ = 3.67 (2 H) and 3.80 (8 H), while the bridge protons are found as an AB system at τ = 7.52 and 8.12 with J = 11.0 Hz (4 H). The position of the proton resonances excludes an aromatic structure with a delocalized 14π electron system *(9)*, and yet a polyene

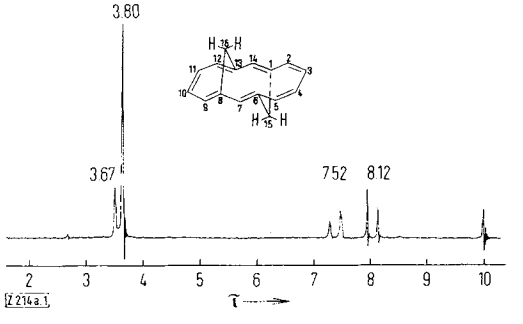
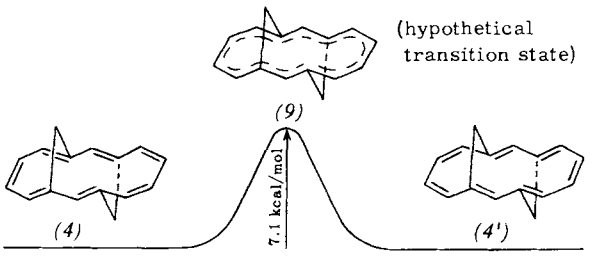


Fig. 1. NMR spectrum of *anti*-1,6:8,13-bismethano[14]annulene *(4)* at room temperature (in $CDCl_3$; 60 MHz, tetramethylsilane as internal standard).

structure with fixed double bonds *(4)*, containing not less than nine different types of protons, cannot be reconciled with the paucity of lines actually observed. Low-temperature NMR measurements cast light upon the structural question: The simplicity of the spectrum is due to a dynamic process which on the NMR time scale confers C_{2h} symmetry on the molecule above −60 °C and, in addition, to an accidental equivalence of the mean values $(\tau_{2,5} + \tau_{9,12})/2$ and $(\tau_{3,4} + \tau_{10,11})/2$ (see below). Between −70 and −120 °C all the signals except the singlet at τ = 3.67 show considerable exchange broadening. The changes in the line shape of the signals cease at about −130 °C, where a spectrum is observed corresponding to the polyene structure *(4)*. This consists of two AA'BB' systems at τ = 3.43 (H-10, H-11) and 3.93 (H-9, H-12), and 3.66 (H-2, H-5) and 4.26 (H-3, H-4), the unchanged singlet at τ = 3.67 (H-7, H-14), and two AB systems at τ = 7.33 and 7.71, as well as 7.61 and 8.53, each with coupling of 11.0 Hz.

The nature of the changes in the line shape of the NMR spectrum of *(4)* caused by lowering the temperature (Fig. 2) leads to the conclusion that the dynamic process is a double-bond migration, *i.e.*, a valence tautomerism [*(4)* ⇄ *(4')*].



To determine the kinetic parameters of the double-bond migration the line shape of the bridge-proton resonances between —70 and —138 °C was simulated by standard techniques[7]. The excellent agreement obtained between the calculated and the experimental spectra is shown in Figure 2. Insertion of the rate constants measured between —84 and —131 °C into the Arrhenius equation gave an activation energy of 7.1 kcal/mole and a frequency factor of $10^{12.2}$.

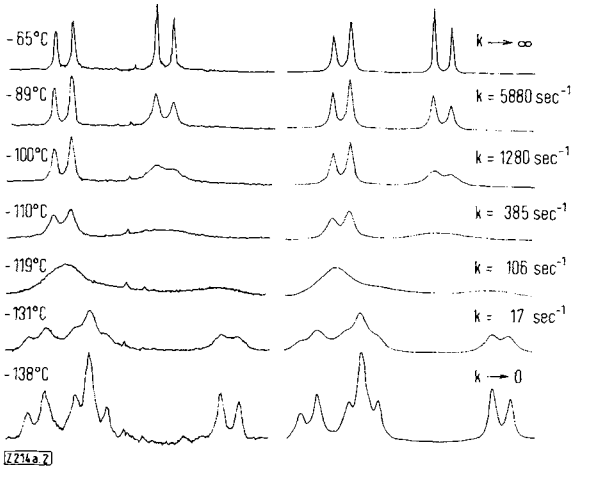


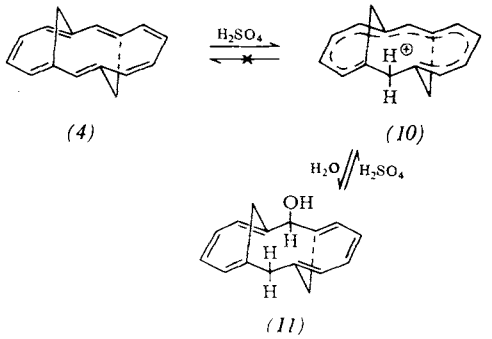
Fig. 2. Absorption of the bridge protons of *(4)* in dependence on temperature [in COS/CS_2 (80 : 20); 100 MHz]; on the left the experimental, on the right the calculated spectra together with the respective rate constants.

The double-bond migration is most plausibly explained by assuming that the resonance hybrid *(9)* constitutes the transition state. An alternative to this would be a series of electrocyclic reactions with the (hitherto unobserved) norcaradiene valence isomer of *(4)* as an intermediate.

anti-1,6 : 8,13-Bismethano[14]annulene satisfies the Hückel rule with respect to the number of π-electrons, yet the hydrocarbon obviously deviates so far from planarity that the delocalization energy is insufficient for equalization of the C—C bonds. Thus in *(4)* the structure with localized bonds is lower in energy than the resonance hybrid.

The UV spectrum of *(4)* can be interpreted in terms of a polyene system [maxima at 217 (ε = 33600), 272 (7800), and 350 nm (4350) (in cyclohexane)].

The olefinic nature of *anti*-1,6 : 8,13-bismethano[14]annulene *(4)* is manifested also in its chemical properties. *(4)* is protonated selectively at C-7 by concentrated sulfuric acid, with formation of the remarkably stable carbonium ion *(10)*. If the dark red solution of *(4)* in H_2SO_4 is added to water, the alcohol *(11)* (m.p. 146—147 °C) is obtained. Analogously, with bromine in methylene chloride at —70 °C *(4)* gives the dibromide *(8)* (steric homogeneity not confirmed) which shows no tendency to form the 7-bromo derivative of *(4)* by elimination of hydrogen bromide.



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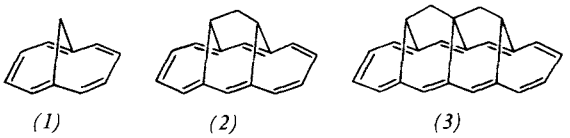
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1,6:8,13-Propanediylidene[14]annulene[1,2]

By *Emanuel Vogel, Axel Vogel, Hans-Klaus Kübbeler*, and *Wolfgang Sturm*[*]

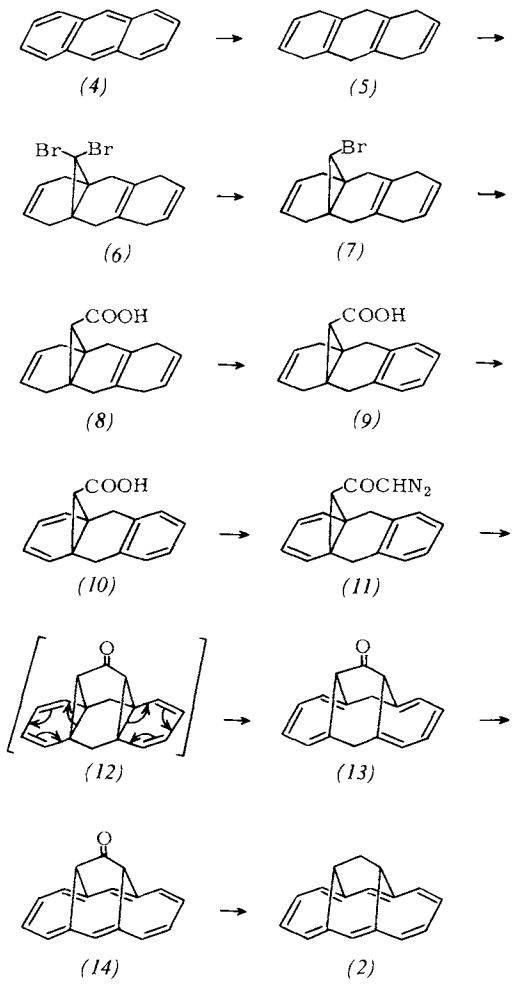
For comparative studies of [4*n* + 2]annulenes it would be desirable to have an annulene series available whose members molecules closely agree in those geometrical properties that are relevant to π-electron delocalization — configuration[3], conformation, and rigidity. In the series of monocyclic [4*n* + 2]annulenes there are considerable differences in this respect[4], so that correlations are possible only to a limited extent.



(1) *(2)* *(3)*

Inspection of models drew our attention to the series 1,6-methano[10]annulene *(1)*[5], 1,6 : 8,13-propanediylidene-[14]annulene *(2)*, and 1,6 : 8,17 : 10,15-pentane-1′,3′,5′-triylidene[18]annulene *(3)*. Since the members of this series show a wealth of common features — they have the same symmetry (acene configuration), have an approximately planar annulene ring, and are completely rigid — they should be particularly suitable for comparison. The synthesis and properties of 1,6 : 8,13-propanediylidene[14]annulene *(2)* justify the expectations placed upon the [4*n* + 2]annulene series *(1)*, *(2)*, and *(3)*.

The synthesis of 1,6 : 8,13-propanediylidene[14]annulene[6] started from 1,4,5,8,9,10-hexahydroanthracene *(5)*[7] which is readily obtained from anthracene *(4)* by way of 9,10-dihydroanthracene. The tetraene *(5)* was treated in tetrahydrofuran with three-molar amounts of bromoform and potassium *tert*-butoxide, thus giving a 20% yield of the 1 : 1 dibromocarbene adduct *(6)*, m.p. 121—122 °C. Reducing *(6)* with tri-*n*-butyltin hydride afforded a product that, according to its NMR spectrum, consisted of the required *endo*-bromide *(7)* (*endo* with respect to the central six-membered ring) and its *exo*-isomer in the ratio 1 : 1. The monobromide mixture was treated at −80 °C with butyllithium, and the resulting organolithium compounds were subsequently allowed to react with solid carbon dioxide at the same temperature. There resulted a 2 : 1 mixture of the *endo*-acid *(8)* [22% based on *(6)*; m.p. 186—188 °C] and the *exo*-acid [m.p. ≈ 200 °C (dec.)], which could be separated by chromatography on silica gel. The configurations of these acids could not be deduced unequivocally from the spectra but follow from bromination studies on the dehydrogenation products [*(9)* and its *exo*-isomer] obtained by means of palladium-charcoal; the dehydrogenated acid [*(9)*; m.p. 180—182 °C] formed in 47% yield from the acid of m.p. 186—188 °C reacted with bromine to give a normal dibromo adduct [m.p. 213—214 °C (dec.)], whereas the isomeric dehydrogenated acid afforded a bromo lactone.



The intention to build the bridge at the *endo*-acid stage *(8)*[8] met with difficulties, for reaction of *(8)* with thionyl or oxalyl chloride gave a β-chloro ketone instead of the expected acid chloride. It was therefore proposed to form the bridge starting from either the acid *(9)* or *(10)*. The dibromo adduct of acid *(9)* was readily dehydrohalogenated by methanolic potassium hydroxide to the acid *(10)* which contained the norcaradiene skeleton [yield 51% based on *(9)*; m.p. 215—217 °C (dec.); NMR ($CDCl_3$), τ = 2.92 (s, 4 arom. CH), 3.7—4.2 (AA'BB' system with a N value of 10.5 Hz, 4 C=CH), 6.45 and 7.09 (AB system with J = 16 Hz, 2 CH_2), 8.92 (s, 1 cyclopropyl-CH); UV (methanol), λ_{max} = 267 (ε = 2700), 272 nm (2770)], and this acid *(10)* was accordingly introduced into the synthesis. Reaction of *(10)* with thionyl chloride was normal, producing the acid chloride, which was next converted by diazomethane into the diazo ketone *(11)* [86% based on *(10)*; m.p. ≈ 100 °C (dec.); IR (CCl_4), CN_2 2120 cm^{-1}]. Copper-catalyzed thermolysis of the diazo ketone resulted in the intended bridge formation to give the ketone *(12)*, which, as anticipated, underwent a spontaneous double norcaradiene-cycloheptatriene valence isomerization to yield *(13)* as the product actually isolated [80%; m.p. 182—183 °C; NMR ($CDCl_3$), τ = 3.5—4.2 (AA'XX' system, 8 C=CH), 6.52 and 6.92 (AB system with J = 15 Hz, 2 CH_2), 7.60 (s, 2 bridge-CH); UV (cyclohexane), λ_{max} = 220 (ε = 39700), 262 nm (7310); IR (KBr), C=O 1730 cm^{-1}]. The dihydro compound *(13)* was dehydrogenated by 2,3-dichloro-5,6-dicyano-*p*-benzoquinone even at room temperature, affording the brilliant orange ketone *(14)* [90%; m.p. 220—221 °C; NMR ($CDCl_3$), τ = 2.09 (s, 2 arom. CH), 1.9—2.6 (AA'BB' system, 8 arom. CH), 10.87 (s, 2 bridge-CH); UV (cyclohexane), λ_{max} = 275 (ε = 21400), 308 (106400), 333 (18200, sh), 365 (8880), 486 (480, sh), 492 (530), 498 (560), 505 (515, sh), 513 (450), 520 nm (360); IR (KBr), C=O 1730 cm^{-1} [9]], and reduction of this ketone by the Huang-Minlon modification of the Wolff-Kishner method gave the desired 1,6:8,13-propanediylidene[14]annulene *(2)* as a stable yellow-orange compound of m.p. 180—181 °C (75%).

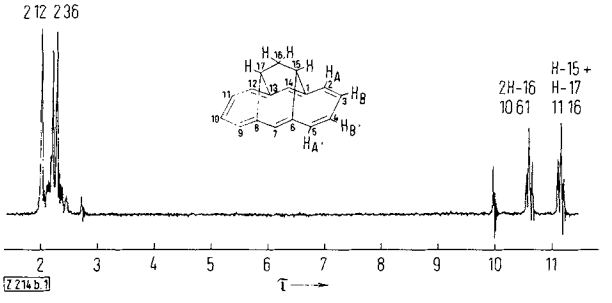


Fig. 1. NMR spectrum of 1,6:8,13-propanediylidene[14]annulene *(2)* (in $CDCl_3$; 60 MHz; tetramethylsilane as internal standard).

The nature of the 14π-electron system in *(2)* is proved above all by the NMR spectrum ($CDCl_3$) (Fig. 1)[10]. The annulene protons appear as a singlet at τ = 2.12 (H-7, H-14) and as an AA'BB' system with τ_A = 2.26 and τ_B = 2.45 (H-2 to H-5, and H-9 to H-12), whilst the bridge protons give rise to two triplets at τ = 10.61 (2 H-16) and 11.16 (H-15, H-17) with J = 2.8 Hz. From the spectrum of the 16,16-dideuterated compound [obtained from *(14)* and tetradeuteriohydrazine] it follows that the triplet at higher field is due to the two outer bridge protons. The absorptions of the annulene protons at relatively low field, together with the strong shielding of the bridge protons, indicate a ring current in the π-electron system and thus show the molecule to be aromatic. The coupling constants of the protons of the AA'BB' system can be interpreted in the same sense (J_{AB} = 9.15 Hz, $J_{BB'}$ = 9.50 Hz, $J_{AB'}$ = 0.41 Hz, $J_{AA'}$ = 1.37 Hz). The annulene protons of *(2)* exhibit approximately the same shifts and coupling parameters as are found for *syn*-1,6 : 8,13-bisoxido-[14]annulene[11], whence it can be concluded that the geometrical and electronic conditions in the C_{14} rings of the two compounds correspond very closely.

The UV spectrum of *(2)* also indicates aromatic character: λ_{max} = 303 (ε = 165000), 322 (23100, sh), 362 (6620), 374 (6560), 480 (410), 486 (435), 492 (440), 498 (385, sh), 506 (300), 513 nm (230) (in cyclohexane).

An X-ray structure analysis of *(2)* proved the approximately planar conformation of the C_{14} ring and the presence of aromatic C—C bonds[12].

Chemically, the aromatic character of *(2)* manifests itself in the formation of substitution products upon treatment of the compound with electrophilic reagents. As in *syn*-1,6 : 8,13 bisoxido[14]annulene[5b], the first substituent preferentially enters at position 2.

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[1] Presented by *E. Vogel* in a lecture at the GDCh General Meeting at Hamburg in September 1969.

[2] Formerly named 1,6:8,13-propano[14]annulene.

[3] *M. J. S. Dewar* and *G. J. Gleicher*, J. Amer. chem. Soc. *87*, 685 (1965).

[4] *F. Sondheimer*, Pure appl. Chem. *7*, 363 (1963).

[5] Reviews: a) *E. Vogel* in: Aromaticity. Special Publication No. 21, Chem. Soc., London 1967, p. 113; b) *E. Vogel*, Chimia *22*, 21 (1968).

[6] *E. Vogel*, Proc. Robert A. Welch Foundation Conferences on Chemical Research, XII. Organic Synthesis, Houston, Texas, 1968, p. 215.

[7] *E. Vogel, M. Biskup, A. Vogel, U. Haberland*, and *J. Eimer*, Angew. Chem. *78*, 642 (1966); Angew. Chem. internat. Edit. *5*, 603 (1966).

[8] See *H. Musso* and *U. Biethan*, Chem. Ber. *100*, 119 (1967).

[9] The C=O frequency of *(14)* – found to be intermediate between those for saturated five-membered and six-membered ring ketones – does not reveal an electronic interaction between the carbonyl group and the 14 π-electron system. As mentioned by *R. B. Woodward* in a discussion (Welch Foundation Conferences on Chemical Research, XII), such an interaction is symmetry-allowed and should result in a polarization of the carbonyl group [cf. the agreement between the UV spectra of *(14)* and *(2)*].

[10] For analysis of the NMR spectrum see *W. Bremser, J. D. Roberts*, and *E. Vogel*, Tetrahedron Letters *1969*, 4307.

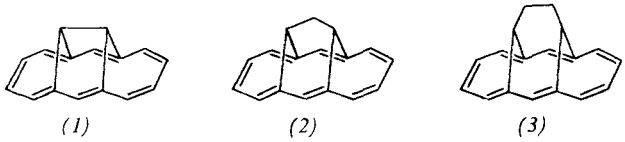
[11] *E. Vogel, M. Biskup, A. Vogel*, and *H. Günther*, Angew. Chem. *78*, 755 (1966); Angew. Chem. internat. Edit. *5*, 734 (1966).

[12] *G. Casalone, A. Gavezzotti, A. Mugnoli*, and *M. Simonetta*, Angew. Chem. *82*, 516 (1970); Angew. Chem. internat. Edit. *9*, 519 (1970); cf. the X-ray structure analysis of *syn*-1,6: 8,13-bisoxido[14]annulene: *P. Ganis* and *J. D. Dunitz*, Helv. chim. Acta *50*, 2369 (1967).

1,6:8,13-Butanediylidene[14]annulene[1]

By *Emanuel Vogel, Wolfgang Sturm*, and *Hans-Dieter Cremer*[*]

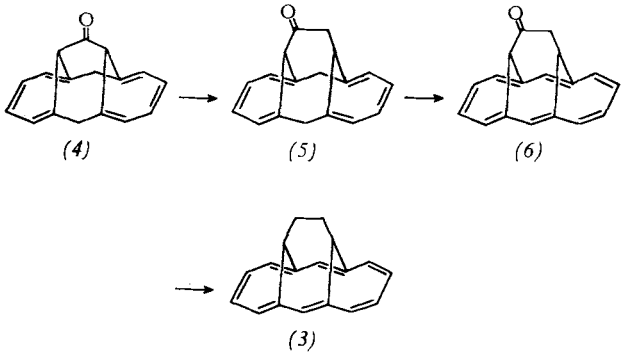
Replacement of the two inner bridge-protons in the as yet unknown syn-1,6 : 8,13-bismethano[14]annulene by one or more CH_2 groups – and, in the simplest case, direct linkage of the two bridging C atoms – leads to the series *(1)*, *(2)*, *(3)*, *etc.* of bridged [14]annulenes, of which one member, 1,6 : 8,13-propanediylidene[14]annulene *(2)*[2], has already been described.



(1) *(2)* *(3)*

From consideration of molecular models it can be predicted that *(2)* has an approximately planar annulene ring[3], whereas for the higher analogs of *(2)* the $(CH_2)_n$ intermediate bridges will compel progressive bending and/or zig-zagging of the peripheral C_{14} skeleton. According to the models it is probable that the lower homolog of *(2)*, *i.e.* 1,6 : 8,13-ethanediylidene[14]annulene *(1)*, will fulfill the steric requirements for delocalization of the π-electrons even better than *(2)* itself. Thus the [14]annulene series *(1)*, *(2)*, *(3)*, *etc.*, opens up the possibility of studying the properties of a cyclic conjugated system in relation to the geometry of the ring skeleton.

The starting point for the synthesis of 1,6 : 8,13-butanediylidene[14]annulene *(3)* was the dihydro[14]annulene ketone *(4)*[2]. Treatment of a solution of the ketone *(4)* in methanol-methylene dichloride (1 : 1) with ethereal diazomethane led to, amongst other products, the required homologous ketone *(5)* [m.p. 131–132 °C; NMR ($CDCl_3$), τ = 3.5–4.2 (multiplet consisting of two partially superimposed AA'XX' systems, 8 C=CH), 6.41 and 7.01 (AB system with J = 13 Hz, 2 allylic CH_2), 6.87 (d with J = 3.5 Hz, bridge-CH_2), 7.22 (s, 1 bridge-CH), 7.80 (t with J = 3.5 Hz, 1 bridge-CH); UV (cyclohexane), λ_{max} = 224 (ε = 30300), 261 nm (7100)], which could be isolated in 7% yield by chromatography on silica gel with methylene dichloride-hexane (2 : 1). 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone dehydrogenated *(5)* in boiling anisole (24 h) to *(6)* [m.p. 164–165 °C; yield 60%; NMR (CCl_4), τ = 2.05 (s, 2 arom. CH), 2.25–2.95 (multiplet consisting of two partially superimposed AA'BB' systems, 8 arom. CH), 8.78 (d with J = 4.0 Hz, bridge-CH), 9.87 (s, 1 bridge-CH), 10.87 (t with J = 4.0 Hz, 1 bridge-CH_2); UV (cyclohexane), λ_{max} = 272 (ε = 8570, sh), 305 (121000), 333 (12900, sh), 360 (7780), 478 (195), 484 (205), 490 (205), 498 nm (170, sh); IR (KBr), C=O 1708 cm^{-1}]. Finally, reducing *(6)* by the Huang-Minlon modification of the Wolff-Kishner reaction afforded the stable yellow hydrocarbon *(3)*, m.p. 175–176 °C, in 66% yield.



(4) *(5)* *(6)* *(3)*

The spectra of *(3)* all indicate the presence of an aromatic compound. The NMR spectrum (CCl_4) (Fig. 1) shows the annulene protons as a singlet at τ = 2.14 (H-7, H-14) and as an AA'BB' system with τ_A = 2.43 and τ_B = 2.88 (H-2 to H-5, and H-9 to H-12), and the bridge protons as two groups of signals at τ = 9.48 (2 H-16, 2 H-17) and 10.96 (H-15, H-18) which, to a first approximation, can be regarded as a triplet and a quintuplet (^3J = 2.4 Hz and ^4J = 1.9 Hz), respectively (relative intensities 2 : 8 : 4 : 2). The coupling constants of the annulene protons H-2 to H-5 (and of H-9 to H-12) are J_{AB} = 9.24 Hz, $J_{BB'}$ = 9.31 Hz, $J_{AB'}$ = 0.21 Hz, $J_{AA'}$ = 1.53 Hz. The absorptions of the annulene- and the bridge-protons at relatively low and relatively high field, respectively, together with the symmetry of the spectrum, indicate that the

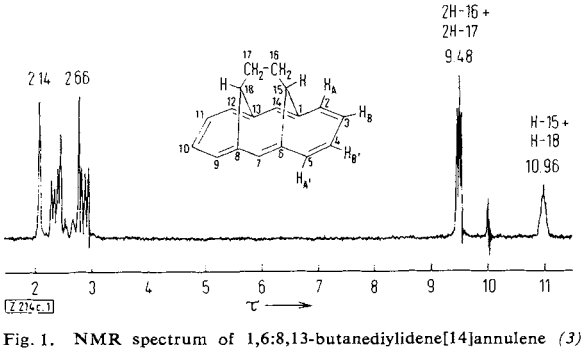


Fig. 1. NMR spectrum of 1,6:8,13-butanediylidene[14]annulene *(3)* (in CCl_4; 60 MHz; tetramethylsilane as internal standard).

π-electron system of the hydrocarbon is delocalized. The UV spectrum of *(3)* can be interpreted in the same terms [λ_{max} = 302 (ε = 145000), 320 (25800, sh), 360 (7450), 373 (7220, sh), 467 (270, sh), 473 (295), 480 (285), 486 (275), 492 nm (215, sh) (in cyclohexane)].

An X-ray structure analysis of 1,6 : 8,13-butanediylidene[14]-annulene *(3)* is not yet available[4], but the geometry of the molecule is already evident from a comparison of its NMR spectrum with that of *(2)*[2,5]. The two compounds have almost identical chemical shifts for the annulene and CH-bridge protons; furthermore, they have virtually the same coupling constants for the annulene protons. However, for *(3)* the signals of the CH_2-bridge protons lie approximately 1.1 ppm farther downfield than for *(2)*. Thence it follows that the annulene ring of *(3)* has almost the same, nearly planar conformation as in *(2)*, and that — contrary to the predictions based on models — it is rather the bridge moiety than the annulene ring that experiences deformation. In the spectrum of *(3)* the absorption of the CH_2 protons is at comparatively low field, indicating that the intermediate CH_2—CH_2 bridge is largely forced out of the space between C atoms 15 and 18. That the conformations of the annulene rings of *(3)* and *(2)* are very similar also follows from the close agreement of the UV spectra of the two hydrocarbons. As far as can be seen, considering the small quantity of *(3)* available up to the present, *(3)* corresponds to its homolog *(2)* also in its chemical behavior.

The spectra of *(3)* show that the tendency of the 14π-electron system for maximal p-orbital overlap determines the geometry of the molecule to a much greater extent than was assumed from consideration of models. Thus, intermediate bridges that are appreciably more rigid and more space-filling than a CH_2—CH_2 grouping will be required to enforce the intended bending of the annulene ring of bridged [14]-annulenes of the present type.

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[1] Previously named 1,6:8,13-butano[14]annulene.

[2] *E. Vogel*, Proc. Robert A. Welch Foundation Conferences on Chemical Research, XII. Organic Synthesis, Houston, Texas 1968, p. 215; *E. Vogel, A. Vogel, H.-K. Kübbeler*, and *W. Sturm*, Angew. Chem. *82*, 512 (1970); Angew. Chem. internat. Edit. *9*, 514 (1970).

[3] This expectation has meanwhile been confirmed by X-ray structure analysis of *(2)*: *G. Casalone, A. Gavezzotti, A. Mugnoli*, and *M. Simonetta*, Angew. Chem. *82*, 516 (1970); Angew. Chem. internat. Edit. *9*, 519 (1970).

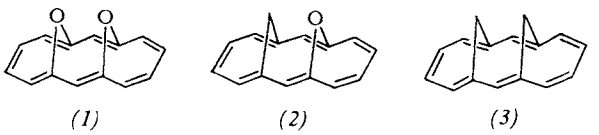
[4] An X-ray structure analysis is currently being performed by Professor *M. Simonetta* at the University of Milan (Italy).

[5] For an NMR analysis of *(2)* see *W. Bremser, J. D. Roberts*, and *E. Vogel*, Tetrahedron Letters *1969*, 4307.

syn-1,6-Methano-8,13-oxido[14]annulene[1]

By *Emanuel Vogel, Ulrich Haberland*, and *Jürgen Ick*[*]

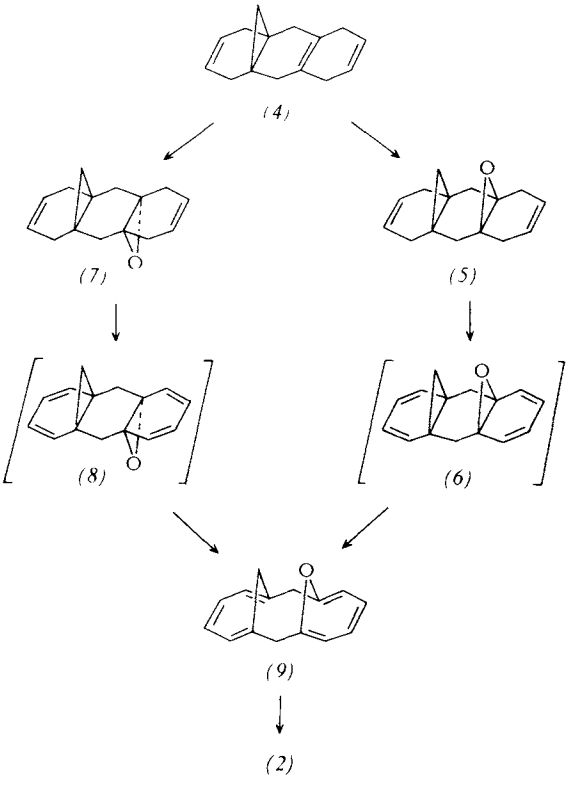
For the aromatic *syn*-1,6 : 8,13-bisoxido[14]annulene *(1)*[2] it was shown by X-ray structure analysis[3] that the annulene ring is approximately planar, that the C—C bonds are of equal length within experimental error, and that the bond lengths (mean 1.392 Å) are almost identical with the C—C distance in benzene. If the two oxygen bridges of *(1)* are replaced successively by the more space-filling CH_2 groups, steric interaction between the bridges increases appreciably. The annulene rings in *syn*-1,6-methano-8,13-oxido[14]annulene *(2)* and *syn*-1,6 : 8,13-bismethano[14]annulene *(3)* should thus experience progressive bending. It seemed interesting to investigate what effects the geometrical changes on going from



(1) *(2)* *(3)*

(1) to *(3)* will have on the physical and chemical behavior of the molecules in question.

This communication concerns the stereoisomeric 1,6-methano-8,13-oxido[14]annulenes [*(2)* and its *anti*-isomer], which were to be synthesized from 1,4,5,8,9,10-hexahydroanthracene[5] in analogy to the preparation of *(1)* and *anti*-1,6 : 8,13-bismethano[14]annulene[2b,4]. It therefore seemed advisable to introduce the bridge functions by cyclopropanation with Simmons-Smith reagent and subsequent peracetic acid epoxidation. When the hexahydroanthracene was treated with a three-fold excess of methylene diiodide and a zinc-copper couple a moderately selective attack at the central double bonds occurred to give the cyclopropane hydrocarbon *(4)* which had to be isolated by chromatography [m.p. 56 °C; yield 23%; NMR (CCl_4), τ = 4.3—4.6 (2 broad singlets, 4 C=CH), 7.5—7.8 (m, 6 CH_2), 9.47 and 9.58 (AB system with J = 3.5 Hz, cyclopropyl-CH_2)]. When *(4)* was treated with one mole of peracetic acid, epoxidation of the residual central double bond was highly selective and there resulted a mixture of the *syn*-epoxide *(5)* [m.p. 79—80 °C; yield 8%;



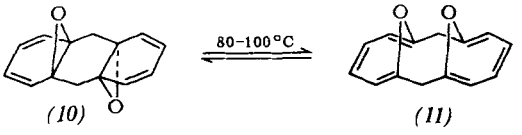
(4) *(7)* *(5)* *(8)* *(6)* *(9)* *(2)*

NMR ($CDCl_3$): τ = 4.5 (s, 4 C=CH), 7.5—8.3 (multiplet, in which an AB system at 7.68 and 8.20 with J = 15.5 Hz can be discerned, 6 CH_2), 8.78 and 9.60 (AB system with J = 3.0 Hz, cyclopropyl-CH_2)] and the *anti*-epoxide *(7)* [m.p. 55—56 °C; yield 66%; NMR (CCl_4): τ = 4.4—4.7 (m, 4 C=CH), 7.5—8.0 (m, 4 CH_2), 8.1 (s, 2 CH_2), 9.25 and 10.01 (AB system with J = 4.2 Hz, cyclopropyl-CH_2)]; these isomers were separated by chromatography on alumina. Structural assignment was based on the assumption that in the *syn*-epoxide the inner cyclopropane proton will absorb at relatively low field since it is certainly subject to deshielding by the oxygen atom.

The *syn*- and *anti*-epoxides [*(5)* and *(7)*] were separately treated in methylene dichloride at —70 °C with 2 moles of bromine, and the resulting tetrabromides [m.p. 140 °C (dec.) and 144—146 °C (dec.), respectively; yield about 50% in each

case] then subjected to dehydrohalogenation by 1,5-diazabicyclo[4.3.0]non-5-ene[6]. Surprisingly, both tetrabromides gave one and the same pale yellow compound [m.p. 80—81 °C, yield 50% in each case; NMR (C_6D_6), τ = 3.7 and 4.2 (AA'XX' system, 4 C=CH of the cycloheptatriene portion), 4.3 and 4.9 (AA'XX' system, 4 C=CH of the oxepin portion), 6.41 and 8.24 (AB system with J = 11.0 Hz, CH_2-bridge protons), 6.80 and 7.35 (AB system with J = 12.5 Hz, 2 CH_2); UV (cyclohexane), λ_{max} = 223 (ε = 26500), 267 (5350), 310 nm (630, sh)], which is shown by spectral data to have the structure of a 7,14-dihydro-1,6-methano-8,13-oxido[14]annulene [*(9)* or its isomer]. Evidently, one is dealing with the *syn*-compound *(9)* since one of the bridge protons absorbs at relatively low field indicating that this proton is close to the oxygen bridge.

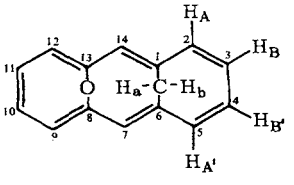
The change of configuration on dehydrohalogenation of the tetrabromide derived from *(7)* can best be explained by assuming that 7,14-dihydro-*anti*-1,6-methano-8,13-oxido[14]-annulene is formed as intermediate and that this compound subsequently isomerizes by flipping of the oxygen bridge (or less probably the CH_2-bridge) through the annulene ring. This interpretation is supported by the reversible isomerization of the *anti*-bis-arene-oxide *(10)*[2b] to the *syn*-bisoxepin *(11)*[2b] observed at 80—100 °C, in which the *anti*-bisoxepin is believed to be an intermediate.



(10) *(11)*

The compound taken as 7,14-dihydro-*syn*-1,6-methano-8,13-oxido[14]annulene *(9)* is dehydrogenated by 2,3-dichloro-5,6-dicyano-*p*-benzoquinone to the orange-red, aromatic *syn*-1,6-methano-8,13-oxido[14]annulene *(2)*, m.p. 118—119 °C (yield 40%).

Taking the reduced molecular symmetry (C_s as against C_{2v}) into account, the NMR spectrum of *(2)* (Fig. 1) corresponds fully to that of the known *syn*-bridged [14]annulenes *(1)* and 1,6 : 8,13-propanediylidene[14]annulene[7]. The absorptions of the annulene protons consist of a singlet at τ = 2.25 (H-7, H-14) and a complex multiplet at τ = 2.2—2.7 composed of two partly superimposed AA'BB' systems (H-2 to H-5, and H-9 to H-12). The calculated chemical shifts and coupling constants for the annulene protons are shown in the Table[8].



	τ_A	τ_B	J_{AB}	$J_{BB'}$
H-2 to H-5:	2.35	2.66	8.8 Hz	9.3 Hz
H-9 to H-12:	2.36	2.57	9.4 Hz	9.1 Hz

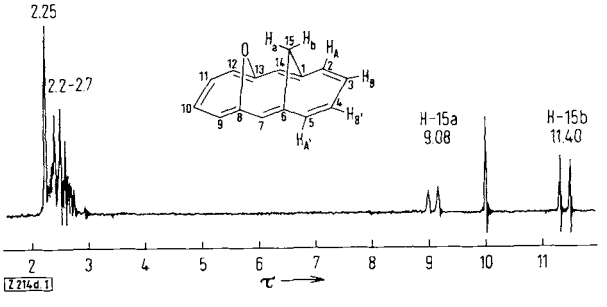


Fig. 1. NMR spectrum of *syn*-1,6-methano-8,13-oxido[14]annulene *(2)* (in $CDCl_3$; 60 MHz; tetramethylsilane as internal standard).

The signals of H-2 to H-5 could be assigned on the basis of a long-range coupling (M mechanism) between H-15a and H-2 and H-5 (J = 1.1 Hz), which was established by a double resonance experiment. As expected from the aromatic character of *(2)* which is indicated by the NMR parameters of the annulene protons, the resonances of the CH_2 bridge protons [the AB system at τ = 9.08 (H-15a) and 11.40 (H-15b) with J = 10.6 Hz[9]] are at relatively high field. The 2.3 ppm difference in the chemical shifts of these CH_2 protons, due mainly to deshielding of H-15a by the oxygen atom, not only proves the *syn*-configuration of *(2)* but also, because of its magnitude, shows appreciable steric interaction between the bridges[10]. From the NMR data for both the annulene and the bridge protons it follows that the molecule rather tolerates a compression of the bridges than a bending of the ring[11].

The UV spectrum of *(2)* has the same shape as that of *(1)* [λ_{max} = 300 (ε = 141700), 330 (17500, sh), 372 (8170), 518 nm (510) (in cyclohexane).

In analogy to *(1)*, *(2)* gives substitution products with electrophilic reagents. As a typical example, Friedel-Crafts acylation with acetic anhydride in the presence of boron trifluoride-ether affords three red monoacetyl derivatives (total yield 66%) which are readily separable by chromatography on aluminum oxide: 2-acetyl- (m.p. 159—160 °C; yield 14%), 9-acetyl- (m.p. 107—108 °C; yield 40%), and 10-acetyl-*syn*-1,6-methano-8,13-oxido[14]annulene (m.p. 117—118 °C; yield 12%). The positions of the substituents are determined by NMR spectroscopy.

An X-ray structure analysis of *(2)* is not yet available, but it is evident from the spectral data alone that the annulene ring of *(2)* has a geometry very similar to that of *(1)*. This result suggests that the steric interference of the two inner bridge-hydrogen atoms in the still unknown *syn*-1,6 : 8,13-bismethano[14]annulene will cause less bending of the annulene ring than is implied by the models.

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[1] Presented by *E. Vogel* in a lecture at the GDCh General Meeting at Hamburg in September, 1969.

[2] a) *E. Vogel, M. Biskup, A. Vogel,* and *H. Günther,* Angew. Chem. *78*, 755 (1966); Angew. Chem. internat. Edit. *5*, 734 (1966); b) *E. Vogel,* Chimia *22*, 21 (1968).

[3] *P. Ganis* and *J. D. Dunitz,* Helv. chim. Acta *50*, 2369 (1967).

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[9] This coupling reflects the expected widening of the CH_2-bridge angle in comparison with that of 1,6-methano[10]-annulene [corresponding coupling 6.9 Hz; *H. Günther,* Z. Naturforsch. *20b*, 948 (1965)].

[10] Such large differences in the chemical shifts of methylene protons due to the proximity of one of these protons to an oxygen function appear to have been observed previously only for some semi-cage compounds with OH and OR groups in the *endo*-position; *S. Winstein, P. Carter, F. A. L. Anet,* and *A. J. R. Bourn,* J. Amer. chem. Soc. *87*, 5247 (1965).

[11] Compare the geometrical conditions in 1,6:8,13-butanediylidene[14]annulene; *E. Vogel, W. Sturm,* and *H.-D. Cremer,* Angew. Chem. *82*, 513 (1970); Angew. Chem. internat. Edit. *9*, 516 (1970).

The Crystal Structure of 1,6:8,13-Propanediylidene-[14]annulene

By *Gianluigi Casalone, Angelo Gavezzotti, Angelo Mugnoli,* and *Massimo Simonetta*[*]

The relationship between the aromatic character and the form of the bridged annulene ring in 1,6 : 8,13-propanediylidene-[14]annulene[1] is of considerable interest.

1,6:8,13-propanediylidene[14]annulene, m.p. 180—181 °C, crystallizes in the orthorhombic space group Fdd2 (C_{2v}^{19}) with 16 molecules in the unit cell, $a = 19.47$, $b = 36.37$, $c = 6.58$ Å, $d_{X\text{-ray}} = 1.244$, $d_{exp} = 1.248$ g cm^{-3}. The intensities of about 1300 independent reflections were recorded on a linear automatic diffractometer using $Mo_{K\alpha}$ radiation.

The orientation of one molecule in the unit cell was determined by an automatic comparison between the experimental three-dimensional sharpened Patterson synthesis calculated near the origin and the intramolecular vector distributions calculated for a plausible molecular model rotating about three mutually perpendicular axes[2]. The position of the reference molecule in the unit cell was then determined by systematic comparison between observed and calculated structure factors, while shifting the oriented model along x and y (z being a polar axis). Some cycles of full-matrix isotropic least-squares refinement on the 826 reflections having $I \geq 2\,\sigma(I)$ led to an R index of 11.5%. Further refinement is in progress taking into account the anisotropy of the thermal vibration.

The molecular conformation (Fig. 1) is very close to the mm2 symmetry, the differences being of the order of the estimated standard deviations as calculated at this point of the refinement. The geometrical features along the annulene perimeter are similar to those previously found for 1,6 : 8,13-bisoxido[14]annulene[3].

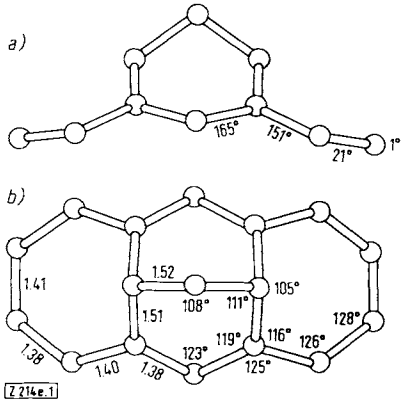


Fig. 1. Crystal structure of 1,6:8,13-propanediylidene[14]annulene. a) Absolute values of torsion angles in the annulene perimeter. b) Mean values of symmetrically equivalent bond lengths and angles.

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[1] *E. Vogel, A. Vogel, H.-K. Kübbeler,* and *W. Sturm,* Angew. Chem. *82*, 512 (1970); Angew. Chem. internat. Edit. *9*, 514 (1970); we are grateful to Prof. *E. Vogel* for supplying us with crystals of 1,6:8,13-propanediylidene[14]annulene.

[2] Program written by *G. Filippini* and *C. M. Gramaccioli,* to be published.

[3] *P. Ganis* and *J. D. Dunitz,* Helv. Chim. Acta *50*, 2369 (1967).

Magnetic Behavior of Alkali-Metal Tetroxocobaltates(v)

By *Claus Brendel* and *Wilhelm Klemm*[*]

Dedicated to Professor Eugen Müller on the occasion of his 65th birthday

A few years ago we reported on potassium tetroxocobaltate(v)[1]. Although a magnetic moment of $\geq 4.9\,\mu_B$ expected for Co^V having the 3d electron configuration $(e)^2(t_2)^2$ with tetrahedral coordination was found for solid solutions of K_3CoO_4 with K_3PO_4, considerably lower values were observed for pure K_3CoO_4, possibly because of interactions between the CoO^{3-} groups.

Since such interactions should be less effective in rubidium and cesium tetroxocobaltate(v) we have now studied the magnetic behavior of these compounds. They were prepared by heating 3 : 1 mixtures of $RbO_{0.7}$ and $CoO_{1.5}$ at 350 °C for 4 h or at 280 °C for 46 h, and 3 : 1 mixtures of $CsO_{0.5}$ and $CoO_{1.5}$ at 300 °C for 2—3 h, respectively, under approx. 0.5 atm of O_2 in a sealed tube. The black products of uniform appearance resulting on quenching to room temperature react with water in the same way as K_3CoO_4. The change in weight incurred during reaction also corresponds to the formation of Rb_3CoO_4 and Cs_3CoO_4. The molar volumes of 97 and 112 cm^3 calculated from the densities of 3.9_0 and 4.6_5 g cm^{-3} are consistent with the molar volume of K_3CoO_4 ($d = 2.7_4$ g cm^{-3}, $v_M = 88$ cm^3). The debyeogram permits no conclusion whether the three compounds are isotypic.

The magnetic behavior of the new tetroxocobaltates(v) is similar to that of K_3CoO_4, as can be seen from the tabulated effective moments:

	μ_{eff} (in μ_B)		
	90 °K	195 °K	293 °K
K_3CoO_4	1.1_8	1.7_0	2.0_8
Rb_3CoO_4	1.3_5	1.7_4	2.0_7
Cs_3CoO_4	1.8_2	2.0_3	2.3_3

As expected, the μ_{eff} values increase on going from the K compound to the Cs compound, *i.e.* the anionic interactions decrease in magnitude. However, the value of μ_{eff} recorded for the Cs compound at room temperature is still far removed from the moment predicted for Co^V.

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[1] *C. Brendel* and *W. Klemm,* Z. anorg. allg. Chem. *320*, 59 (1963).

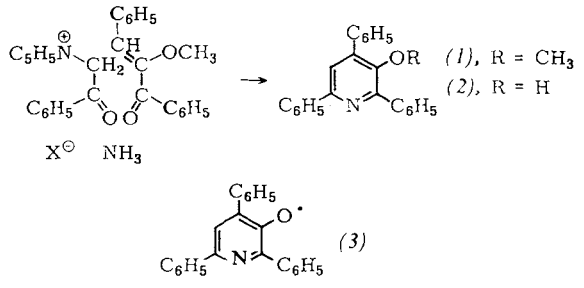
A Stable Aroxyl Radical of the Heteroaromatic Series

By *Hans-Joachim Teuber, Günther Schütz,* and *Hans-Joachim Gross*[*]

Dedicated to Professor Eugen Müller on the occasion of his 65th birthday

Of the isomeric hydroxypyridines, the 3-hydroxy compound shows the closest resemblance to phenol. The phenolic character has now been effectively established by the successful dehydrogenation of its 2,4,6-triphenyl derivative *(2)* to a stable radical *(3)*. This is the first radical of its kind in the heteroaromatic series.

We have synthesized *(2)* from methoxychalcone and phenacylpyridinium bromide *via* the methyl ether *(1)*.



(3)

Isolation of the chalcone is unnecessary if methoxyacetophenone and benzaldehyde are used as starting materials[1]. The pyridine *(1)* can also be prepared by *Weiss*'s modification of the Chichibabin synthesis[2].

The methyl ether *(1)* (colorless needles from ligroin, m.p. 130—131 °C) is cleaved by pyridinium chloride or hydrobromic acid/glacial acetic acid to give the 3-hydroxypyridine *(2)* (yellow needles, m.p. 138—139 °C). Dehydrogenation of *(2)* with potassium hexacyanoferrate(III) or potassium nitrosobissulfate in sodium hydroxide/carbon tetrachloride affords a violet-brown solution of the radical 2,4,6-triphenyl-3-pyridyloxyl *(3)*. Concentration of the carbon tetrachloride solution yields *(3)* as a crystalline yellow dimer (containing 1 molecule of CCl_4) which we formulate as the quinol.

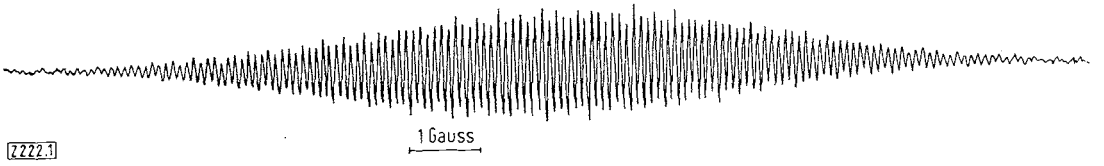


Figure. High resolution ESR spectrum of the radical 2,4,6-triphenyl-3-pyridyloxyl *(3)* in benzene.

In organic solvents the dimer dissociates to the free radical and shows the expected temperature-dependent equilibrium (color deepening on warming). Characteristic quinol absorption bands are present in the IR spectrum of the solid (1707, 1623; 1210 cm^{-1}). The free pyridyloxyl *(3)* gives a UV spectrum containing more bands than the spectrum of triphenylphenoxyl[3] (λ_{max} = 665, 550, 415, 358, 318 nm, in chloroform). The radical, which, unlike 2,4,6-tri-*tert*-butylphenoxyl[4], is completely stable towards oxygen, reacts preferentially as a dehydrogenating agent; it slowly attacks such solvents as acetone, methanol, and chloroform. It obviously has a higher oxidation potential than triphenylphenoxyl. The comparatively low symmetry of *(3)* can be deduced from the ncreased number of lines in the ESR spectrum (see Figure)[5].

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[5] The interpretation of the ESR spectrum will be given elsewhere.

New Aroxyls : Mono-, Di-, and Triradicals. Detection of a Triplet State

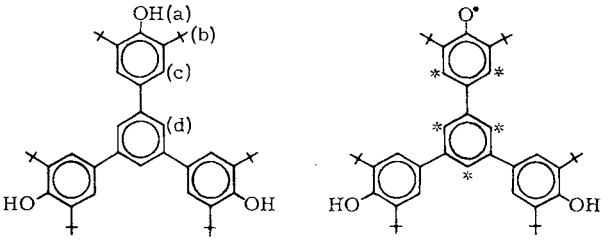
By *Gerd Kothe, Claudia Nowak, Karl-Heinz Denkel, Ernst Ohmes, and Herbert Zimmermann*[*]

Dedicated to Professor Eugen Müller on the occasion of his 65th birthday

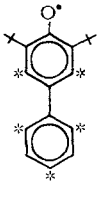
HCl condensation of 4-acetyl-2,6-di-*tert*-butylphenol[1] in dry ethanol at room temperature leads to a small yield of the new triphenol 1,3,5-tris(3,5-di-*tert*-butyl-4-hydroxyphenyl)-benzene *(1)* [colorless crystals, m.p. 313—314 °C (uncorrected); λ_{max} = 271 nm, log ε = 4.74 (ethanol)], from which a number of radicals of the aroxyl series can be derived. The structure of *(1)* follows from elemental analysis, the molecular weight, IR spectrum [ν_{OH} = 3639 cm^{-1} (sharp)], and NMR spectrum [H^a δ = 5.27 ppm (3), H^b 1.49 (54), H^c 7.46 (6), H^d 7.57 (3); δ in $CDCl_3$ with TMS as internal standard].

Dehydrogenation of the triphenol *(1)* with a deficit of lead dioxide in benzene or toluene yields the violet monoradical *(2)*, λ_{max} = 529 nm (in benzene). The color of *(2)* closely resembles that of the radical *(3)*, λ_{max} = 491 nm (in benzene)[2], which was isolated pure by *Eugen Müller et al.*[3].

At low resolution the ESR spectrum of *(2)* in toluene shows six equidistant lines at g = 2 in the intensity ratio 1 : 5 : 10 : 10 : 5 : 1, coupling constant a_H = 1.71 G. The splitting pattern of the signal can be attributed to coupling of the radical electron with five equivalent protons [asterisked aromatic positions in *(2)*]. Similar observations were made in the case of *(3)*[4,5].



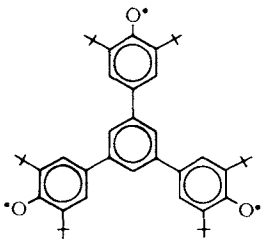
(1) *(2)*



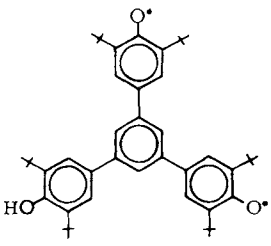
(3)

If the triphenol is dehydrogenated with an excess of lead dioxide in benzene or toluene the orange-brown radical *(4)* is formed whose chemical behavior is consistent with a triradical [λ_{max} = 478 nm with a shoulder at 577 nm (in benzene)].

On iodometric titration[6] of *(4)*, 2.4 to 2.5 equivalents of iodine are liberated. After titration, 96% of the triphenol can be recovered, thus indicating the absence of fragmentation



(4)



(5)

during dehydrogenation. Osmometric molecular-weight determinations in benzene show the triradical *(4)* to be monomeric in solution.

The ESR spectrum of *(4)* in toluene (—70 °C) contains 16 lines at $g = 2$ (Fig 1a). The spectrum can be simulated with two sets of three and six equivalent protons (Fig. 1b) [$a_{H^1} = 1.75$ (3), $a_{H^2} = 0.60$ G (6); half-width of the absorption curve $\Delta H = 0.50$ G; 100% Gaussian curve].

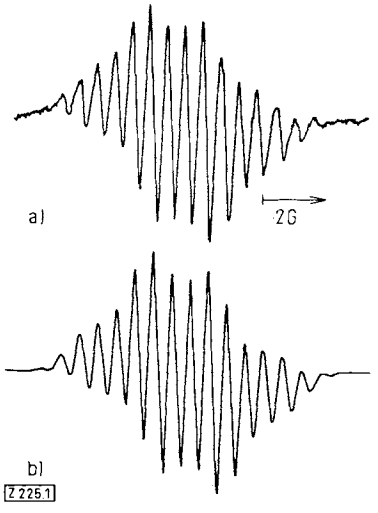


Fig. 1. ESR spectrum of 4,4',4''-(1,3,5-benzenetriyl)tri(2,6-di-*tert*-butylphenoxyl) *(4)* in toluene at —70 °C.
a) Experimental. b) Simulated.

Combination of toluene solutions of the triphenol *(1)* and the triradical *(4)* in the molar ratio 1 : 2 affords a radical solution containing not only *(2)* and *(4)* but also the diradical *(5)* which is present in the triplet state. The triplet state of *(5)* can be deduced from its half-field transition ($\Delta m = 2$) at 1621 G and the corresponding $\Delta m = 1$ lines in the ESR spectrum of a toluene solution frozen to a rigid glass. The high-field ESR spectrum of this glass contains a number of $\Delta m = 1$ lines arranged almost symmetrically with respect to the $g = 2$ transition of *(2)* and *(4)* at 3246 G (Fig. 2).

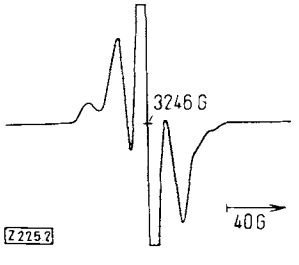


Fig. 2. ESR spectrum of 4,4'-[5-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-phenylene]bis(2,6-di-*tert*-butylphenoxyl) *(5)* in toluene glass at approx. —180 °C.

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[6] *E. Müller* and *K. Ley*, Chem. Ber. *87*, 922 (1954).

Preparation of Cyclic and Acyclic Vinyl Trifluoromethanesulfonates[**]

By *Thomas E. Dueber*, *Peter J. Stang*, *Wolf D. Pfeifer*, *Richard H. Summerville*, *Michael A. Imhoff*, *Paul v. Ragué Schleyer*, *Klaus Hummel*, *Siegfried Bocher*, *Charles E. Harding*, and *Michael Hanack*[*]

We have found that cyclic vinyl trifluoromethanesulfonates (Table) can be prepared in a simple manner by treating cycloalkanones with trifluoromethanesulfonic anhydride.

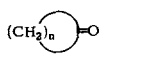
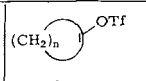
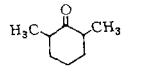
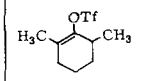
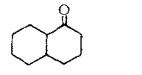
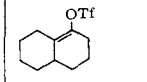
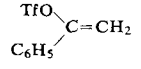
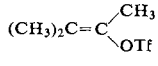
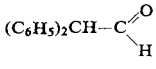
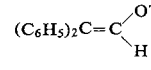
Method 1 (without solvent): Trifluoromethanesulfonic anhydride[1] and an equimolar amount of the cycloalkanone are mixed with stirring at a temperature of —15 to 0 °C. The temperature of the reaction mixture is kept at —5 °C for 2 h and then at 0 °C for 2 to 14 days (Table). For work-up, the reaction mixture is poured on to ice, neutralized with aqueous sodium bicarbonate, and extracted with ether. The ether solution is washed with water, dried, and after removal of the ether the residue is vacuum distilled. The trifluoromethanesulfonate can easily be separated from the distillate by preparative gas chromatography (3 m column, diethylene glycol succinate, 110—140 °C).

Method 2 (with methylene chloride or pentane as solvent): Trifluoromethanesulfonic anhydride (15 mmoles) in methylene chloride (15 ml) is added dropwise within 30 min to a stirred, cold solution (—70 °C) of the ketone (or aldehyde, see Table) (15 mmoles) in methylene chloride (or pentane). Anhydrous sodium carbonate (8 mmoles) is added simultaneously in small portions. During addition of the anhydride a slight increase in temperature is observed. When the reaction mixture has warmed to —10 °C it is yellow or red in color. After one day to three weeks the solution is filtered, washed with water, and dried. The methylene chloride is removed by means of a rotary evaporator and the residue is vacuum distilled. Pure trifluoromethanesulfonate can be obtained from the distillate by preparative gas chromatography, fractional distillation, or chromatography on silica gel (pentane solvent).

Acyclic trifluoromethanesulfonates can be prepared in like manner from acyclic aldehydes or ketones (Table). In addition to the compounds listed in the Table, the corresponding vinyl trifluoromethanesulfonates were prepared from 2,5-dimethylcyclopentanone, *p*-chloroacetophenone, adamantyl methyl ketone, and 1,1-diphenylacetone.

Alkyl trifluoromethanesulfonates solvolyze about 10^4—10^5 times faster than the corresponding alkyl arylsulfonates[2]. Using another method *Stang* and *Summerville*[3] as well as *Jones* and *Maness*[4] prepared for the first time acyclic vinyl trifluoromethanesulfonates. While the acyclic derivatives which they prepared can form the energetically favorable linear vinyl cations[5] on solvolysis[6], it may be possible to generate nonlinear vinyl cations by the solvolysis of the cyclic vinyl trifluoromethanesulfonates described above[7].

Vinyl trifluoromethanesulfonates, prepared by methods 1 and 2.

Ketone or aldehyde	Trifluoromethanesulfonate [a]	Reaction time (days) method 1	Reaction time (days) method 2	Yield (%)	B.p. (°C/torr)	NMR (vinyl-H, τ)	IR νC=C (cm⁻¹)
							
$n = 3$	$n = 3$	2		40	21–23/0.5	4.41 (m, 1 H)	1660 (CCl_4)
$n = 4$	$n = 4$	6		50	78–80/12	4.22 (m, 1 H)	1690 (CCl_4)
$n = 5$	$n = 5$	3		45	71–73/4	4.10 (t, 1 H)	1680 ($CHCl_3$)
$n = 6$	$n = 6$	14	10	40	84–87/4	4.36 (t, 1 H)	1680 (CCl_4)
			14	28	74–76/5	–	1710 (film)
			8	35	196–197/760	–	1695 (CCl_4)
C_6H_5–CO–CH_3			10	40	46–47/0,5	4.59; 4.50 (2d 2 H)	1650 (film)
$(CH_3)_2CH$–CO–CH_3		2 h		18	40–45/10	–	1701 (film)
			10	45	138–140/2.5	2.98 (s, 1 H)	1630 (film)

[a] OTf = OSO_2CF_3.

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Dehydrobenzene from Aromatic Diazonium Salts [1]

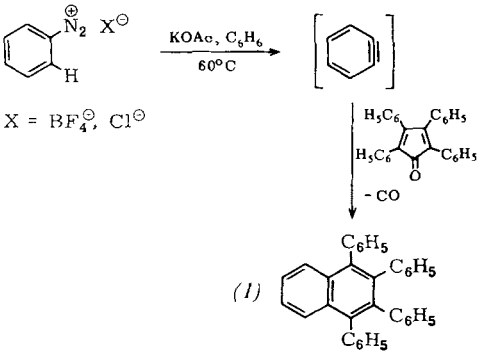
By *Christoph Rüchardt* and *C. C. Tan* [*]

Not long ago we showed that benzenediazonium *p*-chlorobenzoate, which is prepared by isomerization of *p*-chloro-*N*-nitrosobenzanilide in CCl_4, reacts with tetracyclone in CCl_4 at 70 °C to give tetraphenylnaphthalene *(1)* in 46% yield [2].

Compound *(1)* may be synthesized more readily and in better yields by portionwise addition of crystalline benzenediazonium tetrafluoroborate or chloride (10 mmoles) to a vigorously stirred mixture of tetracyclone (1.92 g, 5.0 mmoles), glacial acetic acid (0.1 g), and anhydrous potassium acetate in benzene at 60 °C. Evolution of nitrogen ceases within 2.5 h. After the product had been washed neutral and chromatographed on acidic Al_2O_3, 1.52 g (3.52 mmoles, 70%) or 1.60 g (3.70 mmoles, 74%) of tetraphenylnaphthalene *(1)* could be detected by gas chromatography. The compound was isolated in good yield by concentration and crystallization from dioxane/ethanol. The structure was confirmed by comparison of melting points [197 °C ([3]: 197 °C) and 202 °C ([4]: 204 °C)] and IR spectra, and by C, H analysis.

The analogous reactions of anthracene were found to give 9% and 41% (36% isolated) of triptycene [m.p. 249–251 °C ([3]: 254 °C)].

We interpret this synthesis in terms of formation of dehydrobenzene in an E_2 elimination which is initiated even by the weak base acetate ion owing to the favorable leaving group properties of N_2.



The success of the above reaction suggested that the synthesis of *(1)* (17–34%) and triptycene (1–3%) from *N*-nitrosoacetanilide described by *Cadogan et al.* proceeds not *via* an "arynoid intermediate", as was originally suspected, but rather *via* dehydrobenzene [5]. However, its precursor, benzenediazonium acetate, undergoes rapid, competitive decomposition by a chain reaction in the presence of *N*-nitrosoacetanilide [2b, 6]. If this decomposition is suppressed by slow, dropwise addition of an ice-cold benzene solution of *N*-nitrosoacetanilide (10 mmoles/30 ml or 15 ml, respectively) to a solution of tetracyclone (5 mmoles/30 ml)

or anthracene (5 mmoles 15 ml), to which solid potassium acetate has been added, at 60 °C over a period of 20 min, then 88% of *(1)* (96% found by gas chromatography) or 14–18% of triptycene (according to gas chromatography) may be isolated.

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[1] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

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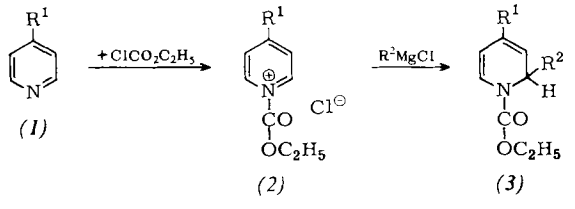
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One-Step Synthesis of 2-Substituted *N*-Ethoxycarbonyl-1,2-dihydropyridines[**]

By *Gideon Fraenkel, J. W. Cooper,* and *C. M. Fink*[*]

Pyridine derivatives react only slowly with Grignard compounds to give poor product yields[1]. The same applies to *N*-acylpyridinium salts[2].

We have now found that pyridine derivatives *(1)* react with ethyl chloroformate and Grignard compounds to give 2-alkyl-1-ethoxycarbonyl-1,2-dihydropyridines *(3)*, the reaction presumably proceeding *via* the pyridinium chloride *(2)*.



(1) *(2)* *(3)*

	R^1	R^2
(a)	CH_3	n-C_4H_9
(b)	$(CH_3)_3C$	$(CH_3)_3H$
(c)	CH_3	C_6H_5
(d)	C_2H_5	n-C_4H_9
(e)	H	n-C_4H_9

Treatment of *(3b)* with *n*-butyllithium in hexane gave a red solution which was found to contain 2,4-di-*tert*-butyl-1,2-dihydropyridyl-1-lithium by NMR spectroscopy[3]. It is converted into 2,4-di-*tert*-butylpyridine when the solution is heated. The low-temperature NMR spectrum of *(3b)* indicates the presence of two rotational isomers.

1-Ethoxycarbonyl-2,4-di-tert-butyl-1,2-dihydropyridine (3b):

To a mixture of 4-*tert*-butylpyridine (1.01 g, 7.5 mmoles) and 20 ml of a 0.75 M solution of *tert*-butylmagnesium chloride in tetrahydrofuran (15 mmoles) is added ethyl chloroformate (0.81 g, 7.5 mmoles) at 0 °C over a period of 10 min. The reaction mixture is hydrolyzed with 1 ml of water at 0 °C, filtered, and the white precipitate is washed with tetrahydrofuran. The washings are added to the filtrate which is then dried with $MgSO_4$ and vacuum distilled. UV: λ_{max} = 2921 Å; IR: $\tilde{\nu}$ = 3000, 1700, 1365, 1300–1275 cm^{-1}: NMR: τ = 5.43, 5.70, 4.70, 3.27, (H-2, H-3, H-5, and H-6, respectively), $J_{2,3}$ = 6.0, $J_{5,6}$ = 7.0 Hz, b.p. 110 °C/0.0014 torr, yield 55%.

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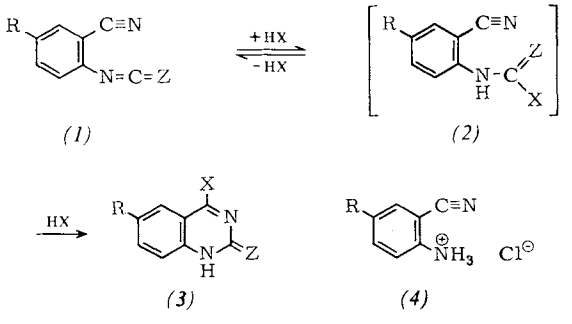
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A New Synthesis of the Quinazoline System

By *Gerhard Simchen, Günther Entenmann,* and *Rolf Zondler*[*]

We recently reported on the synthesis of aza and 1,3-thiaza heterocyclic compounds by cyclizing acylation of ω-cyano and ω-thiocyanato carbonyl halides[1]. We have now found that 1,3-diaza heterocyclic compounds are also accessible by this method. Reaction of *o*-cyanophenyl isocyanates *(1)*, Z = O, and *o*-cyanophenyl isothiocyanates *(1)*, Z = S, with hydrogen halide at room temperature in di-*n*-butyl ether initially affords carbamoyl and thiocarbamoyl halides *(2)*, Z = O and Z = S, resp.[2], which cyclize at about 70 °C in the presence of an excess of hydrogen halide to the hitherto undescribed 4-halogeno-2-quinazolones *(3a)–(3c)* and 4-halogeno-2-quinazolinethiones *(3d)*, respectively.



(1) *(2)* *(3)* *(4)*

	R	X	Z	M.p. (°C)	Yield (%)
(3a)	H	Cl	O	213	87
(3b)	H	Br	O	348–350	78
(3c)	Br	Cl	O	> 350	77
(3d)	H	Cl	S	295–296	70

Ring closure proceeds by nucleophilic attack of the intermediate nitrile-hydrogen halide adducts on the carbamoyl or thiocarbamoyl halide *(2)*. The 4-chloro-2-quinazolines *(3a)* to *(3c)* can also be synthesized without isolation of intermediates by successive passage of phosgene (*ca.* 1 h) and hydrogen chloride (*ca.* 7 h) through a suspension of 2-cyanoanilinium chloride *(4)* in di-*n*-butyl ether at 120 °C and at 80 °C respectively. Nucleophilic substitution of the halogen atoms attached to C-4 of *(3)* proceeds readily.

General procedure:

Compound *(1)*, Z = O or S, (0.01 mole) is suspended in di-*n*-butyl ether (50 ml). HCl or HBr is passed into the suspension at 80 °C for 7 hours. The resulting precipitate is

filtered off, dried at 100 °C in a vacuum for 3 hours, and recrystallized from bromo- or chlorobenzene.

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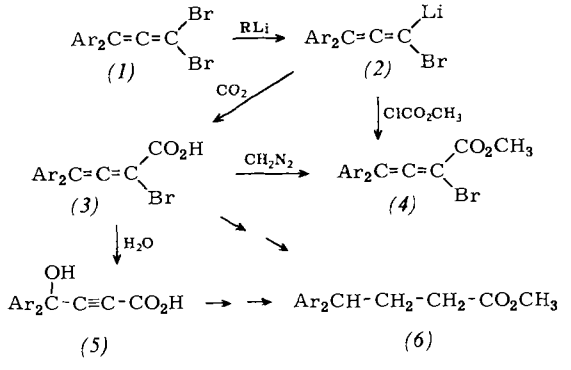
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New Allenes from 1-Bromo-3,3-diphenylallenyllithium [1]

By *Gert Köbrich* and *Ernst Wagner* [*]

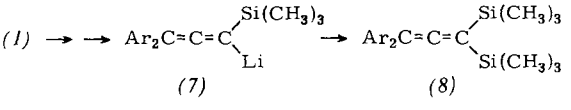
Except for carboxylation, the reactions of the deep violet trichloroallenyllithium — the first metalated haloallene to be prepared [1a] — are very complex. We have now prepared the structurally related and still more thermolabile reddish-black 1-bromo-3,3-diphenylallenyllithium *(2)*, which is found to react in a more comprehensible manner, by exothermal Br—Li exchange between equivalent amounts of 1,1-dibromo-3,3-diphenylallene *(1)* [2] and *n*-butyllithium in 2-methyltetrahydrofuran at —125 °C. *(1)* is characterized by its reaction with methyl chloroformate to give a good yield of the quite stable ester *(4)*, m.p. 125—126 °C, together with 15—25% of unchanged *(1)* [3].



Ar = C_6H_5; R = n-C_4H_9

Carboxylation of *(2)* gives the expected carboxylic acid *(3)*, m.p. 143—145 °C [with which diazomethane gives the ester *(4)*], but also surprisingly the hydroxypropiolic acid *(5)*, $\nu_{C\equiv C}$ = 2200 cm^{-1}. According to control experiments, *(5)* is probably formed during work-up from *(3)*, which thus must be very easily solvolyzed [4]. *(3)* and *(5)* were converted into a common product: 1 mole of *(3)* and 2 moles of butyllithium at —110 °C form a greenish-black organolithium compound [5,6], which is changed to the butyric acid derivative *(6)* [7] on protolysis, catalytic hydrogenation, and esterification with diazomethane. A comparison sample, dec. p. 79—81 °C, identical with *(5)*, was prepared from α-ethynyl benzhydrol by treatment with butyllithium (molar ratio 1 : 2) and subsequent carboxylation; it was converted by catalytic hydrogenation into 4,4-diphenylbutyrolactone [8] and thence by partial hydrogenolysis and esterification into *(6)*.

The disilane *(8)*, b.p. 124—127 °C/0.2 torr (dec.), is formed on treatment of 1 mol. equiv. of *(2)* with 2 mol. equiv. of butyllithium and then 2 mol. equiv. of (chloro)trimethylsilane; the α-metalated silane *(7)* must occur as intermediate.



Like the reaction of *(1)* with butyllithium in ether at +20 °C [2], thermolysis of *(2)* affords approx. 10% of tetraphenylhexapentaene alongside resins.

Methyl 2-bromo-4,4-diphenyl-2,3-butadienoate (4)

The dibromide *(1)* (1.75 g, 5.0 mmoles) in dry 2-methyltetrahydrofuran (60 ml) and light petroleum (10 ml; b.p. up to 40 °C) is treated at —125 °C with butyllithium (5.0 mmoles) for 40—50 min with strict exclusion of moisture. The mixture is stirred for a further 2 hours at the same temperature, and the resulting reddish-black *(2)* is treated dropwise with methyl chloroformate (4.0 g) in light petroleum (15 ml). The whole is kept for a further 3 hours at —105 °C, after which the cooling-bath is removed. The usual work-up gives a red oil (2.04 g), which, when mixed with small portions of ethanol (finally at —20 °C) leaves a total of 52% (0.85 g) of *(4)*, m.p. 125—126 °C (after recrystallization from ethanol).

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Distribution of the Bonding Electrons in Decaborane-14

By *Rudolf Brill, Hans Dietrich*, and *Hinrich Dierks* [*]

The structure of the compound decaborane-14, $B_{10}H_{14}$, is given in Fig. 1 [1]. It contains B—H bonds as well as B—B bonds and hydrogen bridges between two boron atoms. This

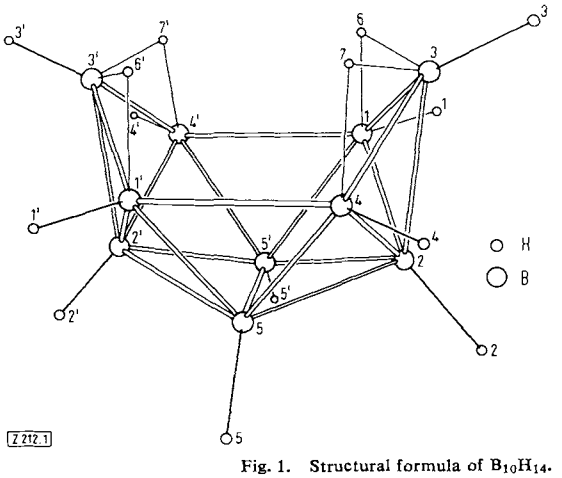


Fig. 1. Structural formula of $B_{10}H_{14}$.

compound, therefore, is especially suited for studies of the electron distribution corresponding to these bond types. In order to achieve the greatest possible accuracy it was necessary to determine the precise nuclear positions and vibrational parameters by means of neutron diffraction. For this purpose the compound consisting of the isotopes ^{11}B and ^{2}H had to be prepared[2]. To keep the thermal vibrations as small as possible the crystals were kept at −160 °C[3,4,5] during the measurement of the neutron- and X-ray diffraction.

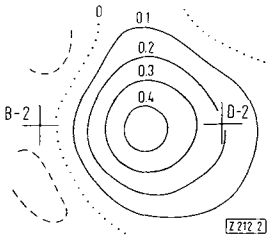


Fig. 2. Longitudinal section through a terminal B—H bond in the difference synthesis (contours at intervals of 0.1 e/A³).

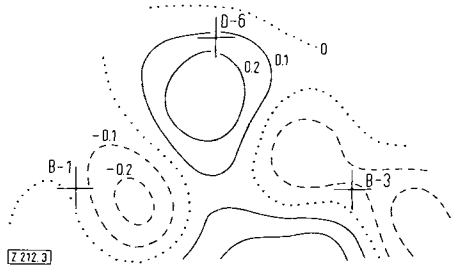


Fig. 3. Section through a three-center bond B—H—B in the difference synthesis (contours at intervals of 0.1 e/A³).

The first difference synthesis of the X-ray data was based on the parameters of the atomic positions as determined by neutron diffraction and also based on atomic scattering factors for neutral atoms[6] (first approximation). In the second approximation the atomic scattering factors were adapted to the charge transfer caused by the chemical bond between boron and hydrogen atoms[7]. In this way a further refinement of the distribution of the remaining bonding electrons was achieved.

The salient results are given in Figs. 2—4. Fig. 2 shows the strong local accumulations of bonding electrons in normal covalent terminal B—H bonds. Fig. 3 shows — also in the first approximation — a maximum of electron density close to the H-atom in the three-center bonds B—H—B. Unlike the minima of equal magnitude in Fig. 3, the maximum is supposed to be real because it appears at the same position in all of the B—H—B bridges of the asymmetric unit.

The distribution of electrons bonding the atoms of the B-skeleton is revealed in the second approximation only. These electrons are smeared over the planes formed by the B-atoms of the skeleton. Fig. 4 shows the cross-section at about the middle between the bottom and the rim of the basket-shaped molecule. The density of these bonding electrons is only of the same magnitude as in the background of a metal. It remains to be seen whether or not a relation exists between the arrangement of the B atoms in $B_{10}H_{14}$ and that in metallic boron. In both cases the atomic arrangement is icosahedral with the same atomic distances. Accumulations of the electrons of the skeleton appear outside the cross-section of Fig. 4, especially on the line B-2 to B-3 (closer to B-3 than to B-2) and, a little weaker, in the middle of the triangle B-2—B-5—B-5′. They are again found uniformly on all chemically equivalent locations of the asymmetric unit and correspond approximately to the electron distribution postulated by *Lipscomb*[8]. We find, however, slight evidence only for a "central" three-center bond in the triangle

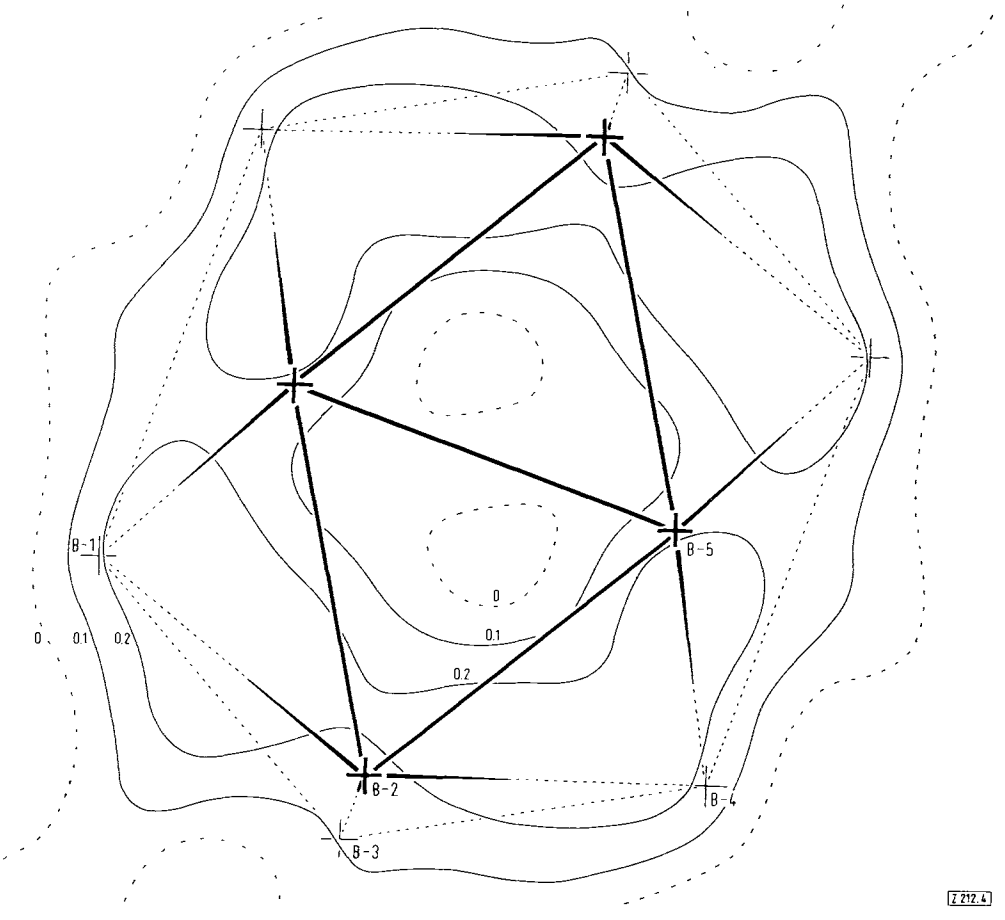


Fig. 4. Section through the boron skeleton of a molecule in the difference synthesis (contours at intervals of 0.1 e/A³).

B-1′—B-4—B-5 and its chemical equivalent in the asymmetric unit of the molecule. Likewise, the B—H—B bonds are not characteristic open three-center bonds. In such a case the bonding electrons are supposed to be concentrated on the lines connecting the atoms B—H—B. Fig. 3 clearly shows that this is not so.

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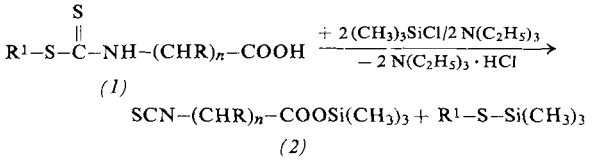
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Isothiocyanato Carboxylic Acids and 2-Thioxo-5-oxazolidones

By *Hans R. Kricheldorf*[*]

Isothiocyanato carboxylic acids *(3)* and 2-thioxo-5-oxazolidones *(4)* can be polymerized with loss of COS to give polyamides or peptides.

The hitherto unknown trimethylsilyl isothiocyanato carboxylates *(2)*, which proved accessible by silylation of *N*-dithiocarboxy amino acid derivatives *(1)*, appeared suitable as starting materials for the preparation of *(3)* and *(4)* (R^1 = $CO—OC_2H_5$[1], C_2H_5[2], $CH_2—C_6H_5$[3]; for R and *n*, see Table).



(1)

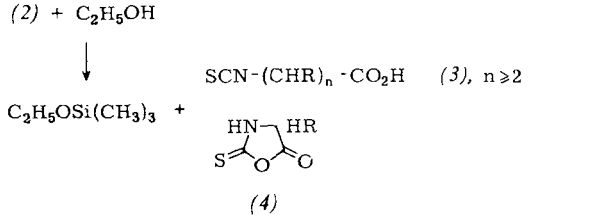
$$SCN-(CHR)_n-COOSi(CH_3)_3 + R^1-S-Si(CH_3)_3$$

(2)

	R	*n*	*(2)* b.p. (°C/torr)	*(3)* m.p. (°C)	*(4)* m.p. (°C)
a	H	1	67–70/1	–	
b	CH_3	1	52–55/10^{-2} [a]	–	
c	$CH_2CH(CH_3)_2$	1	75–78/10^{-3} [b]	–	70–72
d	$CH_2C_6H_5$	1	122–125/10^{-3} [b]	–	93–95
e	H	2	81–84/1	10–12	
f	H	3	70–73/10^{-2}	18–20	
g	H	5	95–98/10^{-3}	32–34	

[a] D,L form. [b] L form.

The carboxylic acids *(3)* can be liberated in 85–95% yield from the silyl esters *(2)* by treatment with ethanol at 0 °C.



(4)

The α-compounds *(2a)* to *(2d)* gave only the 2-thioxo-5-oxazolidones *(4)*. These compounds have a low thermal stability; for example, *(4a)* and *(4b)* decompose within a few hours at room temperature, and, although slower, also at temperatures as low as about −20 °C. Those bearing larger substituents, *e.g.*, *(4c)* and *(4d)*, exhibit a definite melting point and can be kept at −20 °C for several weeks. Decomposition involves loss of COS to give peptides; a concurrent isomerization gives the more stable thiazolidin-2,5-diones, but in far smaller yield.

β-Isothiocyanatopropionic acid *(3e)* also polymerizes in the course of a week at +25 °C to give oligo-β-alanine. In contrast, γ-isothiocyanatobutyric acid *(3f)* and ε-isothiocyanatohexanoic acid *(3g)* (which has already been prepared by another method[4]) are stable at room temperature. The compounds polymerize readily only above about 150 °C or, in the presence of triethylamine (not pyridine!), above 50 °C. Copolymers can be isolated from mixtures of monomers[5].

All the new compounds listed were characterized by C, H, N elemental analysis and IR spectra, and some of them by NMR spectra.

Isocyanato carboxylic acids (3) and 2-thioxo-5-oxazolidones(4)

Triethylamine (2.1 moles) is added dropwise to a warm mixture of *(1)* (1 mole), having R^1 = $CO—OC_2H_5$, C_2H_5, or $CH_2—C_6H_5$, and trimethylchlorosilane (2 moles) in dry toluene (*ca.* 1.5 l) and the reaction mixture is heated to boiling for 2 h. Precipitated triethylammonium chloride is filtered off and the esters *(2)* are isolated in 70–90% yield by fractional distillation.

A solution of *(2)* (0.1 mole) in light petroleum (100–150 ml) is treated at 0 °C with dry ethanol (0.1 mole) and a catalytic amount of dry hydrogen halide, and the solution is stirred at 0 °C until the product [*(3)* or *(4)*] has precipitated (5–30 min). The 2-thioxo-5-oxazolidones *(4)* must be filtered off, dried in a high vacuum, and used immediately. At 20 °C compound *(4b)* yields a solid foam of poly-D,L-alanine within about 20 min of isolation.

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[5] The β-, γ-, and ε-isothiocyanato carboxylic acids and their silyl esters have an extremely powerful urticating action and give rise to painful blisters and wounds, even in high dilution.

Cycloadditions of Vinylcarbenes

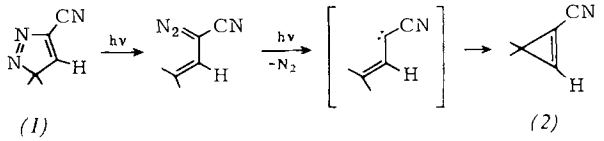
By *Michel Franck-Neumann* and *Christiane Buchecker*[*]

Carbenes that can undergo intramolecular stabilization generally react very reluctantly with other molecules[1]. This appears to be the case, for example, with vinylcarbenes which can give cyclopropenes by intramolecular addition[2,3] and which, to our knowledge, exhibit no intermolecular additions providing proof of carbenoid structure[4].

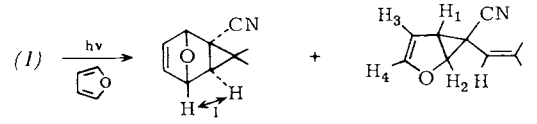
We have now been able to intercept the vinylcarbenes supposed to give rise to cyclopropenes *via* diazoalkenes[3] on photolysis of 5-cyano-3*H*-pyrazoles[5]. This was accomplished by intermolecular cycloaddition to alkenes, alkynes, and dienes to give vinylcyclopropanes, vinylcyclopropenes, and divinylcyclopropanes, respectively.

Two special cases will serve as illustrations: (i) Stereospecific addition to furan and (ii) addition to benzene, which gives a new stable norcaradiene derivative.

If irradiation of 5-cyano-3*H*-pyrazole *(1)*, which gives only the highly unstable 3,3-dimethyl-1-cyanocyclopropene *(2)* [ν (C=C) = 1720 cm^{-1}] when performed in ethereal solution, is carried out in furan, the resulting Diels-Alder adduct *(3)* of cyclopropene (m.p. 52 °C, $J < 0.4$ Hz) is accompanied solely by the 1,2-divinylcyclopropane derivative *(4)* (*cis* or *trans*).



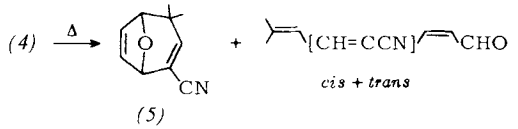
(1) *(2)*



(3) 1:2.5 *(4)*

6-Cyano-6-(2-methyl-1-propenyl)-2-oxabicyclo[3.1.0]hex-3-ene *(4)*, ν (C=C) (vinyl ether) = 1685 cm^{-1}; δ = 1.67 ppm (3 H/d), J = 1.4 Hz; 1.78 (3 H/d), J = 1.2 Hz; 4.54 (1 vinyl H/heptuplet); 3.04 (H^1/dd), J = 2.8 and 5.5 Hz; 4.94 (H^2/d), J = 5.5 Hz; 5.16 (H^3/t), J = 2.8 Hz; 6.24 (H^4/d), J = 2.8 Hz[6].

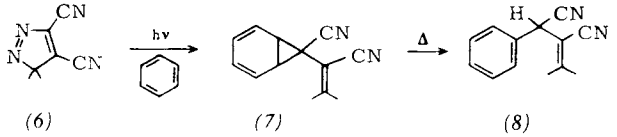
(4) is sufficiently stable to be isolated in pure form (yield 42%), although it gradually rearranges at room temperature to three new substances (halflife 65 min at 50 °C and 23 min at 60 °C). Divinylcyclopropane rearrangement[7] gives 2-cyano-4,4-dimethyl-8-oxabicyclo[3.2.1]octa-2,6-diene *(5)*, δ = 0.88 (3 H); 1.28 (3 H); 4.52 (1 bridgehead H/t), J = 2 Hz; 4.68 (1 bridgehead H/m); 5.95—6.70 (3 vinyl H/m), and furanocyclopropane rearrangement[8] affords a *cis-trans* mixture (1 : 3.4) of two trienealdehydes, ν (C=O) = 1680 cm^{-1}; ν (C=C) = 1600 and 1640 cm^{-1}; λ_{max} (CH_3OH) = 330 nm (ε = 8050); δ (*o*-dichlorobenzene) = 9.60 ppm (aldehyde H/d), J = 7.4 Hz; 10.10 (aldehyde H/d), J = 6.4 Hz.



(5) *cis + trans*

The ready divinylcyclopropane rearrangement cannot be regarded as proof of the *cis* structure of *(4)* in this case (cyano substituent, concomitant isomerization).

Photolysis of 4,5-dicyano-3H-pyrazole *(6)* gives a much more reactive vinylcarbene which even undergoes a C—H insertion reaction with ether. Unlike the carbenes generated from *(1)*, it reacts with benzene to give both the cyclopropene [δ (CH_3) = 1.53], which was not isolated, and the stable norcaradiene derivative *(7)* (one isomer, pure yield 45%), which isomerizes mainly to *(8)* only at elevated temperatures (halflife at 160 °C about 60 min).



(6) *(7)* *(8)*

7-Cyano-7-(1-cyano-2-methyl-1-propenyl)norcaradiene *(7)*, colorless crystals, m.p. 91 °C (from dimethoxyethane), spectroscopic properties similar to those of 7,7-dicyanonorcaradiene[9]: ν (C=C) = 1630 cm^{-1}; λ_{max} (CH_3OH) = 265 nm (ε = 3320); δ = 2.07 ppm (3 H); 2.12 (3 H), 2.93 (2 cyclopropane H/m); 6.20 (4 vinyl H/m).

1,2-Dicyano-3-methyl-1-phenyl-2-butene *(8)*, δ = 2.03 ppm (3 H), 2.15 (3 H); 4.95 (1 allyl H), 7.36 (5 arom. H).

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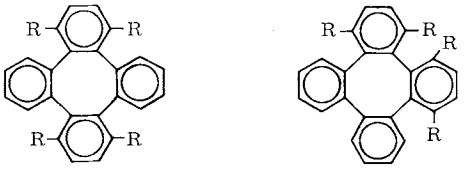
Cyclooctatetraene Systems Flattened by Steric Constraints[**]

By *Dieter Hellwinkel* and *Günther Reiff*[*]

Cyclooctatetraene[1] is a tub-shaped molecule which can assume a planar conformation with predominantly localized double bonds (symmetry D_{4h}) only in a relatively energy-rich transition state (12—15 kcal/mole) during a ring inversion[2]. Flattening of the cyclooctatetraene ring can also be achieved by alteration of the π-electron skeleton (*i.e.* by addition of two electrons[2] and formation of transition metal complexes[3]) the dianion then being structure determining. The same is true for the symmetrical dibenzocyclooctene[4].

The ESR data of the radical anions of the cyclooctatetraene derivatives mentioned above and of the tub-shaped tetrabenzocyclooctene (*o*-tetraphenylene), on the other hand, do not afford definite information about the structure[4,5].

In order to force tetraphenylene, and hence the inherent cyclooctatetraene skeleton, to assume a planar conformation by purely steric means we used as starting materials the tetra-



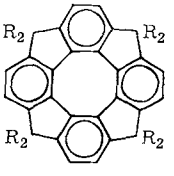
(1) *(2)*

(a), R = CH_3; *(b)*, R = COOH; *(c)*, R = $COOCH_3$

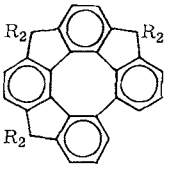
methyltetraphenylenes *(1a)* (m.p. 274 °C) and *(2a)* (m.p. 208 °C), which are accessible in very low yield *via* a multistep synthesis[6]. Oxidation of *(1a)* and *(2a)* with $KMnO_4$ gives the tetracarboxylic acids *(1b)* (dec. pt. 450 °C) and *(2b)* (dec. pt. 380 °C), which react smoothly with diazomethane to give the esters *(1c)* (m.p. 260 °C) and *(2c)* (m.p. 240 °C) respectively.

Treatment of *(1c)* and *(2c)* with polyphosphoric acid (*ca.* 240 °C) yields the orange cyclic ketones *(3)* (subl. > 500 °C, νC=O = 1720 cm^{-1}) and *(4)* (subl. ≈ 380 °C, νC=O = 1720 cm^{-1}) whose monomeric structures have been established by mass spectrometry[7]. Interestingly, in the IR spectrum of *(3)* the characteristic strong γCH bands for 1,4-di- and 1,2,3,4-tetrasubstituted benzene derivatives are shifted to 740 cm^{-1}. The IR spectrum of *(4)* contains a very intense multiply-split band in this region having a maximum at 739 cm^{-1}.

Reduction of the ketones *(3)* and *(4)* with hydrazine hydrate/sodium diethylene glycolate[8] affords 1,16;4,5;8,9;12,13-tetramethano-*o*-tetraphenylene *(5)* (subl. 380 °C) and 4,5;8,9;12,13-trimethano-*o*-tetraphenylene *(6)* (m.p. 240 °C) in good yields; the molecular weights of *(5)* and *(6)* have been determined by mass spectrometry[7]. The IR spectrum of *(5)* exhibits very few lines and shows an unusually large shift of the intense γCH bands (775 cm^{-1}) towards longer wavelengths.



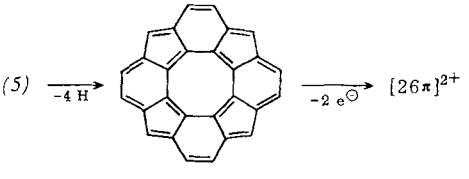
(3), R_2 = O
(5), R_2 = 2 H



(4), R_2 = O
(6), R_2 = 2 H

The UV spectra of *(5)* and *(6)* ($HCCl_3$) resemble very closely those of fluorene and indeno[2,1-*c*]fluorene, yet all maxima, and in particular the two at the longest wavelength, show increased intensity and considerable bathochromic shifts as a result of the greatly extended conjugated system. [*(5)* λ_{max} (log ε): 262 (4.63); 275 (4.67); 285 (4.70); 343 (4.24); 358 (4.50); (6): 275 (4.84); 285 (4.80); 335 (4.25); 348 (4.32).]

The mass spectrum of *(5)* affords an indication of the stability of the potential dehydrogenation products of *(5)*, *i.e.* of the tetramethinotetraphenylene *(7)*[7]. [M^+ = 352, 100%; $(M-1)^+$, 35%; $(M-2)^+$ 25%; $(M-3)^+$, 27%; $(M-4)^+$ = $(7)^+$, 25%; M^{2+}, 36%; $(M-1)^{2+}$, 27%; $(M-2)^{2+}$, 51%; $(M-3)^{2+}$, 48%.] A relative intensity of 100% is observed for $(M-4)^{2+}$ = $(7)^{2+}$; this is four times greater than the intensity of the accompanying singly charged fragment ion $(M-4)^+$!



(7), 28π

This behavior seems to indicate the tendency of the non-Hückel 28π electron system *(7)* to be transferred, following the loss of two electrons, into a 26π electron system obeying the Hückel rule[9].

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[**] This work was supported by the Deutsche Forschungsgemeinschaft.

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[7] We are indebted to Farbenfabriken Bayer AG, Leverkusen, for the recording of the mass spectra.

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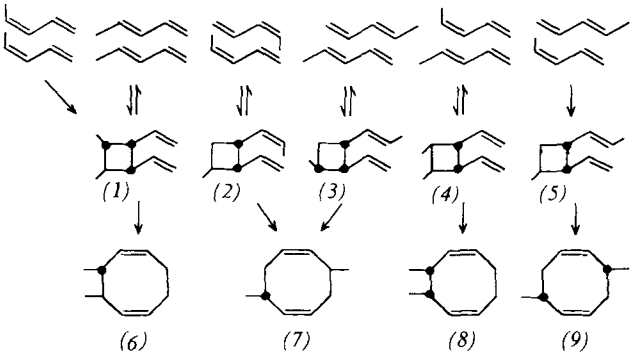
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Stereochemistry of the Catalyzed Cyclodimerization of Piperylene

By *Paul Heimbach* and *Hansjörg Hey*[*]

The cyclodimerization of butadiene in presence of nickel-ligand catalysts affords *cis*-1,2-divinylcyclobutane in yields of up to 40% together with *cis,cis*-cycloocta-1,5-diene if the reaction is carried out to 85% conversion of butadiene[1,2]. We have now investigated the stereochemical course of this catalyzed synthesis of four- and eight-membered rings, using as example the cyclodimerization of the piperylenes (1,3-pentadienes)[3].

In addition to the eight-membered rings *(6)*—*(9)*, five of the ten possible isomeric dimethyl derivatives of *cis*-1,2-divinylcyclobutane are formed stereospecifically in yields of 16—92%.



Two molecules of *trans*-piperylene give the four-membered rings *(1)* and *(3)*, whereas two molecules of *cis*-piperylene give the four-membered rings *(1)* and *(2)*, and one molecule each of *cis*- and *trans*-piperylene afford the four-membered rings *(4)* and *(5)*.

The yields are dependent on the type of ligand (phosphines or phosphites) in the nickel catalyst, on the composition of the piperylene, and on the conversion of the 1,3-diene.

The structures and the configurations of the isolated four-membered ring derivatives were determined by IR- and ^{1}H-NMR spectroscopy; they are in agreement with the behavior of the compounds *(1)*—*(5)* in the thermal Cope rearrangement[4].

In the course of these investigations a *thermodynamic equilibrium between 1,3-dienes and cis-1,2-divinylcyclobutanes* was observed for the first time.

Thus, *e.g.* the shape of the concentration-time curve for the four-membered ring *(1)* (see Fig. 1) obtained on reaction of *trans*-piperylene in presence of nickel-tricyclohexylphosphine catalyst can only be explained by an equilibrium between the 1,3-diene and the corresponding *cis*-1,2-divinylcyclobutane.

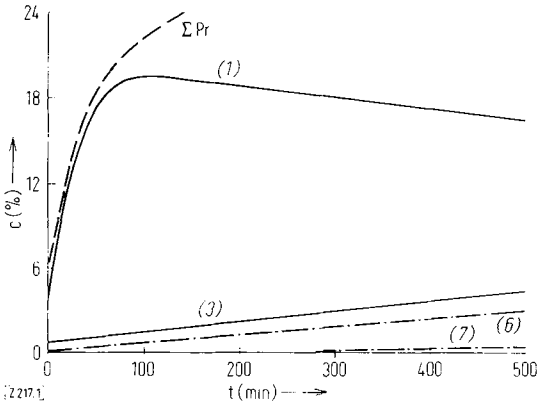
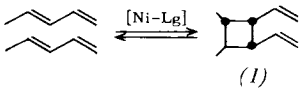


Fig. 1. Concentration-time curves for the four- and eight-membered rings obtained from *trans*-piperylene in presence of nickel-tricyclohexylphosphine catalyst. Temperature. 30 °C; Ni:diene = 1 : 48. ———: four-membered rings, — · · —: eight-membered rings.



(1)

$$K = \frac{[\text{four-membered ring } (1)]}{[\textit{trans}\text{-piperylene}]^2}$$

The equilibrium constant K has a value of $(2.3 \pm 0.3) \times 10^{-2}$ l/mole at 30 °C irrespective of the type of ligand in the nickel catalyst. At lower temperatures the equilibrium shifts in favor of the four-membered ring *(1)*.

The catalysts give rise not only to addition but also to an *isomerization of cis- to trans-piperylene via the four-membered ring (1)*. This novel type of isomerization is apparent in particular from the kinetics of the cyclodimerization of pure *cis*-piperylene.

Reaction of two molecules of *cis*-piperylene in presence of nickel-tricyclohexylphosphine catalyst leads, in the first instance, to slow formation of the four-membered ring *(1)*. Reaction of one molecule each of *cis*- and *trans*-piperylene proceeds about three times as fast, but with a distinct incubation period, to give the four-membered ring *(4)*. The *trans*-piperylene necessary for the formation of *(4)* is available only after cleavage of *(1)*.

The catalyzed retrocleavage of the pure four-membered rings *(2)—(4)* also proceeds stereospecifically. The above mentioned stereospecific formation of the four-membered rings is therefore confirmed. Unambiguous results are obtained, however, only if the 1,3-diene formed is immediately withdrawn from the reaction mixture at 30 torr. In addition, the corresponding eight-membered rings *(6)—(8)* are formed stereospecifically by a catalyzed Cope rearrangement [5].

Mango suggests that the *cis*-1,2-divinylcyclobutane is formed in a suprafacial concerted process [6]. The stereospecificity found for formation of the four-membered rings from piperylene is not in agreement with this hypothesis.

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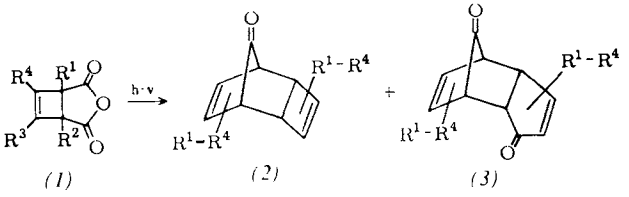
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Alkyl-Substituted Cyclobutadienes[1][**]

By *Günther Maier, Giselher Fritschi*, and *Bernd Hoppe*[*]

The photofragmentation of cyclobutenedicarboxylic anhydrides at room temperature leads to products whose formation can readily be interpreted in terms of the intermediacy of cyclopentadienones and cyclobutadienes [1b, 1c].

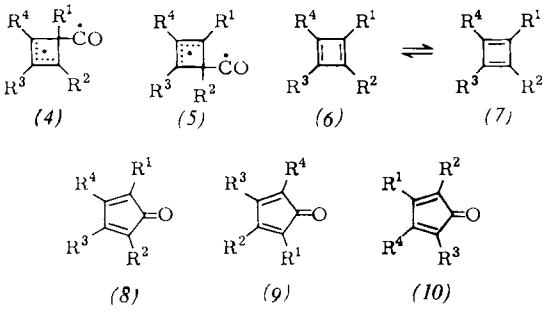
When the anhydrides *(1a)—(1c)* are irradiated in a tetrahydrofuran matrix at —196 °C a deep yellow color appears; this disappears immediately when the matrix melts, or, more



	(a)	(b)	(c)	(d)
R^1	CH_3	H	H	H
R^2	CH_3	CH_3	H	H
R^3	CH_3	CH_3	CH_3	$C(CH_3)_3$
R^4	CH_3	CH_3	CH_3	$C(CH_3)_3$

exactly, at a temperature when the organic glass just becomes mobile. The cyclobutadiene-cyclopentadienone adducts *(2)* and the dimers *(3)* of the cyclopentadienones are the sole products that can be isolated from the low-temperature photolysis.

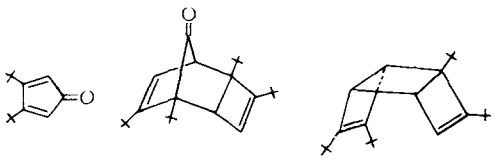
This is not only true for the anhydrides *(1a)* and *(1c)* [1a] but also for the trimethyl derivative *(1b)*. The distribution of the methyl groups in the products suggests that, in the irradiation of the anhydrides, CO_2 is first eliminated and the diradical fragments *(4)* and *(5)* formed subsequently lose CO to give



the cyclobutadienes *(6)* and *(7)* — in the case of singlet cyclobutadienes, two valence isomers come into consideration — or cyclize to give the isomeric bicyclo[2.1.0]pentenones, which can isomerize *via* ring opening to the cyclopentadienones *(8)*, *(9)*, and *(10)*. The fact that the isolated adducts *(2)* and *(3)* are formed by a Diels-Alder type reaction and have an *endo* configuration suggests that the cyclobutadienes and cyclopentadienones have singlet character and are stable as monomers when frozen into a matrix at —196 °C.

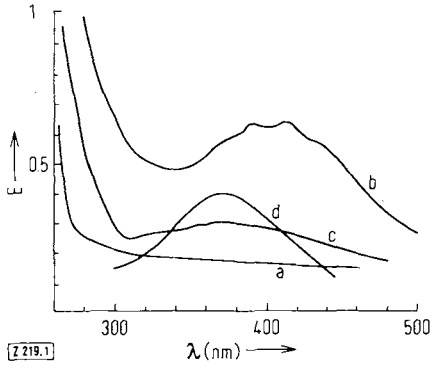
Supporting evidence for this concept can be gained from spectroscopic investigations: In the IR spectra recorded during the low-temperature irradiation, the anhydride bands disappear and a carbonyl stretching vibration characteristic for cyclopentadienones appears at 1700—1710 cm^{-1}. This is an indication that the yellow glasses probably do not contain any compounds having a carbonyl group other than starting anhydrides and cyclopentadienones.

In the case of the anhydride *(1d)* [2], it is of particular importance for the spectroscopic detection of the cyclobutadienes that the 3,4-di-*tert*-butylcyclopentadienone *(8d)* [m.p. 47.5—48.5 °C; IR(CCl_4): 1708 cm^{-1}; UV(ether):



(8d) (11) (12)

λ_{max} = 365 nm, ε = 80; NMR(CCl_4): τ = 4.65 (2 H/S); 8.64 (18 H/S)] can be isolated. It is therefore possible to compare the UV spectrum of the dienone *(8d)* with the total absorption of the primary products occurring in the photofragmentation of the anhydride. The Figure shows quite clearly that the



Low-temperature irradiation of 3,4-di-*tert*-butylcyclobutenedicarboxylic anhydride (1d) in 2-methyltetrahydrofuran (3.7×10^{-2} mole/l); a) before irradiation: b) irradiated two hours (low-pressure Hg lamp, Vycor); c) after warming to room temperature; d) isolated 3,4-di-*tert*-butylcyclopentadienone *(8d)*.

yellow color observed in the low-temperature irradiation of *(1d)* not only stems from *(8d)* — and consequently not from *(9d)* — but must originate predominantly from another species having a structured absorption band in the visible region (maximum at 410 nm). In the case of the anhydrides *(1a)*—*(1c)*, spectra of the same type are found under analogous conditions; only the position of the maxima is bathochromically shifted with increasing number of methyl groups.

We ascribe these absorptions to the cyclobutadienes and believe that this is the first successful direct spectroscopic detection of simple substituted cyclobutadienes.

The low-temperature photolysis of *(1d)* affords *(8d)* and two further products: the monoketone *(11)* [m.p. 140 °C; IR(CCl_4): 1765 cm^{-1}; NMR(CCl_4): τ = 3.53 (1 H/D) (J = 4.5 Hz); 4.45 (1 H/S); 7.15 (1 H/S); 7.27 (1 H/D) (J = 4.5 Hz); 8.67 (18 H/S); 8.94 (9 H/S); 8.97 (9 H/S)] and the hydrocarbon *(12)* [NMR(CCl_4): τ = 4.18 (1 H/S); 7.0—7.7 (3 H, ABX system); 8.85 (18 H/S); 8.90 (9 H/S); 9.01 (9 H/S)]. Apparently the 3,4-di-*tert*-butylcyclopentadienone *(8d)* does not dimerize, even at room temperature, because of steric hindrance in the transition state of the Diels-Alder reaction. It does not even add di-*tert*-butylcyclobutadiene; only 2,3-di-*tert*-butylcyclopentadienone *(9d)* can react with the 1,2-di-*tert*-butylcyclobutadiene. The unconsumed cyclobutadiene dimerizes to the tricyclic compound *(12)*. The formation of *(11)* and *(12)* indicates that the equilibrium *(6d)* $\rightleftharpoons$ *(7d)* lies on the side of the valence isomer *(7d)*, in which the bulky groups are further removed from one another.

In the series of methyl-substituted anhydrides, the C=O band belonging to the cyclopentadienones is rapidly lost on thawing out, and the signals expected for the adducts *(2)* and *(3)* are formed. Similarly, the UV absorption in the region > 350 nm disappears as soon as the matrix begins to melt. On the other hand, in the case of the anhydride *(1d)* a residual yellow color remains even on warming because of the dienone that is still present; the maximum at 410 nm, however, vanishes completely. At the same time, the carbonyl absorption in the IR spectrum decreases only slightly and a weak band, which can be ascribed to the adduct *(11)*, appears at 1765 cm^{-1}.

In the ESR spectrum[3] — irradiation of the anhydride *(1a)* and recording of the spectrum were carried out at the temperature of liquid nitrogen — there are no signals to be seen other than a septet, which can be ascribed to the radical[4] occurring by cleavage of hydrogen from 2-methyltetrahydrofuran. It is almost certain, therefore, that neither triplet molecules nor any other sufficiently long-lived diradical intermediates are present in the yellow matrix.

The chemical and spectroscopic[5] findings can, in our opinion, be interpreted as follows: alkyl-substituted cyclobutadienes are highly reactive substances which are detectable only under extreme conditions *e.g.* when frozen into a matrix at the temperature of liquid nitrogen. They have a singlet ground state for which theory demands a rectangular geometry and alternating single and double bonds. They are to all appearances[6] yellow owing to a characteristic absorption between 400 and 430 nm.

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] Small Rings, Part 8. — Part 7: a) *G. Maier* and *U. Mende*, Tetrahedron Letters *1969*, 3155; b) see also: Angew. Chem. *81*, 114 (1969); Angew. Chem. internat. Edit. *8*, 132 (1969); c) Angew. Chem. *80*, 532 (1968); Angew. Chem. internat. Edit. *7*, 537 (1968).

[2] *R. E. K. Winter*, St. Louis, Missouri (USA), first prepared this anhydride and found that *o*-di-*tert*-butylbenzene is formed when it is irradiated at room temperature (private communication).

[3] We are indebted to Dr. *K. Eiben*, Karlsruhe, for the recording of the spectrum.

[4] *F. S. Dainton* and *G. A. Salmon*, Proc. Roy. Soc. (London) Ser. *A 285*, 319 (1965).

[5] *N. L. Allinger*, *C. Gilardeau*, and *L. W. Chow*, Tetrahedron *24*, 2401 (1968), have calculated the UV spectra of triplet- and singlet-cyclobutadiene. The latter cannot give rise to an absorption in the region 200—400 nm; however, two forbidden transitions ought to be observed at 439 and 487 nm. The maxima > 400 nm observed by us, as well as the relatively small extinction coefficients (crudely estimated as a few hundred at most), are in agreement with these calculations.

[6] The longwave absorption could possibly be due to a charge-transfer complex between a cyclopentadienone and a cyclobutadiene molecule. An orientation of the anhydride molecule would then have to take place in the matrix before the irradiation. Furthermore, if this were the case it would be difficult to explain why the two closely neighboring, highly reactive partners are not converted into the adducts *(2)* before the thawing-out.

Macromolecular Colloquium

The Macromolecular Colloquium was held at Freiburg/Br. (Germany), February 26–28, 1970.

From the lectures:

Preparation of Monodisperse Polyethylene Oxides by Gel-Chromatographic Separation of Discontinuous Polymer-Homologous Series

By *Bruno Bömer* (lecturer), *Walter Heitz*, and *Werner Kern*[*]

We have been able to prepare monodisperse polyethylene oxides HO–[CH_2–CH_2–O–]$_n$–H having molecular weights of up to 2000, corresponding to degrees of polymerization $n \leq 45$, by the triplication process on a preparative scale.

In this process, both condensation components are derived from the same oligomer, so that the condensation gives a mixture of the members of a discontinuous polymer-homologous series.

The polyethylene oxides are synthesized from di-*p*-toluenesulfonates and sodium alkoxides of the same diols at room temperature, *e.g.*

$$\begin{aligned} &HO\text{–}[\text{–}CH_2\text{–}CH_2\text{–}O\text{–}]_3\text{–}Na + \\ &TsO\text{–}[\text{–}CH_2\text{–}CH_2\text{–}O\text{–}]_3Ts + NaO\text{–}[\text{–}CH_2\text{–}CH_2\text{–}O\text{–}]_3\text{–}H \\ &\qquad\downarrow \\ &HO\text{–}[\text{–}CH_2\text{–}CH_2\text{–}O\text{–}]_{3n}\text{–}H \\ &n = 2, 3, 4, 5, \ldots \end{aligned}$$

The purity of the triethylene glycol was verified by gas chromatography of the bis(trimethylsilyl) ethers. The gel-chromatographically uniform compounds nonaethylene glycol ($n = 9$, molecular weight = 414) and pentadecaethylene glycol ($n = 15$, molecular weight = 678) were obtained from the reaction mixture of the first triplication step by molecular distillation.

The nonaethylene glycol was used as the starting material for the second triplication stage. The resulting polymer homologs of nonaethylene glycol were separated by preparative gel chromatography on a polystyrene gel crosslinked with 2% of divinylbenzene, the pure monodisperse hepteikosaethylene glycol ($n = 27$, molecular weight = 1207) and pentatetrakontaethylene glycol ($n = 45$, molecular weight = 2000) being obtained on the preparative scale. Samples of up to 5 g in 50 ml of THF could be separated on a 200 × 5 cm column.

In the separation of industrial polyethylene oxides prepared by polymerization, it was found that the resolving power of the separation arrangement used extended up to $n \approx 27$.

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Physical Structure of Secondary-Valence Crosslinking in Urethane Elastomers

By *R. Bonart*[*]

Elastomers crosslinked by secondary valences are generally block copolymers of "hard" and "soft" segments, which must be substantially insoluble in each other. Owing to the weakness of secondary-valence interactions technologically satisfactory crosslinking is obtainable only if a large number of interactions contribute simultaneously and cooperatively to each crosslink, *i.e.* if the "crosslinks" are formed by crosslinking regions that are spread out in space. Elastomers crosslinked by secondary valences are therefore always two-phase systems of hard and soft segment regions. The soft segments are in the molten state at the service temperature and make the material extensible, whereas the hard segments are vitreous, crystalline, or paracrystalline, and in addition to effecting the crosslinking, they also have a certain filler character. This should be remembered in particular in the discussion of stress softening, which is often wrongly attributed to a fundamental weakness of secondary-valence crosslinking, whereas it is really due to the filler action of the hard segments. Attempts to optimize the technological properties of elastomers crosslinked by secondary valences by additional principal-valence crosslinking have therefore often been unsuccessful.

In the urethane elastomers, polyethers or polyesters having an average chain length of about 150–200 Å are generally used as the soft segments. The hard segments, on the other hand, generally result from the reaction of diisocyanates with diamines or diols as chain extenders. They contain urethane or urea groupings, and are therefore capable of forming hydrogen bonds. Information about the phase separation of the hard and soft segments is obtained by X-ray small angle scattering, while the mutual arrangement of the hard segments in space within the crosslinking regions is shown by special wide angle reflections. According to these reflections, the segregated hard segments are generally not crystalline in the conventional sense, but form paracrystals in Hosemann's sense, the statistical structural principle (referred to by *Hosemann* as the coordination statistic) of which depends on the chain extender, *i.e.* on the steric conditions for the formation of hydrogen bonds between adjacent hard segments. Even with a constant concentration of urethane or urea groupings, the conditions for the formation of hydrogen bonds are sometimes favorable and sometimes less favorable, depending on the steric structure of the chain extender. This leads to differences in the stability of the crosslinking regions and to differences in the solubility or phase separation of the hard and soft segments, and hence to differences in the number of crosslinking regions despite the constant ratio of the components. Both factors affect the mechanical behavior and the softening by heat.

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Oligomer Formation in the Thermal Polymerization of Styrene

By *K. Kirchner* and *K. Buchholz* (lecturer)[*]

In the thermal polymerization of styrene, small quantities of oligomers are formed as undesirable by-products[1,2]. 0.023% of dimer and 0.082% of trimer are formed in pure styrene at 137 °C and 10% total conversion. These oligomers consist mainly of cyclic compounds with no olefinic double bonds. Kinetic measurements showed that there are essentially two independent reactions taking place. Firstly, a cycloaddition with the Flory diradical as an intermediate leads to *cis*- and *trans*-1,2-diphenylcyclobutane, and secondly, two styrene molecules from the unstable Diels-Alder adduct formulated by *Mayo*, which can enter into three secondary reactions: 1. Addition of a further molecule of styrene leads

to trimers. This reaction predominates at high monomer concentrations. 2. By migration of a H atom, the adduct is stabilized as 1-phenyltetralin. 3. A H atom is transferred to a third styrene molecule so that two monoradicals are formed. This reaction occurs to a relatively small extent [5].

The results of the kinetic measurements on oligomer formation agree with the investigations on the thermal polymerization [3]. *Brown*'s arguments [4] are discussed.

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Light Scattering by Branched Systems

By *Walter Burchard* (lecturer), *Kanji Kajiwara*, and *Beate Pfannemüller* [*]

The interpretation of solution properties of branched macromolecules meets with difficulties for two reasons. Because of the formation conditions, products are formed having

a) extremely broad molecular weight distributions (M_n/M_w about 200–1000) and

b) a large number of isomers.

Owing to these difficulties, investigations have recently been carried out on the chemistry and theory of uniform macromolecules having specific branching, *i.e.* star and comb polymers. According to *Good* [1] and *Gordon* [2], however, the properties of randomly branched chains can also be calculated by means of "generating functions". These functions themselves generate the required broad molecular weight distributions with the corresponding isomer distributions. To set up the functions, one need only know the probabilities with which the reactive groups of a polyfunctional fundamental unit may have reacted. In this way, *Gordon* was able to calculate various average values of the molecular weight and of the mean square radius of gyration.

After generalization of the generating functions, it was possible to derive an expression that allows the calculation of the scattering functions for light and small-angle X-ray scattering in addition to the average values already known; the rigidity of the chains can be taken into account in this calculation [3].

Four examples were discussed:

1. Polyfunctional homopolycondensations.

2. Cocondensation of trifunctional with bifunctional monomer units of the types A—$\langle^{A}_{A}$ and A—A (Stockmayer model).

3. Condensation of trifunctional monomer units of the type A—$\langle^{B}_{C}$, where A can react with B and C, but B cannot react with C and like groups cannot react with one another (French-Erlander model).

4. Condensation of A—$\langle^{B}_{C}$ with A—B, where A can again react with B and C, while all other combinations are impossible.

Examples 1 and 2 give straight lines in the Zimm plot and indicate the same angle dependence as for linear chains. Type 3, however, gives plots with a strong upward curvature, while type 4 can exhibit all intermediate forms between the Stockmayer and French-Erlander models, depending on the reaction conditions.

Models 2 to 4 are applied to light scattering measurements on amylopectin tricarbanilate. The results are best described by model 4.

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[2] *M. Gordon*, Proc. Roy. Soc. (London) Ser. *A 268*, 240 (1962).

[3] *K. Kajiwara*, *W. Burchard*, and *M. Gordon*, British Polymer J. *2*, 110 (1970).

Segment Mobility in Polyethylene Terephthalate According to NMR Measurements

By *Uwe Eichhoff* (lecturer) and *Hans Gerhard Zachmann* [*]

The thawing of segment mobility can be seen in the NMR spectrum of semicrystalline polymers from a pronounced decrease in line width and in the second moment in the region of the glass transition temperature, as well as in the appearance of a narrow component.

For polyethylene terephthalate, irrespective of prior and subsequent heat treatment, a maximum of the transition temperature is found at crystallization temperatures of 200 and 220 °C. It can be shown on the basis of X-ray measurements that a large number of very small crystallites is formed at these temperatures. The strains in the small crystallites are responsible for the maximum of the transition temperature.

A process has been reported for the separation of the components of the spectrum, which permits the determination of the correct absolute value of the mobile component, free from experimental effects. By subtracting the mobile component from the noncrystalline fraction found by density measurements, one obtains the immobile noncrystalline component. This has a maximum at crystallization temperatures of 200–220 °C. In agreement with the interpretation of the maximum of the transition temperature, it must be assumed that at these temperatures the crystallization gives rise to strains that hinder the thawing of the segment mobility in these regions, even at high temperatures. If the samples are swollen in deuterated acetone after crystallization, this maximum disappears.

It can be shown by calculation of the line form of the spectra and comparison with the measurements that hindered rotation already exists for all the CH_2 groups up to the start of the glass transition. Above the glass transition, rotation of the benzene rings in the noncrystalline regions begins, and this changes into a microbrownian movement of the chain segments as the temperature is further raised.

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Investigations on the Sequence Length Distribution of Copolymers of α-Methylstyrene and Butadiene

By *K. F. Elgert* (lecturer), *E. Seiler*, and *Horst Friebolin* [*]

The butyllithium-initiated copolymerization of α-methylstyrene (A) and butadiene (B) in THF at −75 °C is described by the copolymerization parameters $r_A = 0.017$ and $r_B = 2.8$. The sequence length distribution was investigated by 220 MHz NMR measurements. Analysis of the in part strongly overlapping band systems with a curve simulator allowed the quantitative determination of the frequencies of the AAA, BBB, BBA, and ABA triads as a function of composition and conversion. The experimentally determined triad frequencies agree well with those calculated from the *r* parameters.

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High-Resolution NMR Studies on Cellulose Derivatives

By *Horst Friebolin* (lecturer), *Gunda Keilich*, and *Egon Siefert*[*]

Tests were carried out to determine whether the proton magnetic resonance method (measuring frequency 220 MHz) can be used to elucidate the structure of polysaccharides. Acetyl and benzoyl derivatives of cellulose were used as model substances, since in addition to their better solubility in organic solvents (*e.g.* $CDCl_3$), these compounds also exhibit spreading of the ^{1}H-NMR signals of the seven ring protons.

For the cellulose derivatives with molecular weights of several hundred thousand, all seven ring protons are separately visible in the spectra. However, the coupling constants, which are important for the determination of the configuration and conformation, cannot be determined because of the large line width.

The spectra of the cellulose derivatives with degrees of polymerization between about 50 and 100, on the other hand, exhibit such sharp lines that it has been possible to assign all the ring proton signals by means of the coupling constants. The chair conformation of the monomer units, glucose, and their β-glucosidic linkage were definitely confirmed. The 1,4-linkage of the glucose units is conclusively demonstrated by comparison of the chemical shifts of the protons in the 1 and 4 positions with those of the corresponding glucose and cellobiose derivatives; the structure that has been assumed for cellulose until now is thus confirmed.

The ^{1}H-NMR signals of the three acetyl groups of cellulose triacetates give three separate lines in the 220-MHz spectrum, which can be assigned to the acetyl substituents in positions 2, 3, and 6.

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Structure of Phenylalanine-Specific Transfer Ribonucleic Acid from Baker's Yeast

By *Friedrich von der Haar*[*]

Transfer ribonucleic acid (tRNA) has a dual function in protein biosynthesis. Firstly, a specific tRNA binds, and hence activates, only the corresponding amino acid (acceptor function), and secondly the resulting activated amino acid is introduced into the ribosomal apparatus and built into the growing protein chain (transfer function). Whereas very detailed views exist on the second step (codon-anticodon interaction), the details of the course of the specific aminoacylation are unknown. In particular, there is no explanation at present for the very high specificity of the reaction, which must proceed with an error rate of less than 10^{-4}. In this connection it is important to clarify the three-dimensional structure of tRNA, which must be a globular molecule[1].

We therefore investigated tRNA by oxidation with monoperoxyphthalic acid. Under strictly defined conditions, this reagent specifically oxidizes non-base-paired adenines to adenine 1-*N*-oxide, which can be readily detected analytically. All the tRNAs that have been sequenced so far can be folded back by optimum base pairing in the Watson-Crick sense to give a planar clover-leaf structure, as was first suggested by *Holley* for $tRNA^{Ala}$[2]. In such a structure, nine adenines should be oxidizable in $tRNA^{Phe}_{Yeast}$. We found that only four of these bases are oxidized; the other five must therefore be protected by hydrogen bonds. Three of the oxidizable adenines are situated in the anticodon loop, while the fourth is at the 3′-terminal end of the $tRNA^{Phe}_{Yeast}$.

This result can be readily explained by folding of the dihydro-U-loop and of the T—Ψ—C loop to the 3′-terminal end. New interloop base pairs are then formed by proximity in space, the stability of these base pairs arising from optimum stacking.

Investigations by *Litt* on the guanosine-specific reagent ketoxal[3] and biochemical[4] and physicochemical[5] measurements confirm these views, which can be applied to all other tRNAs.

We have now succeeded in crystallizing $tRNA^{Phe}_{Yeast}$[6], and there is thus a possibility that its structure can be elucidated by X-ray analysis.

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The Influence of Electron Donor-Acceptor Complexes on Cationic Polymerization

By *Manfred L. Hallensleben*[*]

We have investigated the cationic polymerization of styrene and α-methylstyrene in solution in the presence of organic electron acceptors that form an electron donor-acceptor complex with the monomer (monomer-acceptor complex, MA complex). In inert solvents such as carbon tetrachloride, the MA complex decomposes at low acceptor concentrations after initiation *e.g.* with $BF_3 \cdot O(C_2H_5)_2$, and a new electron donor-acceptor complex is formed with the negatively charged ion (anion-acceptor complex, AA complex). The separation of the ion pair by this AA complex increases the polymerization rate. Its increase is a linear function of the acceptor strength. At high electron acceptor concentrations, the MA complex causes retardation or even inhibition of polymerization.

In aromatic solvents such as benzene or toluene, which can compete with the monomer as electron donors, the influence of the electron acceptor on the polymerization is small.

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Influence of Polymer and Copolymer Microstructure on the Chemical Reactivity of Polymers

By *H. James Harwood* (lecturer), *Edwin Thall*, and *Arthur B. Robertson*[*]

Investigations of the kinetics of reactions involving functional groups attached to polymer chains and studies of the limiting conversions obtained in such reactions suggest that polymers may contain groups with considerably different reactivities, depending on their environment in the polymer chain. These studies suggest that information about the stereoregularity of homopolymers and the distribution of monomer sequences in copolymers can be obtained from studies of their chemical reactivity.

The reactivity of polymers is influenced by many factors other than microstructure, however, and the influence of

these other factors changes with the extent of reaction. For this reason, kinetic and limiting conversion data should not be used for the characterization of microstructure.

A radiotracer procedure has been developed for detecting groups present in polymers which have different reactivity. The procedure provides information about the relative amounts of the various groups present and their relative reactivity.

When this procedure was used to study the reactivity of MMA units in styrene-methyl methacrylate copolymers, all the MMA units were found to have the same reactivity. Similarly, all the units in conventional poly(methyl methacrylate) were found to have the same reactivity.

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The Structure Rule of Antibodies and the Antibody Problem

By *Norbert Hilschmann* (lecturer), *Herwig Ponstingl*, *Maxime Hess*, *Ludwig Suter*, *Heinz Ulrich Barnikol*, *Knut Bazcko*, *Shitsu Watanabe*, and *Dietmar Braun* [*]

Comparative structure analysis of monoclonal, *i.e.* chemically uniform, immune serum globulins have shown that

1. antibodies with different antigen specificities have different amino acid sequences, and

2. these structural differences are confined to the variable part of the immune globulin chains.

In the light (L) chains (molecular weight 24000), this variable part corresponds to the N-terminal half, while in the heavy (H) chains, which are approximately twice as long (molecular weight 50000), it is the N-terminal quarter of the molecule. The variable parts are thus of the same size in both chains, and contain 110 to 120 amino acid residues. The structural differences in the variable part involve several exchanges of amino acids and a few deletions.

To gain an insight into the causes of this antibody variability, we have studied other variable parts of immune globulin L chains over the past few years. We found that the amino acid exchanges in the variable part that determine the specificity follow an ordering principle. The ordering principle is the number of amino acids exchanged.

Several "subgroups" of chemically related proteins occur, in which at most 25% of the amino acids are exchanged. Proteins of various subgroups differ in an exchange of 50% of the amino acids. We have found three such subgroups in the $\varkappa$ chains and four in the λ chains.

This degree of order is understandable only if one assumes that the antibody variability has arisen by evolution and that the chains are derived from a common basic form after the fashion of a phylogenetic family tree. If this "variability rule" is confirmed by further investigations, particularly for proteins within the subgroups, this would mean that the information for the specificity of the antibodies is genetically fixed, and is thus not an acquired property, but an inherited one.

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Mosaic Structure, Grain Boundaries, and Paracrystalline Distortions in Polyethylene Single Crystals

By *Rolf Hosemann* [*]

Some interesting properties of polyethylene single crystals can be deduced from the X-ray small angle and wide angle interferences.

If X-rays pass through a bundle of parallel oriented single crystals of this type, the small angle scattering appearing on the meridian points to a "long period" of 100 to 300 Å or more, depending on annealing, and gives the distance between neighboring crystal platelets (from center of gravity to center of gravity). The widths of the first layer line wide angle reflections, on the other hand, give direct information about the thickness of the crystallites [1]. The thickness of the "amorphous" intermediate layer in the single crystals of linear polyethylene (Lupolen 6011 H, BASF) studied here can then be calculated and is only a few Å. The crystals were prepared isothermally from 0.01% xylene solution at 85 °C, filtered and washed in acetone for 24 hours at the same temperature, and finally dried for 3 days under vacuum.

The width of the equatorial wide angle reflection gives the dimension of the lattice regions perpendicular to the chain direction. Careful consideration of the *h*00 and *hk*0 reflections showed that the structure probably consists of mosaic blocks whose grain boundaries are often formed by (310) planes, the diameters in the *h*00 and 0*k*0 directions being about 340 and 840 Å respectively [2]. On annealing at 125 °C, both quantities and the crystallite thickness increase to approximately the same degree, after 10^4 min, for instance, by about 30%. It is therefore permissible to speak of a type of equilibrium form, and to apply the Wulff equation. From the surface energy of the frontal faces (≈ 39 erg/cm^2), the surface energy within the lateral grain boundaries was found to be 68 ± 7 erg/cm^3. Since the intramolecular energy of a 2*g*1 kink, according to ref. [3], is about 38×10^{-14} erg, we find a two-dimensional kink concentration of 0.77×10^{14} cm^{-2} if these kinks are alone responsible for the distortions at the grain boundaries.

Comparing this quantity with the number of chain units $(CH_2)_3$ immediately adjacent to or lying in the (310) plane one obtains a kink concentration of about 24%. This agrees very well with the picture reported by *Pechhold et al.* for the concentrations of "jogs" in the grain boundaries. We find a different situation for the kink concentration inside the mosaic blocks; these can be calculated from the widths of the *hk*0 and *h*00 wide angle reflections with the aid of the paracrystal theory. The so called *g* value of the paracrystals, which characterizes the relative fluid-like statistical fluctuations of the distances between the planes, is found by X-ray studies to be 1.4 and 1.8% respectively for the (110) and (200) planes. A rough calculation on this basis gives a three-dimensional kink concentration of a least 0.14% inside the mosaic blocks.

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Light Scattering Measurements on Polymer Solutions in the Pressure Range 1–1000 atm

By *M. Lechner* (lecturer) and *G. V. Schulz* [*]

Very extensive data exist on light scattering measurements on solutions of macromolecules as a function of composition and of temperature, the pressure generally being kept constant. For a complete knowledge of such systems, it is necessary to abandon the accidental external condition of atmospheric pressure and to introduce pressure as an available independent variable. We have therefore constructed a photometer that allows the measurement of the scattering intensity at a scattering angle of 90° up to pressures of about 1000 atm [1]. To determine the dimensions of the dissolved molecules, the dependence of the scattered light on the wavelength was measured instead of its angle dependence.

In this way we have measured the second virial coefficient of the osmotic pressure A_2 and the radius of gyration $\bar{r}$ as a function of pressure between 15 and 50 °C for the following systems[2–4]: the two endothermic systems polystyrene/*trans*-decalin (Θ = 20 °C at 1 atm) and polystyrene/cyclohexane (Θ = 36 °C at 1 atm); the athermic system polystyrene/toluene; and the exothermic system polystyrene/chloroform.

We have obtained the following results:

1. All the solvents examined become thermodynamically poorer with increasing pressure, *i.e.* the Θ temperature (A_2 = 0) increases, and all the systems examined become more endothermic.

2. The radius of gyration, which was measured for the systems polystyrene/*trans*-decalin and polystyrene/toluene, decreases continuously with increasing pressure for both systems between 15 and 40 °C.

3. The excluded volume model satisfactorily represents the observed behavior of the systems in the vicinity of the Θ temperature. At greater distances from the Θ temperature, the deviations become greater, *i.e.* agreement with the experiments can be obtained only if the unperturbed dimensions decrease with increasing pressure.

4. The free volume theory fairly accurately reproduces the temperature and pressure dependence of the thermodynamic properties even for athermic and exothermic systems.

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Notes on the Determination of the Heterogeneity of the Chemical Composition of Copolymers by the Light Scattering Method

By *Pavel Kratochvíl* and *Zdeněk Tuzar*[*]

The molecular weight (M_w) and the parameters Q and P characterizing the chemical heterogeneity of binary copolymers can be determined by measurement of the scattered light intensity in at least three solvents having different refractive indices[1]. The refractive indices of the components A and B of the copolymer should differ as much as possible.

We have investigated the question of the optimum conditions for the determination of M_w, P, and Q. It was found that the three solvents should satisfy the following conditions. First solvent: both refractive index increments (ν_A, ν_B) should have large absolute values and the same sign; second solvent: $|\nu_A|$ large, $\nu_B = 0$; third solvent: $\nu_A = 0$, $|\nu_B|$ large.

It is generally difficult to achieve the optimum conditions with single-component solvents. If ν_A and ν_B are virtually equal, analysis is impossible. However, it is possible to obtain mixed solvents[2] with differing values of ν_A and ν_B, provided that they are measured after establishment of the dialysis equilibrium between solvent and solution. This effect is based on the different selective sorption of the components of the mixed solvent on the components A and B of the copolymer. It should accordingly be possible, in principle, to determine the chemical heterogeneity even of copolymers whose components have very similar refractive indices.

Our investigations on the light scattering from solutions of copolymers in mixed solvents have shown that the classic relations derived for single solvents by *Bushuk* and *Benoît*[1] are also valid for systems of this type; however, it is necessary to use the ν values determined after dialysis, in order to take into account the optical effect of the selective sorption.

These views have been tested for model mixtures of polymethyl methacrylate, polyethylene glycol monomethacrylate, and their copolymers in methyl cellosolve/α-bromonaphthalene. The copolymer components have very similar refractive indices in this case. The satisfactory agreement of the calculated and experimental M_w, P, and Q values confirms the importance of mixed solvents in the determination of the chemical heterogeneity of the copolymers.

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Synthesis and Conformation of Collagen Models

By *Manfred Rothe* (lecturer), *Rainer Theyson*, *Klaus-Dieter Steffen*, *Hans-Jürgen Schneider*, *Mohammed Zamani*, *Michael Kostrzewa*, and *Wolfgang Schindler*[*]

In its nonpolar regions, collagen has an ordered structure with the regularly repeating tripeptide unit –glycine-proline-X–. Polytripeptides having this sequence with different X can help, as models, to elucidate the molecular basis of the biological function of collagen.

Since the polytripeptides investigated so far have not always been suitable, because of low molecular weights in most cases, partial incorporation of the condensing agent, and broad molecular weight distributions, pure, defined oligotripeptides having the sequence H(Pro-Gly-Gly)$_n$OH *(1)* up to $n \approx 8$ were synthesized in a chromatographically pure state after *Merrifield*.

Conformation studies by CD measurements showed that ordered structures as in the polymer occur at least beginning with the heptamer *(1)*, n = 7, in trifluoroethanol [three Cotton effects at 203–205 (weakly positive), 223 (weakly negative), and just below 185 nm (strongly negative), polytripeptide: 206, 230, <185 nm]. However, the first effects already occur with the tetramer *(1)*, n = 4. In hexafluoroacetone, on the other hand, the CD curves point to the absence of secondary structure.

In the stiff-chained oligoprolines H(Pro)$_n$OH, which were obtained by the same route in an electrophoretically uniform state up to n = 17, helices are found even for shorter chains. As in the case of polyproline, two conformations with *cis*- or *trans*-peptide linkages, different helical sense, and different residue translations, depending on the solvent, occur beginning with the tripeptide. This is shown by the molar rotations, the UV, NMR, and CD spectra in solution, and the IR spectra in the solid state. Interconversion of the two helices is possible by changing the solvent, as is shown by remarkable changes in the optical rotation (mutarotation).

Further models for the polymers are cyclopeptides with a rigid arrangement of the amino acids, *e.g.* cyclotri-L-prolyl and cyclo-L-prolyl-ε-aminocaproyl, as is shown by the optical data.

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Some Polymeric Complex Formers

By *Georg Manecke*, *Hans-Uwe Schenck* (lecturer), and *Hans-Peter Aurich*[*]

The coordination behavior of 3(5)-pyrazolecarboxylic acid, 3(5),4-pyrazoledicarboxylic acid, their esters, 3(5)-pyrazolyl alkyl(aryl) ketones and 3(5)-pyrazolecarbaldehyde oxime was

investigated. 1 : 1 or 1 : 2 (M^{2+} : pyrazole derivative) complexes were obtained with Cu^{2+} and other transition metal ions.

3(5)-Vinylpyrazole derivatives have been obtained in good yields by 1,3-dipolar addition of vinyldiazomethane to sufficiently activated acetylene derivatives such as propiolic esters and ethynyl alkyl(aryl) ketones. Where these vinyl compounds were readily soluble in dimethylformamide, they could be homopolymerized in this solvent by a free-radical mechanism.

Both the copolymer of ethyl 3(5)-vinyl-5(3)-pyrazolecarboxylate with 2.5 mole-% of bis[3(5)-vinyl-5(3)-pyrazolyl] ketone and that of 3(5)-vinyl-5(3)-pyrazolyl methyl ketone were prepared. In both cases, crosslinked products exhibiting only limited swelling were formed. Alkaline hydrolysis of the polymeric vinylpyrazolecarboxylate gave a chelate-forming ion exchanger having a high capacity.

Polymerizable 5-vinyl derivatives were obtained from 5-acetyl-8-alkoxyquinoline and 5-acetyl-8-alkoxyquinaldine by reduction of the acetyl group to form the alcohols followed by dehydration with Al_2O_3. The 8-hydroxy-5-vinylquinoline obtained on hydrolysis of the phenol ester did not polymerize. Copolymers of 8-benzyloxy-5-vinylquinoline and 8-benzyloxy-5-vinylquinaldine with divinylbenzene lost the benzyl residue quantitatively on treatment with 5 N HCl. Peptides could be synthesized on the quinaldine resin.

The quinaldine and quinoline resins, as well as the C-7-brominated resins, were examined for complex formation with Cu, Ni, and Zn. The resins had higher capacities than one would have expected from the heterocycle content on the basis of the formation of 2 : 1 (ligand : metal) complexes. It is assumed that 1 : 1 complexes are formed. The copolymer of 8-ethoxy-5-vinylquinaldine (8-ethoxy-5-vinylquinoline does not polymerize well) with divinylbenzene takes up bromine as an adduct from aqueous solution.

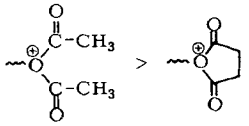
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Investigations on the Course of the Cationic Copolymerization of Tetrahydrofuran with Dicarboxylic Anhydrides

By *Waldemar Öchsner* (lecturer) and *Karl-Heinz Reichert* [*]

The cationically initiated reaction of tetrahydrofuran with dicarboxylic anhydrides leads *via* a ring-opening copolymerization to polyesters with ether units in the polymer chain [1]. The reaction was investigated in the system tetrahydrofuran (THF)/succinic anhydride (SA) and in the low molecular weight model system THF/acetic anhydride (AA), in most cases with PF_5 as the initiator. The induction period observed in the homopolymerization of THF with Lewis acids in the absence of cocatalysts could be avoided by prepolymerization of THF and addition of the comonomer after depolymerization of the polytetrahydrofuran formed.

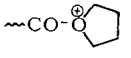
Kinetic studies with various initial monomer concentrations in dichloroethane at 80 °C showed that the rate-determining step involves only THF, and not the anhydride monomer. By comparison of the overall rates of the copolymerization and the model reaction, this slowest step was identified as a nucleophilic attack by THF on the anhydride oxonium ion. The relative reactivities of the anhydride oxonium ions *(1)* and *(2)* towards THF were determined from the ratio of the overall polymerization rates. The results agree favorably with those obtained on sterically hindered acid hydrolysis of butyrolactone and on similar reactions of five-membered rings compared with reactions of unstrained systems [2].



(1) > *(2)*

For a detailed structure analysis, the alkaline hydrolysis products of the copolymer were acetylated to the same oligoether diacetates $CH_3CO-[O(CH_2)_4-]_nOCOCH_3$, which are formed directly in the model reaction. As expected from the polymerization equilibrium of THF, the diacetate distribution showed that above the ceiling temperature of THF (84 °C) the reaction leads mainly to the diacetate with $n = 2$ (BEDA) together with that having $n = 1$ (BDA). Considerable amounts of diacetates with longer ether sequences ($n \geqslant 3$) are formed only below this temperature.

Conclusions as to the relative reactivities of the two monomers (THF and anhydride) in a competitive addition to the oxonium ion *(3)* can be drawn from the molar ratio BEDA/BDA above the ceiling temperature, taking the initial monomer ratio into account. Structural unit analysis of the oligomeric diacetates of a copolymerization product and of a model reaction product, prepared in dichloroethane at 80 °C, gave higher values for BEDA/BDA in the model system THF/AA than in the copolymerization of THF/SA. The results indicate that succinic anhydride is more reactive than acetic anhydride in attacking the oxonium ion *(3)*, as was also to be expected from the carbonyl absorption frequencies of 1865 and 1782 cm^{-1} (SA) and 1825 and 1748 cm^{-1} (AA).



(3)

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Determination and Comparison of the Number of Active Centers in the Polymerization of Ethylene, Propylene, and 1-Butene with Ziegler-Natta Catalysts

By *Karl A. Jung* and *Hans W. Schnecko* (lecturer) [*]

The reaction constants for the polymerization of the three monomers mentioned in the title can be determined from the initial polymerization rate, the viscosimetric molecular weights, and the complete chain termination at given times. The ^3H method is much more suitable than *e.g.* reaction with iodine for the measurement of the last process; though iodine can be quantitatively determined both by microtitration and by activation analysis, the termination reaction is not quantitative.

In view of the strong transfer reaction at the beginning of polymerization, it is necessary to extrapolate the number of active centers to the start of polymerization. This gives the following values for the three monomers: $C^* = 6.9 \times 10^{-3}$ mmole/mmole of $TiCl_3$ for ethylene, 5.3×10^{-3} for propylene, and 3.5×10^{-3} for 1-butene.

Moreover, these monomers behave quite differently during the polymerization, as can be seen in the different rate and molecular weight curves, as well as in the values of the polymerization and transfer rates and of the lifetime of growing chains. It may be assumed that the differences are due to the differences in the structures of active centers for the various monomers.

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Optically Active Poly-β-amides

By *Erwin Schmidt*[*]

Optically active β-lactams with one and with two centers of asymmetry in the lactam ring have been polymerized alone and as mixtures of enantiomers of various optical purities. The properties of the polymers, their solubility and behavior in solution, as well as structural features, were described.

The optically active poly-β-amides have higher melting points and are less readily soluble than the corresponding optically inactive polymers. The optically active poly-β-aminobutyric acids, which can be made into fibers and films, have been studied in most detail. The textile properties do not differ appreciably from those of poly(+)-β-aminobutyric acid.

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Problems in the Kinetic Evaluation of the Thermogravimetric Degradation of Polymers

By *Ion Adam Schneider*[*]

Thermogravimetric measurements on the stability of polymers have frequently been evaluated kinetically during the last decade. However, these methods can hardly be described as absolute, since the kinetic parameters obtained may depend both on the conversion and on the heating rate. The reason for these peculiarities is that observations based on the isothermal degradation kinetics were applied uncritically to complicated degradation reactions occurring under conditions of rising temperature. The thermal degradation reactions are heterogeneous, and so probably also may depend on transport phenomena. Moreover, it must be noted that the degradation process of polymers is not a simple reaction. Even if *e.g.* the polymer is degraded by a simple chain mechanism comprising at least the three phases initiation, depolymerization, and termination, it cannot be assumed that quasi-steady states are formed under conditions of steadily rising temperature, since, in particular, the rate of the initiation reaction, and hence the concentration of the chain carrier, increases exponentially according to the Arrhenius equation, until the influence of the decreasing concentration of the polymer becomes noticeable.

It can thus be readily shown that under thermally dynamic conditions, the activation energy of chain reactions must decrease with the conversion. According to the Flynn-Wall equation

$$\frac{d \log \beta}{d(1/T)} = -(0.457/R)E_a$$

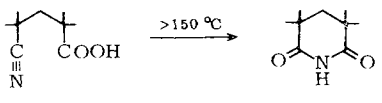
where β is the constant heating rate, it can be seen indirectly that the heating rate also influences the activation energy. In our opinion, therefore, thermogravimetry is kinetically only a relative method.

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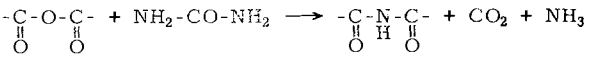
Polymer-Analogous Formation of Imido Groups in Methacrylic Acid/Methacrylonitrile Copolymers

By *G. Schröder* (lecturer), *W. Gänzler*, *P. Huch*, and *W. Metzger*[*]

When copolymers of (meth)acrylonitrile and (meth)acrylic acid are heated, adjacent nitrile and acid groups react above about 150 °C to form glutarimide units.



Reactions of this type have been known in low molecular weight chemistry since 1868 through the work of *Gautier*. In macromolecular chemistry they provide a simple route for the preparation of polymers with cyclic di(meth)acrylimide units. The number of imido groups formed depends on the composition of the initial copolymer, its sequence length distribution, the heating temperature, and the heating time. If there are long nitrile sequences, more or less pronounced discoloration is observed as a result of the well-known polymerization of the nitrile groups. Glutaric anhydride units can be formed from adjacent acid groups by elimination of water. The glutaric anhydride units can react with urea, in accordance with the following equation



When suitable (meth)acrylonitrile/(meth)acrylic acid copolymers (which can be prepared by bulk polymerization) containing urea are heated, therefore, they give foams containing imides, the pores of which are filled with CO_2. In the absence of urea and other foaming agents, yellowish, clear plastics are formed. All polymers containing (meth)acrylimide are characterized by high softening points, high mechanical strength, and resistance to most organic solvents.

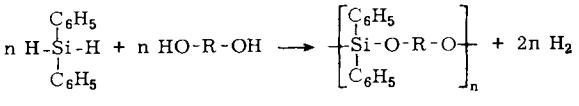
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Poly(dioxyarylene)diphenylsilanes

By *Klaus-Dieter Steffen*[*]

High molecular weight thermoplastic poly(dioxyarylene)-diorganosilanes (also known as polyorganosilicic esters) can be prepared by polycondensation of bis(anilino)diorganosilanes with diphenols[1].

In another process known from the preparation of simple organosilicon compounds, high molecular weight poly(dioxyarylene)diphenylsilanes are obtained from diphenylsilane and diphenols by elimination of hydrogen.



The polycondensation can be carried out in solution or in the melt after the addition of catalysts.

Twelve poly(dioxyarylene)diphenylsilanes were prepared by polycondensation of bis(anilino)diphenylsilane or diphenylsilane with diphenols. The glass transition and Vicat temperatures (43—208 °C), viscosities [$\eta_{sp/c}$ = 0.4—1.5 dl/g (0.5% in THF)], and molecular weights (20×10^3 — 200×10^3) of the twelve polymers were determined. Thermal stability measurements were carried out on the polymers by determining the loss of weight and the decrease in viscosity as a function of time.

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[1] *W. R. Dunnavant, R. A. Markle, R. G. Sinclair, P. B. Stickney, J. E. Curry*, and *J. D. Byrd*, Macromolecules *1*, 249 (1968).

Constitution of the Styrene Oligomers Formed on Thermal Polymerization

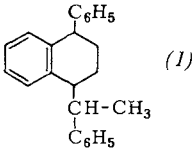
By *Joachim Kurze, Dieter J. Stein* (lecturer), *Petr Šimák*, and *Rudolf Kaiser*[*]

In the thermal polymerization of styrene, oligomers are formed in a side reaction. According to *Mayo*[1], these are saturated and unsaturated dimers and trimers of styrene; this

author assumes a close relation between oligomer formation and the initiation reaction of the thermal polymerization of styrene. Later investigations by other authors on the structure of the dimers led to contradictions.

By independent synthesis of the oligomers, we have largely confirmed the assignment suggested recently by *Brown*[2]: the principal components of the dimer fraction are *trans*- and *cis*-1,2-diphenylcyclobutane in a ratio of about 3 : 1; 2,4-diphenyl-1-butene and 1-phenyltetralin were also detected in smaller quantities.

The principal object of this work was to elucidate the structure of trimeric styrenes. We were able to verify the assumed presence[3] of 2,4,6-triphenyl-1-hexene by synthesis; this compound forms about 30% of the trimer fraction. We also showed that the trimeric styrenes without olefinic double bonds (about 65% of the trimer fraction) are the four isomeric optically inactive 1-phenyl-4-(1-phenylethyl)-1,2,3,4-tetrahydronaphthalenes *(1)*. The structure was demonstrated by dehydrogenation to obtain the optically inactive 1-phenyl-4-(1-phenylethyl)naphthalene, which was compared with an authentic sample.



(1)

We believe that the tetrahydronaphthalenes are formed by recombination, in the solvent cage, of the initiating radicals that are responsible for the thermal polymerization.

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[1] *F. R. Mayo*, J. Amer. chem. Soc. *75*, 6133 (1953).

[2] *W. G. Brown*, Makromolekulare Chem. *128*, 130 (1969).

[3] *D. J. Stein* and *H. Mosthaf*, Angew. makromolekulare Chem. *2*, 39 (1968).

Polymerization of 4-Methyl-1-pentene with Ziegler Catalysts

By *Heinrich Weber* (lecturer), *Günther Kiessling*, and *Eberhard Blanck*[*]

The polymerization of 4-methyl-1-pentene with the catalyst α-titanium trichloride/diethylaluminum chloride yields crystalline, isotactic poly-4-methyl-1-pentene. With titanium tetrachloride/triethylaluminum, depending on the temperature (−20 to +60 °C) and Al/Ti ratio (0.2 : 1 to 2 : 1), the reaction yields low molecular weight hydrocarbons (olefins and paraffins), atactic poly-4-methyl-1-pentene, and isotactic poly-4-methyl-1-pentene. The composition of the reaction products changes considerably when the catalyst is aged, *i.e.* the components of the catalysts can react at 60 °C/30 min in toluene. No low molecular weight reaction products but only alkylated toluenes are formed in this case.

It was found that the low molecular weight olefins and paraffins do not consist only of dimers, trimers, and higher oligomers of 4-methyl-1-pentene, but that *trans*-olefins and paraffins containing two C atoms more than oligomers are also formed. These two C atoms come from the ethyl groups of the triethylaluminum. The ratio of *trans*-olefins to paraffins depends strongly on the nature of the solvent used; the amount of paraffin is higher in aromatic than in aliphatic solvents.

Experiments in which tris(ethylphenyl)aluminum was used instead of triethylaluminum and others that were terminated with H_3COD support the view that the ethyl groups are derived from organotitanium groups as reaction products from the catalyst components. The proposed reaction course also explains the formation of *trans*-olefins and paraffins.

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Anionic Polymerization of Methacrylonitrile

By *H. Vankerckhoven*, *M. Van Beylen* (lecturer), and *G. Smets*[*]

The anionic polymerization of methacrylonitrile was studied kinetically in toluene at low temperature (approx. −75 °C). 1,1-Diphenylhexyllithium and *n*-butyllithium were used as initiators. The reaction was found to be second order with respect to the initiator in both cases.

In the polymerization with butyllithium as the initiator, induction periods occur at low initiator concentrations. To obtain more information about the initiation stage, the decrease in the butyllithium concentration was followed as a function of time by gas chromatography. Only a small part of the initiator is consumed in the polymerization, and the greater part remains unchanged. The efficiency of the initiators was calculated from the molecular weights of the polymers (about 2000–8000), and it was found that the growing chains are "living".

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Limits in the Scope of Gel Chromatography

By *Wolfram Gerlich*, *Helmut Determann*, and *Theodor Wieland* (lecturer)[*]

Regenerated cellulose gels in bead form (obtained from tetramminecopper(II) hydroxide or from xanthate solution at various concentrations) were calibrated as media for gel chromatography with a total of 21 substances having radii of 1–1000 nm by recording the elution parameter K_{av} as a function of the particle radius.

The bead gels obtained from xanthate by precipitation with acetic acid are comparable in their separation range and separation efficiency with the well-known weakly crosslinked dextran or agarose gels, but are superior in their mechanical stability. Very large particles such as bacteriophages, mitochondria, and even bacteria can be chromatographically separated on particularly wide-pored gel beads precipitated from the solution containing copper. However, the use of gel chromatography for particle radii greater than 200 nm is restricted by substantial irreversible adsorption.

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Crosslinking Reactions in Fibrous Proteins under the Action of Monofunctional Reagents

By *Helmut Zahn* (lecturer) and *Dietrich Brandenburg*[*]

After exposure to the action of monocarboxylic acid chlorides in dimethyl sulfoxide and pyridine (2–24 hours, 20–65 °C), wool[1], silk, and collagen gave the analytical data for the crosslinked protein. Only a small proportion of the carboxylic

acid residues is firmly bound by the proteins (*e.g.* by *N*-acylation). The principal reaction is the formation of N_ε (γ-glutamyl- or β-aspartyl)-lysine bridges. It is assumed that these carboxamide bridges are formed *via* mixed anhydrides from the carboxylic acids and the free carboxyl groups of the glutamyl or aspartyl residues.

Self-crosslinking has also been observed, though only as a side reaction, on reaction of wool with *p*-nitrophenyl esters. Fluorodinitrobenzene causes crosslinking on reaction with wool in the presence of acetate buffer at pH values below 7. Self-crosslinking of insulin has been observed on reaction with active esters of Boc-amino acids and with *tert*-butyl trichlorophenyl carbonate; monomeric and dimeric insulin derivatives with additional carboxamide bridges have been isolated.

[VB 228 IE]

German version: Angew. Chem. *82*, 553 (1970)

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Technischen Hochschule
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[1] *H. Zahn, H. Beyer, M. M. Hammoudeh*, and *A. Schallah*, Melliand Textilber. *50*, 1319 (1969).

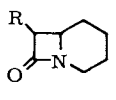
Synthesis and Reactions of Penicillin-Like Compounds

By *Friedrich Moll*[*]

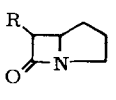
Penicillins and cephalosporins contain, as essential structural component, a β-lactam ring (azetidinone ring), which is fused to a five-membered ring and an unsaturated six-membered ring, respectively. The high reactivity of this fused azetidinone ring towards nucleophiles plays a decisive role in the blocking of bacterial cell-wall synthesis by β-lactam antibiotics. In the case of penicillin, *Woodward* has offered two possible explanations for this marked reactivity: a) Linkage of the azetidinone ring with a second ring increases the ring strain (increased energy content of the bicyclic ring system and change of the amide resonance); b) neighboring group participation of the acylamino side chain enhances the reactivity of the azetidinone ring to the observed level.

The neighboring group effect has received detailed attention in the production of semisynthetic penicillins. In contrast, the extent of the "ring-strain effect" was hardly known until recent syntheses and reactivity studies on penicillin-like compounds bearing no side chains permitted an assessment of its significance.

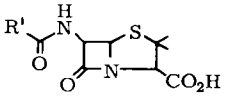
Carbocyclic analogs of the penicillin and cephalosporin skeletons can be synthesized by cycloaddition or by acid cyclization. [2 + 2] Cycloaddition of ketenes and cycloimines only gave the desired bicyclic compounds when the ring member β to the nitrogen was geminally substituted. Acid cyclization, however, proved generally applicable. It was possible to prepare the azabicyclo[4.2.0]octanones *(1)* (R = H, C_6H_5, NH_2) and the azabicyclo[3.2.0]heptanones *(2)* by synthesis and cyclization of correspondingly substituted 2-piperidyl- and 2-pyrrolidinylacetic acids.



(1)



(2)



(3)

Comparison of the reactivity of the new bicyclic compounds towards nucleophiles on the basis of the rate constants of alkaline hydrolysis led to an interesting result: The reactivity of the azetidinone ring increases by about 10^2 on fusion with a five-membered ring instead of a six-membered ring. Whereas the rate constant for azabicyclo[4.2.0]octanone *(1)*, R = H[1], is similar to the corresponding constants for monocyclic azetidinones, that for azabicyclo[3.2.0]heptanone *(2)*, R = H[2], is of the same order of magnitude as for the penicillins *(3)*.

Since neighboring group effects cannot operate in the case of *(1)* or *(2)*, it follows for the structure-activity relationships in β-lactam antibiotics that the enhanced reactivity of penicillins and cephalosporins must be due to a ring strain set up when the azetidinone ring is fused to another ring that is already strained. The neighboring-group effect, which can be controlled by variation of the side chains, plays a modifying role.

Lecture at Braunschweig on May 11, 1970 [VB 241 IE]
German version: Angew. Chem. *82*, 523 (1970)

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[1] *F. Moll*, Z. Naturforsch. *21b*, 297 (1966); Arch. Pharmaz. *301*, 230 (1968).

[2] *F. Moll* and *H. Thoma*, Z. Naturforsch. *24b*, 942 (1969).

Chemical Changes in Radiation-Preserved Foods

By *J. F. Diehl*[*]

Since treatment of foods with ionizing radiation is forbidden in the Federal Republic of Germany and exceptions are likely to be made only for specific foodstuffs, methods must be devised whereby a previous irradiation can be detected. In our laboratory we have found that deoxy sugars are formed on irradiation of carbohydrate-rich foodstuffs and that this can be detected very sensitively as malondialdehyde formed on oxidation by periodic acid[1]; in protein-rich foodstuffs, protein aggregates are produced that can be detected by electrophoresis and by thin-layer gel chromatography[2]. In dry foods a content of free radicals can be demonstrated by ESR measurements months after the irradiation[3].

The extent of changes induced by radiation depends on the dose given. In the region required for sterilization, *i.e.* for killing of all microorganisms, the requisite dosage (1--5 Mrad) can be demonstrated for most foods by the above methods. In the region 0.1—1 Mrad (radiation-pasteurization) the chemical changes are so small that detection is still uncertain. For the region below 0.1 Mrad (pest control in grain, prevention of sprouting of potatoes) there is still no usable method of detection.

It is also of interest how far the radiation destroys essential ingredients. The effect on vitamins has been the subject of numerous studies[4], which, however, have been confined to determination of the vitamin contents before and immediately after irradiation. However, the important matter is the vitamin content at the time of consumption. The finding that vitamins E and B_1 are strongly degraded further, even after irradiation, during storage and preparation of the food[5], leads to the question, still unanswered, whether radicals, traces of peroxides, or other radiation-produced compounds, are responsible for this. The matter is our particular present interest. In respect to the sensitivity of essential amino acids to irradiation it has been repeatedly determined that no loss worth mentioning occurs even with the dosage of about 5 Mrad[6].

Lecture at Würzburg on April 24, 1970 [VB 240 IE]
German version: Angew. Chem. *82*, 522 (1970)

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[1] *H. Scherz*, Nature (London) *219*, 611 (1968).

[2] *B. J. Radola*, Kältetechnik *21*, 333 (1969).

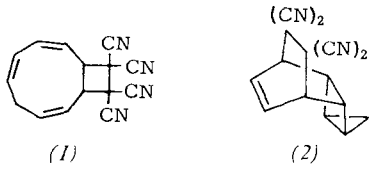
[3] *J. F. Diehl* and *S. Hofmann*, Lebensmittel-Wiss. Technol. *1*, 19 (1968).

[4] *J. F. Diehl*, Therapiewoche *18*, 1146 (1968).

[5] *J. F. Diehl*, Food Irradiation *10*, No. 1, p. 2 (1969).

[6] *E. Sickel, J. F. Diehl*, and *Th. Grünewald*, Z. Tierphysiol., Tierernähr. Lebensmittelkunde *25*, 258 (1969).

Reactions of bicyclo[6.1.0]nona-2,4,6-triene with dienophiles have been studied by *W. H. Okamura* and *T. W. Osborn* and by *C. S. Baxter* and *P. J. Garratt*. According to the conditions, the reaction with tetracyanoethylene gives *(1)* or *(2)*.

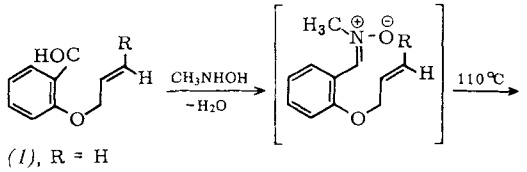


(1) *(2)*

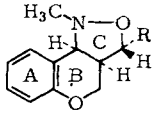
With maleic anhydride the bicyclic compound gives products that, like *(2)*, are derived from tricyclo[4.3.0.0^{7,9}]nona-2,4-diene. No product retaining the original bicyclic skeleton was obtained in reactions with these or other dienophiles. / J. Amer. chem. Soc. *92*, 1061, 1062 (1970) / —Kr.

[Rd 196 IE]

Intramolecular nitrone-olefin cycloadditions leading to heterocycles have been discovered by *W. Oppolzer* and *K. Keller*. For example, these workers obtained benzopyrano[4,3-*c*]isoxazole *(2)* (yield 80%, m.p. 184—185 °C) from *o*-(allyloxy)-benzaldehyde *(1)* and *N*-methylhydroxylamine by way of a nitrone intermediate. This type of synthesis can be effected



(1), R = H
(3), R = CH_2Cl

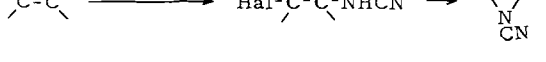


(2), R = H
(4), R = CH_2Cl

with numerous derivatives of *(1)* and with, *e.g.*, the naphthalene derivative and with *o*-(*N*-allylformylamino)-, *o*-(3-butenyloxy)-, and *o*-(vinyloxy)benzaldehyde. *W. Oppolzer* and *H. P. Weber* determined the X-ray structure of the product *(4)* from *(3)* and *N*-methylhydroxylamine and this showed that rings B and C are always *cis*-fused independently of the conformation of the olefinic compound. The conformation at C-3 and C-3a corresponds to the conformation of the starting material. / Tetrahedron Letters *1970*, 1117, 1121 / —Kr.

[Rd 197 IE]

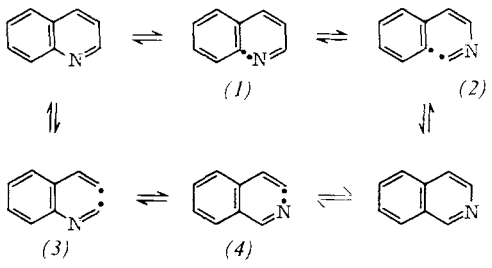
Vicinal halo(cyanoamines) and *N*-cyanoaziridines were obtained by *K. Ponsold* and *W. Ihn* by simultaneous addition of cyanamide and compounds containing positive halogen to olefins. The stable chloro cyano amines can be converted by alkali into the aziridine derivatives. Bromo cyano amines



readily react further to give the aziridines. Examples (cyanamide added in all cases): *trans*-stilbene + *N*-bromosuccinimide → 1-bromo-2-(cyanoamino)-1,2-diphenylethane (21% yield); cholesterol + dichlorourethane → 5α-chloro-6β-(cyanoamino)cholestan-3β-ol (21%); cholesteryl acetate + *N*-bromosuccinimide → 3β-acetoxy-5,6β-(cyanoimino)cholestane (62%). / Tetrahedron Letters *1970*, 1125 / —Kr.

[Rd 198 IE]

Mutual thermal interconversion of quinoline and isoquinoline was investigated by *J. M. Patterson*, *C. H. Issidorides*, *E. P. Papadopoulos*, and *W. T. Smith jr.* At 850 °C quinoline is converted into isoquinoline to the extent of 0.7%, and isoquinoline affords 2.3% of quinoline. Only hydrogen cyanide

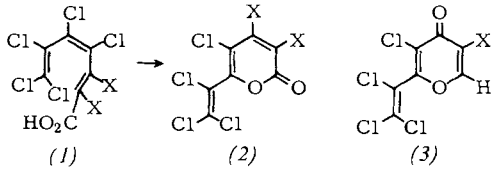


(1) *(2)* *(3)* *(4)*

and acetylene are formed as gases. The mass spectra of quinoline and isoquinoline, and of the by-products of the pyrolysis, make it probable that reaction occurs by way of *(1)* and *(2)* and/or *(3)* and *(4)*. / Tetrahedron Letters *1970*, 1247 / —Kr.

[Rd 199 IE]

Cyclization of the 2,3-dihalo-4,5,6,7,7-pentachloro-*cis*,*cis*-2,4,6-heptatrienoic acids *(1)* was studied by *A. Roedig*, *G. Märkl*, and *H. Schaller*. On thermal decomposition, *(1)* (prepared from perchloro-*cis*-2,4-pentadienal by chain elongation) affords the α-pyrone derivative *(2)*, together with a small amount of the hexahalobenzene. However, amides and anilides of the trienoic acids *(1)* cannot be cyclized. Aldehydes corresponding to *(1)* are converted into γ-pyrone



(1) *(2)* *(3)*

(a), X = Cl *(b)*, X = Br

derivatives *(3)* by proton catalysis. Thus these authors did not find the 1,7-heptatriene-oxygen shift expected from analogy with the 1,5-pentadiene-oxygen shift of perchloro-*cis*-2,4-pentadienal. / Chem. Ber. *103*, 1011 (1970) / —Kr.

[Rd 200 IE]

The cation S_4^{2+}, in the form of the compounds $S_4(SO_3F)_2$ and $S_4(SbF_6)_2$, was obtained by *J. Barr*, *R. J. Gillespie*, and *P. K. Ummat* on oxidation of sulfur. On treatment of sulfur with a solution of $S_2O_6F_2$ in fluorosulfuric acid there were formed first S_{16}^{2+} and S_8^{2+} (detected spectroscopically) and finally, with an excess of $S_2O_6F_2$, a colorless solution of S_4^{2+} (λ_{max} = 330 nm). When an excess of $S_2O_6F_2$ is condensed on powdered sulfur in liquid SO_2 at −196 °C and the mixture is allowed to warm slowly to −23 °C a solid, pale yellow, diamagnetic compound $S_4(SO_3F)_2$ is obtained. $S_4(SbF_6)_2$ is formed as a white powder from sulfur and SbF_5 in liquid SO_2 after several days' heating at 140 °C. / Chem. Commun. *1970*, 264 / —Kr.

[Rd 201 IE]

N-Chlorodifluoromethylenamine *(2)*, the simplest *N*-chloroperfluoroalkylenamine, was prepared by *D. E. Young*, *L. R. Anderson*, and *W. B. Fox* by thermolysis of *N,N,C*-trichlorodifluoromethylamine *(1)*. Compound *(1)* was obtained from cyanogen chloride and chlorine fluoride.

$$ClC{\equiv}N + 2\,ClF \xrightarrow{25\,^{\circ}C} CF_2Cl{-}NCl_2$$
(1), >90%

$$CF_2Cl{-}NCl_2 \xrightarrow[4\,h]{100-150\,^{\circ}C} CF_2{=}NCl + Cl_2$$
(1) *(2)*, ≈80%

(2) was freed from chlorine by means of mercury and was purified by gas chromatography. Azo and azino compounds RN=NR and R=N—N=R were not among the thermolysis products. *(2)*, b.p. ≈5 °C, has a very simple IR spectrum and gives almost all the possible ions in the mass spectrum. / Chem. Commun. *1970*, 395 / —Kr. [Rd 203 IE]

The diffusion constant of mobile electrons in anthracene was measured by *N. Karl*, *E. Schmid*, and *M. Seeger*. Plane-parallel crystal plates of the highest purity available are silver-coated on both sides by evaporation. If by a short flash of UV light a certain number of electron-hole pairs are generated on one side of the crystal, and an electric field is applied across the crystal, current carriers will drift through the crystal in the direction of the field. With increasing distance from the starting area, the current pulse corresponding to the moving carriers will be broadened by, among other factors, the diffusion of carriers. Quality criteria for the crystals to be used in these measurements are given together with experimental conditions that render carrier diffusion the major factor of current pulse broadening. The diffusion constant (in the crystallographic *a* direction) of 0.06 $cm^2\,s^{-1}$ is in good agreement with the independent value derived from drift mobility. As shallow traps would decrease the mobility, but increase the apparent diffusion constant, the agreement is a good argument that the electrons are actually free. / Z. Naturforsch. *25a*, 382 (1970) / —Hz. [Rd 205 IE]

A device for thermal analysis at temperatures up to 3000 °C is described by *N. L. Baldwin*, *S. Langer*, *F. L. Kester*, and *C. Hancock*. The samples (10—30 g) are heated in a high vacuum induction furnace. The radiation emitted from the sample impinges on a lead sulfide photoconductive cell placed in one leg of a bridge circuit. The imbalance signal is processed so that the sample temperature or its first time derivative can be recorded. A chopper system is provided allowing radiation from sample and standard to impinge alternately on the detector for differential thermal analysis. The lead sulfide photoconductive cell is especially well suited for this purpose because of its spectral sensitivity from 0.25 to 3.5 μm allowing the detection of black-body radiation at 100 to 3000 °C. Investigations of the phase transitions in the system

$$a\mathrm{U(liquid)} + \mathrm{UO_{2-}}_x\mathrm{(solid)} = \mathrm{U_{1+}}_a\mathrm{O_{2-}}_x\mathrm{(solid)}$$

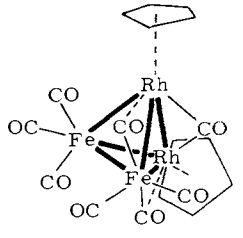
as functions of temperature and O : U ratio showed that isothermal enthalpy changes down to 7 cal can be detected if the derivative of the sample temperature is recorded. / Rev. Sci. Instruments *41*, 200 (1970) / —Hz. [Rd 206 IE]

Silver ketenide *(1)* has been synthesized by *E. T. Blues*, *D. Bryce-Smith*, *H. Hirsch*, and *M. J. Simons* by reaction of Ag salts with ketene or acetic anhydride in pyridine at room temperature:

$$2\,AgOCO{-}CH_3 + (CH_3CO)_2O \xrightarrow{(py)} Ag_2C{=}C{=}O(py) + 3\,CH_3COOH$$

(1) and its pyridine adduct are yellow, non-melting, explosive substances. *(1)* reacts with HCl gas (diluted with N_2) to give acetyl chloride, and with Br_2 in CCl_4 at room temperature to give tribromoacetyl bromide (>90%), and with CH_3I in octane at 90 °C to yield tetramethylcyclobutane-1,3-dione. Both Ag atoms of *(1)* are bonded covalently to the terminal C atom. The rapid thermal decomposition of *(1)* at 150 °C under argon affords carbon suboxide almost quantitatively. X-ray and electron-diffraction studies show *(1)* to have a layer structure in which the Ag atoms of a layer are separated by 2.84 Å and the interlayer distance amounts to 5.846 Å. / Chem. Commun. *1970*, 699 / —Ma. [Rd 215 IE]

A tetrahedral metal cluster is present in the center of the compound $(\pi\text{-}C_5H_5)_2Rh_2Fe_2(CO)_8$ *(1)*, which *J. Knight* and *M. J. Mays* obtained along with other compounds of the same type by reaction of $(\pi\text{-}C_5H_5)Rh(CO)_2$ with $Fe_2(CO)_9$ and which has now been subjected to X-ray structural analysis



(1)

by *M. R. Churchill* and *M. V. Veidis*. *(1)*, a = 17.979, b = 12.079, c = 9.386 Å, has space group Pnma (D_{2h}^{16}, No. 62) and C_s symmetry. The two unsymmetrical carbonyl bridges are particularly noteworthy. / Chem. Commun. *1970*, 529 / —Kr. [Rd 217 IE]

BOOK REVIEWS

Einführung in die Strahlenchemie (Introduction to Radiation Chemistry). By *A. Henglein*, *W. Schnabel*, and *J. Wedenburg*. Verlag Chemie GmbH, Weinheim/Bergstr. 1969. 1st Edit., x, 400 pp., 124 figures, 29 tables, plastic cover DM 45.—.

Radiation chemistry in its present state appears in very many guises. This is partly due to the fact that chemical reactions can be induced by high-energy radiation in nearly all substances, whether they are inorganic, organic, or macromolecular, and irrespective of their aggregation state. This last point leads to fundamentally new possibilities for investigations in solid phases, and in the form of the matrix isolation technique it has greatly increased our knowledge of the properties and behavior of highly reactive intermediates such as free electrons, radical-ions, and free radicals. The pulse radiolysis technique, which allows the direct investigation of the kinetic behavior of the short-lived intermediates mentioned by ESR- and absorption-spectroscopic and electrochemical methods of analysis, is also important to general chemistry.

This diversity of radiation chemistry is clear from a shortened list of topics dealt with in 23 chapters of roughly equal length in *Henglein*'s book: types of radiation, radiation sources,

chemical dosimetry, specific energy losses of charged particles, elementary processes, formation and reactions of excited molecules, free radicals, and carbons, the technique of pulse radiolysis and its use, and electrons and ions in solids. In addition to these chapters, which are concerned with the fundamentals of radiation chemistry, the application of radiation in a number of fringe fields is also discussed. Topics represented include chemical aspects of radiation biology, the action of radiation on polymeric systems, and industrial radiation chemistry.

It is obviously not easy to present these many facets in an easily understood manner in a book of 400 pages. However, this enterprise has been successful for two reasons. First, the book is intended mainly for students and learners, including chemists, physicists, biologists, and physicians who wish to acquire a knowledge of the fundamentals and the present state of radiation chemistry. The book does not aim to replace textbooks by means of the many special chapters that it contains. This has made it possible to keep the various chapters short and concise, and this has greatly benefitted understandability and educational requirements. Another factor that undoubtedly helps in this respect is the fact that the book is made up from lectures that have been in use over a long period at the Berliner Technische Universität. Secondly, the authors have gone to some trouble to ensure clarity and simplicity. This has made it possible for the reader to obtain a rapid grasp of radiation chemistry, though this is generally regarded as a difficult field. Further assistance is provided by the references that are added to each chapter, and which are consequently arranged in a clear manner. The reader is also led up to the latest position of knowledge in this field and introduced to the problems on which research is currently being carried out. A great help to those who wish to learn about radiation-chemical methods will be the mathematical and experimental problems given at the end of most chapters, which are taken directly from radiation-chemical practice.

On the whole this book, when judged in relation to its aims, is very successful. It can be recommended to anyone who wishes to gain an insight into modern radiation chemistry and its problems.

Dietrich Schulte-Frohlinde [NB 874 IE]

Stabilisierung und Alterung von Plastwerkstoffen. (Stabilization and Aging of Plastics). Vol. 1. Stabilisierung und Stabilisatoren von Plastwerkstoffen (Stabilization and Stabilizers for Plastics). By *K. Thinius*. Verlag Chemie GmbH, Weinheim Bergstr. 1969. 1st Edit., 720 pp., 80 figures, 58 tables, linen DM 84.—.

The systematic review of literature on the stabilization of plastics started only a few years ago, and involves the difficult tasks of critically examining a practically endless and constantly growing mass of empirical results, deriving general rules that can be applied in practice, and explaining the observed effects as consistently as possible. The present book is particularly remarkable in that it is based on work carried out by the author over decades, and thus provides a valuable presentation of the results of research by an outstanding authority on the problem of the stability of plastics.

The book is divided into eight chapters, which differ considerably in size. The first chapter explains the concepts stability, stabilization, stabilizers, and aging. The second chapter is rather vaguely entitled "Measures for the stabilization of plastics", and deals with the modification of the intrinsic stability of the polymeric raw material by impurities in the starting materials, by the production process (only in the case of nitrocellulose), and by the isolation process. Stabilization by chemical modification, *e.g.* the blockage of end groups, which is important in polyacetal technology, is also discussed here. Details of geat practical interest are to be found in the third chapter ("Interrelations between the stability of the plastic and the parameters of its processing to form a molding composition"). The fourth chapter, again under a very general title "Stabilizers for plastics and their efficiency", provides information about the mode of addition of stabilizers to plastics and a collection of methods for testing their efficiencies. This collection is very detailed with respect to thermal and thermooxidative aging, and is particularly recommended to those who are interested in testing techniques.

The principal chapter of the book, which comprises more than 70 % of its volume, is the fifth chapter ("The effectiveness of the various groups of stabilizers"). All types of stabilizers are described here, together with investigations on their effectiveness, the stabilizers being arranged according to their chemical constitution, which experience has shown to be the most suitable basis for classification. In the description of the stabilizers, in addition to a relatively complete coverage of patent and journal literature, the author devotes considerable space to his own results, some of which are of great importance. Special mention should be made of the extensive studies on the stabilization of PVC. Unfortunately, too little emphasis is placed on the stabilizer systems that are important in modern industrial practice, the specific importance of which cannot be guessed by the reader from the comprehensive material. Thus the great importance of the benzotriazole UV absorbers and their structural variants reported by Geigy is allotted too little space, apart from the mention of Tinuvin P (though the structural formula given is wrong, and the text might give the impression that it resulted from the work of Japanese authors). The same is true of the phenol esters of carboxylic acids, which currently hold a considerable share of the market in commercial antioxidants for polyolefins. On the other hand, from the space given to the stabilization of polyolefins with amines, the reader might be led to wrongly assume that this is currently of considerable industrial importance. In a field as closely linked with practice as this, more attention should have been paid to the additives that have proved themselves in industry and that are commercially available.

In the sixth chapter the author discusses "Theoretical views and experimental results on the mechanism of action of stabilizers", dealing separately with purely thermal degradation, thermooxidative degradation, photooxidative degradation, and synergism. In view of the far-reaching, more or less speculative theories on degradation and stabilization mechanisms, particularly in the fields of autoxidation processes and the decomposition of PVC, this chapter has been kept relatively short. The mechanisms are mainly indicated qualitatively, and reaction formulas are usually not given; kinetic equations are totally avoided. However, this is not a disadvantage, if one considers the very arbitrary character of most current theories of stabilization and the fact that their prognostic value is small. Certain fundamental physicochemical concepts, such as the criteria of autocatalytic reactions, the stability period, and the critical stabilizer concentration, should however have been defined clearly at a suitable point.

The seventh chapter is devoted to the "Analysis of stabilizers". This chapter is too short to present more than very general considerations, together with brief notes on the methods for a few selected analyses, with references to the original literature. The discussion of the "Toxicity of stabilizers" in the eight chapter is thorough and careful. The ninth part of the book, which is headed "Index", is an alphabetic index of keywords. This is the only index in the book, apart from the list of contents. The absence of a general bibliography or author index is regrettable. Since the references are scattered throughout the book, it is practically impossible to obtain information about a given publication or patent without considerable search. The references to literature and patents attached to each sub-chapter, which can only be found from the text, cover the journal literature up to 1965, and in a few cases up to 1966, and patent applications up to about 1963, again with occasional exceptions of more recent date. Literature from the German Democratic Republic and Eastern European countries is generally covered up to later

dates. The references are accurate, but more care should have been taken in spelling the authors' names.

On the whole, the book will be an excellent source of knowledge for the reader who is particularly interested in obtaining a general picture of the field, and will provide him with a good knowledge of the fundamental relationships and of the author's results. The practical worker, on the other hand, will have difficulty in finding information on methods of stabilizing a given plastic or on a processing or application problem. A short chapter showing the present position with regard to the stabilization of certain types of plastics, with reference to particular technical requirements, would greatly enhance the usefulness of a book of this type.

The presentation is excellent.

Joachim Voigt [NB 875 IE]

Chemische und biologische Laboratorien. Planung-Bau-Einrichtung (Chemical and Biological Laboratories. Planning-Building-Equipment). By *W. Schramm*. Verlag Chemie GmbH., Weinheim/Bergstr. 1969. 3rd Edit., 412 pp., 1200 figures, linen DM 98.—.

This standard work, which is important because of its comprehensive details and examples of plans for the construction of chemical and biological laboratories that have already been executed, has been out of print for several years, and is now available in a fully revised and enlarged 3rd edition[1].

The arrangement of the subject matter follows the same successful pattern as earlier editions, but a great improvement results from the use of the decimal classification system.

The material in the 20 chapters is based on the latest experience and technical developments in laboratory construction. Some of these chapters are considerably longer than in the 2nd edition, and a number of topics also appear in the book for the first time; in particular, these are Part 2 "General planning principles", Part 3, "Principles of the dimensioning and furnishing of laboratory rooms and buildings", and Part 4 "Guide to space requirements and floor layout in laboratories" Reference is made in Chapter 2 to the questions of flexibility, prefabrication, execution by general contractors, and the formulation and programming of the problem and of the design principles, which is essential for planning ahead.

With the aid of instructive drawings, the author deals with suitable dimensions for the laboratory, widths of passages, furnishing schemes of single and large rooms, and laboratory boxes. A noteworthy feature is a table giving the room, and bench dimensions of 50 laboratory buildings for predominantly chemical and biological fields of specialization; because of the numerous examples, this makes it easier both for the owner of the building and for the planner to visualize the space requirements.

The guiding values given in the fourth chapter for space requirements and outlay also provide pointers and possibilities of comparison for the assessment of designs.

In later sections, the advantages and disadvantages of the various types of buildings (low buildings and multistorey buildings are critically weighed). A distinction is drawn in the construction of buildings between conventional and industrialized building methods; as is shown by the photographs and drawings, increasing use is being made of prefabricated constructions in laboratory buildings.

As might be expected on grounds of importance in the laboratory, the book devotes considerable space to Chapter 7 "Technical supply equipment and installations". In addition to the two basic pipe arrangements, *e.g.* vertical and horizontal installation systems, good summaries are given for the first time of the possible combinations for the arrangement of the entire supply systems; the problems of drying, aeration and deaeration, and air conditioning of laboratories are also discussed in detail.

The questions of sound and vibration damping, protection against corrosion and acids, safety appliances, fire prevention, and protection against radiation, which are usually treated very cursorily, are discussed in great detail in Chapters 8 to 10.

The consumption figures, connected loads, and isochronism factors, which are important for the determination of the power requirements, are summarized in another chapter, making more accurate calculation of the requirements possible.

The discussions on the wide and many-layered field of laboratory fittings make it easier for the reader to judge and select from the designs that are currently available.

The chapters on "Laboratory rooms", "Subsidiary rooms", and "Animal rooms" have also been revised in the present edition, and contain an abundance of information, recommendations, and hints for arrangement, installation, and fitting; the information on climatic conditions for research animals, the space required by the animals, and cage dimensions and axis dimensions of animal rooms is extremely useful to the designer. The "open system" and the "closed system" described for SPF plants for animal rooms also provide useful hints for the less common special stalls.

Another new inclusion is Chapter 19 "Greenhouses".

The example part is greatly enlarged; it shows many laboratory buildings for a wide range of specialized fields and tasks. The new examples are all of buildings erected since 1960, and are therefore very up-to-date. The fact that they are confined to Central European installations is no disadvantage to the designer.

The present 3rd edition has not only been revised and enlarged by more than 60 pages as compared with the last edition, but has also been given a new, clear, and pleasing make-up. In this volume the author has provided a good, comprehensive source of advice on questions of laboratory construction. The interested reader should use and consider the copious factual information and the many suggestions and examples in this book as valuable aids in his future planning.

Oskar Grüneis [NB 872 IE]

Coordination Chemistry in Non-Aqueous Solutions. By *V. Gutmann*. Springer-Verlag, Vienna-New York 1968. 1st Edit., viii, 174 pp., 10 figures, bound DM 48.—.

The present book is remarkable in two respects. 1. It was written in English by an Austrian. Though some linguistic weaknesses must be taken into account, it is pleasing to find English gaining ground as a language for chemical communication in the German-speaking countries. 2. It classifies a large number of non-aqueous solvents (mainly covalent oxides, halides, oxide halides, and organic solvents containing functional groups, and less comprehensively the "water-like", ionizing solvents) and their chemistry purely on the basis of coordination chemistry, instead of according to the usual approach.

The discussion is based on the Lewis acid (acceptor)-base (donor) concept (Chapter I). Donor solvents (which preferentially solvate cations) and acceptor solvents (which preferentially solvate anions) are distinguished, and each of these types is divided into aprotic and protonic solvents (Chapter II). The Brønsted concept is also used for the protonic solvents; in general, however, the acid-base reaction is regarded only as part of the coordination chemistry, which is classified by the Lewis theory. The donor strength of an aprotic solvent is measured by the donor number DN (Chapter II), which is defined as the negative enthalpy of formation of $SbCl_5$·Donor in dichloroethane.

The acceptor solvents discussed are the hydrogen halides, HCN, H_2SO_4, HNO_3, H_3PO_4, HSO_3F, HSO_3Cl, HPO_2F_2,

[1] Cf. Angew. Chem. *74*, 334 (1962).

$H_2S_2O_7$ (Chapter IV), SO_2, ClF_3, N_2O_4, BrF_3, IF_5, AsF_3, and covalent chlorides, bromides, and iodine (Chapter V). This is followed by the discussion of the donor solvents (DN in parentheses) NH_3 (a more detailed treatment of the ammines passing beyond the qualitative would have been desirable in a book on coordination chemistry), N_2H_4, H_2S, $HC(O)NH_2$, $CH_3C(O)NH_2$, HCOOH, CH_3COOH, alcohols (Chapter III), and oxide halides (particularly $POCl_3$ (11.7), which has been investigated by *Gutmann*, originally on the basis of the solvent concept and his concept of ionotropy; he defends his results in detail against American workers) (Chapter VI). A series of solvents with increasing DN from ClH_2CCH_2Cl (0.1) *via e.g.* CH_3NO_2 (2.7), CH_3CN (14.1), $(C_4H_9O)_3PO$ (23.7), $HC(O)[N(CH_3)_2]$ ($\approx$ 27) to $[(CH_3)_2N]_3PO$ (38.8) follows (Chapter VII).

The coordination chemistry of the transition metal halides in donor solvents, which is discussed particularly fully and summarized in many tables (Chapters II, VI, VII, VIII) essentially involves three equilibrium reactions: 1. Formation of a complex anion by addition of an anion donor, 2. autocomplexing, and 3. ionization. Which reaction predominates depends on the relative donor strengths of the halide ion and of the donor solvent. The donor strength of the solvent C_6H_5COCl (2.3), for example, cannot compete with that of the chloride ion, so that the formation constant for $[FeCl_4]^-$ from $FeCl_3$ and Cl^- is greater than 10^{-4}. The donor competition of the solvent $(CH_3O)_3PO$ (23), on the other hand, leads to autocomplexing:

$$2\ FeCl_3(TMP) \rightarrow [FeCl_2(TMP)_2]^+ + [FeCl_4]^-$$

Finally, $FeCl_3$ is completely ionized in the strong donor solvent $(CH_3)_2SO$ (29.8):

$$FeCl_3 + 6\ DMSO \rightarrow [Fe(DMSO)_6]^{3+} + 3\ Cl^-$$

It follows *e.g.* that a solvent with a low DN should be used for the preparation of complex compounds, and a solvent with a high DN to eliminate unwanted hydrates.

This is a useful book, from which not only students, but also trained chemists can learn, and not least because of the plentiful references to the original literature.

Jochen Jander [NB 882 IE]

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Present-Day Communication in Chemistry – Problems and Possibilities

By Günter Kresze [*]

This article deals with the problems and possibilities in the present-day communication of chemical results and opinions. Personal communications as well as primary and secondary literature have to be supplemented in the future by documentation and information services which use modern electronic data processing equipment.

1. Classical Methods for the Communication of Information in the Field of Chemistry

The problem of communication in all branches of science is closely connected with the development of our thinking. People everywhere are challenging the validity of concepts and objectives that date from a period when the world was scientifically naive by today's standards; methods which were formerly adequate for solving problems are now proving inadequate. In the field of communication, especially in the natural sciences, these problems were recognized at a relatively early stage. An attempt will be made in this article to survey some of the basic problems and to give an idea of the main possibilities in this field.

The first category of problem is that of large numbers. According to the National Science Foundation's estimates there are 500000–700000 chemists and chemical engineers working in the world today. How does this number affect communication in chemistry? The "most natural" means of communication in any field is speech (Fig. 1), the direct communication of a result or an opinion. Speech plays an essential role even today.

The many conferences, for example, are proof of the importance accorded to oral communication. Direct oral or written discussion can meet the information needs of the chemist who receives it only if he knows all the people working in the same field. In individual fields of intensive research, *e.g.* biochemistry, where the research is directed toward a specific end, this requirement is still approximately satisfied. In most fields, however, the large numbers of chemists involved make this situation impossible.



Fig. 1. The "most natural" method of communication: speech (illustration: Daumier).

In general, therefore, communication is only possible through the intermediary of "exchanges". The classical medium for such communication is the primary chemical literature: journals, patents, monographs (Fig. 2). Communication thus becomes more indirect

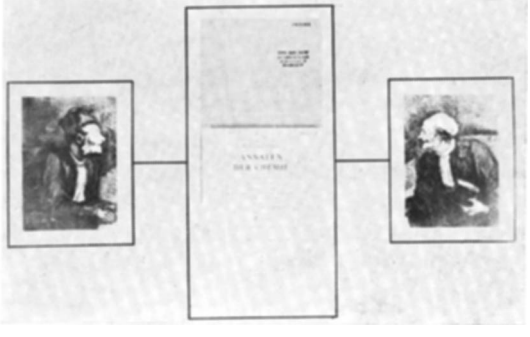


Fig. 2. The primary chemical literature as a communication medium.

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and more impersonal, but it is only in this way that it is possible at all. Let us consider the wishes of those involved in this type of communication and examine how far the primary literature is capable of fulfilling its tasks. First and foremost every author's wish is to communicate his results to all interested parties; he wants a target-oriented form of communication. The wish of every reader must be to find *all* the material that interests him in response to a specific inquiry. These wishes should be taken particularly seriously in the field of chemistry: the results of others are a considerable help to the chemist in his own work, and frequently have a decisive influence on the further course of this work.

How far are today's journals capable of acting as communication "exchanges"? According to the National Science Foundation's "Overview of World Wide Chemical Information Facilities and Resources" the total number of journals in the field of chemistry is at present 12000; about 300000 articles and 50000 patents appear every year. An estimated 25% of publications in the field of chemistry are contained in only 50 journals, 50% in about 250 journals and 75% in about 1300 journals. Furthermore, it is obvious that the individual chemist does not have to read all – or even the majority of – chemical journals to get the fullest information possible on his particular sphere of interest. The number is limited by the mere fact that many of these journals carry mostly articles from narrowly specialized fields, and this trend has recently been increasing. Nevertheless, one only has to compare the number of journals in existence with the number which, according to the 1967/68 questionnaire [*] sent out by the Gesellschaft Deutscher Chemiker (GDCh), the average chemist reads (eight) to see that the "comprehensive information" requirements cannot be even approximately met by the reading of journals alone.

For a long time, therefore, a further means of communication has been used in addition to journals, *i.e.* secondary chemical literature, lists of titles, or abstracting journals (Fig. 3). This means that there is another relay station in communication and hence a further depersonalization, as well as a further time lag. Even more stringent checks must be made on how far the introduction of a secondary service at least meets the requirement of specific and comprehensive information. Here we immediately encounter the second problem of communication in chemistry: information retrieval *i.e.* chemical *documentation.* Chemical results keep their value for a long time. Methods of preparation, data on the properties of compounds, and reactions can often still be used for one's own work even if they were first reported a hundred years ago.



Fig. 3. The secondary chemical literature as a communication medium.

The fullest possible retrieval of all earlier results, together with that of up-to-date information, is therefore an aim which the chemical communications services must achieve. This was the original objective of the abstracting journals which, like the handbooks, were intended to facilitate comprehensive and summary searches for compounds and factual data by means of their indexes. To ensure that *every* later search will bring to light all the available information, all relevant data must be extracted from a publication and reproduced by the abstractor. There is, however, much doubt as to whether this is necessary at all, and such an analysis in depth takes considerable time. The attempt to meet *documentation* requirements, despite the ever-increasing number of publications (nowadays the volume of chemical literature doubles every eight to ten years) and despite the fact that the number of processors is not increasing at the same rate, has led to the abstracting journals being behindhand in their work, something which has often been criticized in the past, and therefore to their being ineffective as vehicles of up-to-date information.

One way of using the secondary literature effectively as an exchange for communication in chemistry is to dispense with the task of documentation [1].

Briefly, we have seen that the increase in the amount of material to be communicated not only reduces the comprehensiveness of communication but also makes the communication aids used *qualitatively* incapable of fulfilling their function in the field of up-to-date information. Moreover, we are still faced with the fundamental problem that as the number of intermediaries involved in communication increases, so also does the possibility of falsification and delay.

The obvious conclusion is that traditional customs must be abandoned in the search for new ways of conveying up-to-date information which, although even more depersonalized than those used hitherto, will nevertheless probably be able to meet the main demands for the speedy dissemination of specific and comprehensive information. Such methods will be described in Section 4.

2. Requirements for a Communication System in Chemistry

While the welter of material has an adverse effect particularly on the speed and comprehensiveness of its communication, the second category of problems, the

[*] Summarized by *Ch. Weiske*, Nachr. Chem. Techn. *18*, 250 (1970).

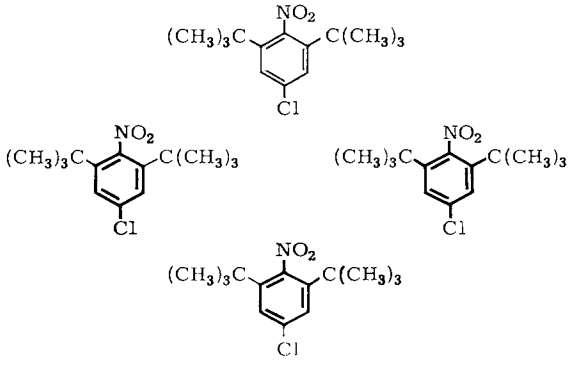
[1] For current work, see *Ch. Weiske*, Angew. Chem. *82*, 569 (1970); Angew. Chem. internat. Edit. *9*, 550 (1970).

change in the nature of inquiries, affects particularly the specificity and completeness of information. In the field of chemistry inquiries have been and are being received relating to substances, structures, and properties both in respect of up-to-date information and in respect of retrieval (retrospective search). The significance of these categories has, however, changed in recent years as a result of the development of chemistry from an empirical to a deductive science. This can be seen from a glance at the results of the GDCh's questionnaire (Table 1).

Table 1. Subjects of chemical documentation searches. (Evaluation of the Gesellschaft Deutscher Chemiker questionnaire.)

Searches for:	Answers (%)
1. Individual compounds	25
2. Partial structures	23
3. Reactions	22
4. Properties	7
5. Applications	5
6. Combinations of 1–5	17

Almost the same number of requests are received for information on *classes* of compounds with a common structural element, *i.e.* for "partial structures", as for information on individual compounds. Properties or applications alone, however important the search for them might be, are requested much more rarely than, for example, the combination of properties and structural characteristics. Searches for reactions (relation between the structures of the starting material and the end product) should also be regarded as combination inquiries of this type. A modern chemical documentation system must be capable of answering such inquiries. One way to achieve this is to arrange its contents in a systematic manner. A principle of arrangement is the basis of every documentation system. Arrangement systems which are still valid today have been created for chemical compounds in the handbooks. These allow compounds with common structural elements to be grouped together insofar as these correspond to the arrangement system used. When one realizes, however, how many groupings and how many partial structures could be of interest in later searches in the case of a relatively simple compound, *e.g.* 1,3-di-*tert*-butyl-5-chloro-2-nitrobenzene (chloronitrobenzene derivatives for the person interested in the S_N reactions of the aromatic nucleus; 1,2,3,5-tetrasubstituted benzenes for the molecular spectroscopist; *o*-*tert*-butylnitrobenzenes for the chemist working on



sweetening agents), it becomes clear that no linear arrangement system, however perfect, will allow a search for *all* conceivable groupings in a handbook or index. Every arrangement system must of necessity be *mono*dimensional, while present day inquiries demand *multi*dimensional search possibilities.

The situation is even worse when it comes to factual content; the indexes of monographs are mostly still in the form of compilations of words that are considered to be important and that have been extracted from the text, arranged solely on the alphabetic principle. The user is expected to find *the* word that has been used in the text for the concept he is looking for or to be able to think of words of a similar or the same meaning. There is a certain standardization for the indexes of abstracting journals: references are given for synonyms, *i.e.* words of the same meaning. They consist of collections of designations of facts (a "thesaurus"). Nevertheless, in searches for factual content – a property or an application – there is always the risk that some information will be missed if the traditional documentation aids, particularly indexes, are used. Furthermore, a desire for general information is often concealed behind the special formulation of enquiries relating to factual content. For example, an inquiry may be received that relates specifically to the antipyretic action of a substance, while, in the wider sense, information on other pharmaceutical applications may also be of interest. As with chemical structures, the documentation system must allow facts to be grouped together. Systems for the arrangement of the designations of facts, *i.e.* classifications, that make it possible to use more general or more specific concepts, as desired, in the formulation of an inquiry, have been under development for only a relatively short time in the field of chemistry. Such systems of classification, however, are essential for a specific and comprehensive search. Moreover, such systems must be constructed on a multidimensional basis; the traditional methods of documentation cannot meet this requirement.

Finally, conventional methods do not solve the problem of answering combination inquiries. In this case, as in searches for partial structures, the problem cannot be solved with a monodimensional register.

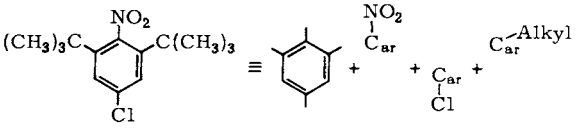
To sum up, conventional methods of chemical documentation enable one to find answers only to some of the questions which are important today. These shortcomings have come to be recognized during the past twenty years. This has led to severe criticism of the existing organs of communication, but it has also led to attempts to develop an adequate information and documentation system in the field of chemistry. Generally speaking it is certain that the systems of classification will have to be reconsidered before the problems described can be solved [2]. This specialist task can be performed only with the use of new *technical* methods.

[2] For re-examination of the objects and methods of communication in chemistry, see *R. Fugmann*, Angew. Chem. *82*, 574 (1970); Angew. Chem. internat. Edit. *9*, 555 (1970).

3. Computer Oriented Description of the Structures of Organic Compounds

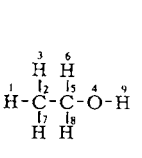
Electronic data processing machines, which offered a solution both to the problem of the welter of material and to that of polydimensional searches, fortunately appeared on the scene just when the communication problem was becoming acute in the field of chemistry, with the result that the technical means of solving the problem was on hand. However, the information to be communicated clearly could not be simply fed into a computer in the usual way in the hope that an inquiry will then meet with success. The information had to be transformed in such a way that it could later be found by computer. This means that a new *language* had to be created for describing chemical structures and factual data, and that arrangement systems had to be devised for chemical structures and factual data which allow full use to be made of the ability of electronic data processing machines to deal with combination inquiries; in short, that there had to be a reappraisal of chemical expressions. Taking the example of the description of the structures of organic compounds, the ways in which such descriptions are arrived at will now be briefly described.

One of the ways is based on the idea of characterizing the conceivable fragments in a structural formula by code symbols and using the sum of these code symbols as a description of the compound. In such fragment codes, for instance, we would indicate that the compound in our example contains a benzene ring substituted in the 1,2,3,5-positions, has a nitro group bound to an aromatic C atom and a chlorine atom similarly bound, and has one or more alkyl groups on the aromatic nucleus.



Many suggestions have been made for such fragment codes in recent years; within the range of fragments in the code they allow searches for partial structures. One of the most advanced codes of this type, the GREMAS system, is used by a European industrial chemical documentation enterprise, the IDC (Internationale Dokumentationsgesellschaft für Chemie mbH, Frankfurt) [3]. The advantage of such a fragment code lies in a structural description which is familiar to the chemist; this allows the clear formulation of inquiries that can be answered quickly and therefore cheaply with the aid of data processing machines, even when there is a large amount of material. The disadvantage lies in the fact that the translation of a structural formula into such a description, *i.e.* the coding, is an intellectual exercise which must be performed by specialists with a thorough knowledge of the often very complicated coding rules, and is a very arduous and expensive process where large amounts of material are concerned.

The second fundamental possibility for the description of chemical structures is the abstract summation of the atoms of the molecule in their relation to one another, *i.e.* topology. Figure 4 shows the principle of this technique.



a)

1	4	2	000
2	1	1	357
3	4	2	000
4	2	5	900
5	1	8	264
6	4	5	000
7	4	2	000
8	4	5	000
9	4	4	000

b)

Fig. 4. The instructions are as follows:

a) Draw the structural formula and number the atoms in any order (example: ethanol).

b) Write the numbers allocated to the atoms underneath each other, together with the element symbols (in the example, the figures 1 for carbon, 2 for oxygen, and 4 for hydrogen) and also the numbers allocated to the ligand atoms that are bound to the atom concerned.

The result is a sequence of numbers known as a matrix. This description is quasi-mathematically equivalent to a "graph", *i.e.* a system of straight lines (the bonds) and nodes (the atoms). This equivalence makes it particularly easy to process the description on an electronic computer. No knowledge of complicated coding rules is necessary for the topological description of structures [4], and it is even possible nowadays to automate the process to a large extent by using formula-reading machines. When the topological system is used, therefore, input is very simple and cheap, even where large quantities of material are involved. However, the retrieval of information is often very complicated. The partial structures, *i.e.* the groups of compounds, constituting the content of the inquiry have to be assembled in the data processing machine from many individual records. Searching is more arduous and more expensive than with fragment codes. The IDC has now succeeded in combining the two systems.

Topological input is followed by nonrecurring machine conversion into the well-developed fragment code, the GREMAS system. In the majority of searches, only this code is consulted. Thus, even when there are large quantities of data (more than 800000 structures are stored at present), rapid and cheap retrieval is possible.

The development in the description of the structure of a chemical compound, from the name through the fragment data to the topology, is an abstraction process and also a development of the ideas of chemistry. An analogous abstraction process, again using mathematical methods based on graph theory, can be seen in the preparation of factual content codes for processing in electronic computers. In this case the

[3] For the IDC System, see *M. A. Lobeck*, Angew. Chem. *82*, 598 (1970); Angew. Chem. internat. Edit. *9*, 576 (1970).

[4] For the topological description of structures, see *E. Meyer*, Angew. Chem. *82*, 605 (1970); Angew. Chem. internat. Edit. *9*, 583 (1970).

task was even more difficult; many, frequently inadequate or variously defined concepts, which furthermore vary in meaning over a period of time, had to be incorporated into a logical system [5].

To sum up, it is technically possible to overcome the difficulties described at the beginning of this article by the use of electronic data processing machines in conjunction with arrangement and description systems for chemical structures and factual data. The relevant information can be retrieved speedily and reliably from large quantities of material; it is possible to answer inquiries that are now comparable in importance with the so-called "classical inquiries", *i.e.* for groups of compounds of any type, or for combinations of structures and factual data.

Special mention should be made of one possibility in particular. Searches of this type can be formulated in such a way as to cover the entire field of interest of an individual worker, *i.e.* his "interest profile". If all the publications in one field are fed into a data processing machine as soon as they appear, then, by immediate searches for the topics of interest to the various participants, up-to-date information can be supplied by a communication system of this nature; furthermore, only the relevant information is supplied to individuals on a selective and specific basis. This is the principle of the "selective dissemination of information" (SDI) which is already used in many centers of industrial chemical documentation.

4. Information and Documentation Services of the Present and Future

The new technical scope for communication makes reconsideration necessary from another point of view. In this connection brief mention should be made of a problem concerned not primarily with communication itself but rather with the apparatus used in the conveyance of information. The diversity of the fields of interest and the different tasks involved in modern information and documentation, among other things, have led to the situation where at present many general or specialized information and documentation services exist *side by side*. Each of these centers evaluates the primary literature and analyzes it; for many publications this intellectual work is carried out twice, three times, or even more often. This has the advantage, particularly in the case of the specialized services, that they can to a large extent be adapted to suit the needs of their subscribers. On the whole, however, it means that both labor and money are wasted. If the traditional mode of communicating information proves to be inadequate, at all events when it is subjected to a thorough critical appraisal, then the information services must sooner or later go over to using methods which allow rapid selective dissemination of comprehensive information; *i.e.* they must operate a computerized documentation system. This means greater costs for the running of information and documentation services, and this increase in cost is intensified if many services are being operated side by side and if the same material is processed many times. If the very necessary conversion to modern working methods is not to be hindered by financial considerations, the mode of communication *must* be organized differently.

This reorganization has been a moot point for a fairly long time. Two concepts that regularly arise are the information *center* and the information *network*. Fundamentally one can imagine all primary chemical literature being evaluated in a single center. This center then operates information services, ideally for *all* chemists, or, by means of searches conducted on the collections of material stored immediately after evaluation, publishes target-oriented information in the form of notes relating only to the sphere of interest of the individual chemist, *i.e.* it operates an SDI.

The material stored at the center also serves for later comprehensive searches; it is the foundation stone of the documentation system. A center of this nature on a worldwide scale has come to be accepted as a near impossibility. In its place many centers concerned with the problem of the organization of documentation in the natural sciences, in technology, and especially in chemistry recommend a merger of the existing services. Such a merger would also be made technically much easier by the use of machine methods; an exchange of information based on computer tapes involves the use of very little language (or language that is easy to translate) and entails less difficulty than, for example, the exchange of abstracts, provided that a *uniform* system is used. Such collaboration has already been realized many times on a small scale. Thus, large European companies have come together in the IDC in order jointly to run a machine documentation system primarily in the field of low molecular weight organic chemistry. A similar system of collaboration is also getting under way in those services available to the chemical public. A first step toward such collaboration was the arrangement between the American Chemical Society and the British Chemical Society whereby agreements were reached on the joint processing of the primary literature and the creation of national centers to undertake machine searches. A similar agreement was reached in 1969 between the American Chemical Society and the Gesellschaft Deutscher Chemiker. It is to be hoped that this is the beginning of a modern worldwide chemical documentation system that is capable of meeting today's requirements.

A future chemical information network of this type might, for example, take the following form. Communication by means of lectures, conferences, and journals is supplemented by the dissemination of information by special high-speed abstracting services which, relieved of the documentation tasks that have hitherto fallen to the abstracting services, provide fast and specific reports on the primary literature in specific fields. By the use of machine aids in producing these

[5] For the graphical method of representing relations between concepts in mechanized chemical documentation, see *R. Fugmann, H. Nickelsen, I. Nickelsen*, and *J. Winter*, Angew. Chem. *82*, 611 (1970); Angew. Chem. internat. Edit. *9*, 589 (1970).

services it would be possible to produce indexes for abstracting journals and to keep the individual chemist up to date on the work of special interest to him with the aid of standing inquiries, *i.e.* to offer an SDI.

Apart from the up-to-date information, there will probably be only *one* general chemical documentation service, which will be operated on an international cooperation basis. It will be possible to search these documents by means of a computer; area centers will be set-up for such searches. The Gesellschaft Deutscher Chemiker, in collaboration with other German scientific societies and documentation enterprises, is planning to set up such a center with governmental support.

For the individual chemist this will definitely mean a wider scope for obtaining information and, to some extent, a change in his information habits. Up-to-date briefing will in the future be obtained through the intermediary of an SDI, as well as through reading journals and through special information services. Comprehensive literature searches in the library will frequently be replaced by machine searches in the documentation center.

The success of such a reorganization depends primarily on us all. Even the best, technically perfect system is useless if people fail to use it or do not use it enough; this is a sad observation that has often been made in the field of documentation. However, so that the individual can also make satisfactory use of the information services, he must see that, within reason, they will meet his requirements. This is also a problem of communication, of the contact between those who operate the information and documentation services and those who use them.

This active interest is also important from another point of view. A prerequisite for the use of a method is knowledge of it. The young chemist going into industry should know what possibilities are open to him for obtaining information. Not everyone has to know the details of the machine process, since this task is taken over by experts in practice. However, recruits must be available in relatively large numbers to take over from these experts. This does not mean that there should be special chairs for documentation in the universities. In the USA there are courses for the propagation of knowledge relating to information methods and the principles of machine methods. Such courses are also being planned in Germany.

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Chemical Information Services

By Christian Weiske [*]

The definition of information services derives from the demarcation between documentation and information. The main criteria for information services are up-to-dateness, clarity, manageability, relevance, and flexibility. In addition to the printed information media (tables of contents, lists of titles, abstract journals) services have been offered in recent years which are prepared with the aid of data processing machines and which operate on the basis of data tapes (SDI, profile searches).

1. Introduction: Information – Information Service

While documentation is generally understood to be a method for storing information or the systematic collection of published research results which can be consulted on specific subjects, information is variously defined as the end product of documentation [1], as the communication of news coupled with a literature-processing procedure [2], or in general as the reduction of uncertainty [3]. In this article the word will be interpreted as "apprizal" or "instruction" in accordance with the Late Latin meaning of the word "informare".

Taking this definition, the information services are media for the propagation of information. The media may differ, but they all have a common aim, namely to show scientists a way out of the dilemma of having to keep continually up to date but not being able to do so because of the large number of publications [4].

It is very necessary to have information so that one can press on with one's own scientific work, keep abreast of developments in one's own particular field,

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[1] *E. Pietsch*, Nachr. Dokumentation *19*, 199 (1968).

[2] *U. Bischoff*: Die Informationslawine. Econ-Verlag, Düsseldorf 1967, p. 12.

[3] *G. Wersig* and *K.-H. Meyer-Uhlenried*, Nachr. Dokumentation *20*, 199 (1969).

[4] *G. Kresze*, Angew. Chem. *82*, 563 (1970); Angew. Chem. internat. Edit. *9*, 545 (1970).

build foundations for theories and ideas, guard against avoidable financial losses, *etc.* [5–7].

Thus, according to the survey by the Gesellschaft Deutscher Chemiker in 1967 [8], chemists spend 6 hours a week on keeping up to date with current developments; this amounts to 15% of their working time for a 40-hour week. It is therefore extremely important that the information should be prepared and presented in such a way that the recipient can use the time available to him as effectively as possible.

If they are to be of use to the research chemist, information services, whatever their form, must be suited to the needs of the users and must therefore fulfill a number of conditions. The survey shows how few people recognize or take notice of this fact. About a third of the chemists consulted were dissatisfied with the information services available to them.

2. The Requirements of a Chemical Information Service

2.1. Up-to-dateness

One of the most important prerequisites of an information service is that the information it supplies must be fully up to date. Because of the very rapid development in almost all fields of chemistry (about 30–35 new publications are registered every hour) it is essential that information be the very latest. Although the time taken for publications to become outdated is a few years on average, it can be as little as a few months in special fields *e.g.* biochemistry. Another benefit to be gained from up-to-date information is the reduction of the delay between a new discovery and its use. *Voigt* [9] coined the term "technertia" to describe this phenomenon.

The basic problem is thus to minimize the time lag between the publication of a scientific document and the publication of the information. Since the information services are consequential upon the primary publications (journals, patents, reports, *etc.*) their up-to-dateness depends on the nature and depth of the evaluation of the primary publications and on how the results are produced (photochemical reproduction, offset printing, letterpress). Collections of tables of contents (*e.g.* Current Contents, Isotope Titles) require relatively little intellectual work, the depth of evaluation is not very great, and technical production is possible with very little loss of time. Collections of titles, *e.g.* Chemical Titles, the Signal Information from the All-Union Institute for Scientific and Technical Information, Moscow, Current Chemical Papers, and Chemical Biological Activites (with keywords), are certainly more demanding, but because their evaluation is not very deep and because of the low production costs they can be more up to date than information services based on abstracts. However, they can only be used as an aid to orientation. This is also echoed in the survey [8], according to which 73.5% of those consulted used abstracting services to keep up to date, while only 24.5% used lists of titles. This is partly because of other features demanded of the information services and partly because of the steady improvement of up-to-dateness that has been possible in the abstracting services. Thus only two months are required for the scientific and technical production of the Chemischer Informationsdienst, which first appeared in 1970, as compared with the three months required for the Schnellreferatedienst of the Chemisches Zentralblatt published until 1969.

2.2. Clarity

Another important factor for an information medium is good readability and clarity both in the organization of the information and in its arrangement. Thus *Erbersdobler* [7] claims that information work is facilitated by a layout with visual impact. General mention is made of typographically emphasized titles (*e.g.* by using semi-bold type faces). If the texts of the abstracts are supplemented with structural formulas, the readability of the abstracts is further improved for the chemist, and therefore the amount of time spent in sifting through the information is considerably reduced. Structural formulas are the lingua franca of the chemist. Examples are the Fortschrittsbericht of the Farbenfabriken Bayer AG, the Index Chemicus and the Chemischer Informationsdienst published jointly since 1970 by the Gesellschaft Deutscher Chemiker and Farbenfabriken Bayer AG.

The short abstract as defined by *Harbeck* and *Lutterbeck* [10], which should tell the reader whether it is worth his while to read the original itself, is normally sufficient for information purposes. The abstracts should be concise, indicative, and to the point, *i.e.* they should contain no superfluous material [11]. The reading speed can be further increased if the abstracts are introduced by a heading indicating the main content of the work. Abstracts of this type may be thought of as position abstracts [12]. An example is given in Figure 1.

The individual pieces of information in the information media can be arranged according to journals, *e.g.* collections of tables of contents (Current Contents *etc.*), or according to subjects, *e.g.* collections of titles and abstracting services, the arrangement by subject naturally being more useful for the reader. Therefore

[5] *R. Fugmann*, Angew. Chem. *82*, 574 (1970); Angew. Chem. internat. Edit. *9*, 555 (1970).

[6] *B. L. Mathers, H. B. King*, and *J. C. Rea*, Unclassified report, AD 650901, April 1967, Clearinghouse for Federal Scientific and Technical Information.

[7] *H. Erbersdobler*, Nachr. Dokumentation *16*, 200 (1965).

[8] *Chr. Weiske*, Nachr. Chem. Techn. *18*, 250 (1970).

[9] *O. Voigt*, Nachr. Dokumentation *19*, 5 (1968).

[10] *R. Harbeck* and *E. Lutterbeck*, Nachr. Dokumentation *19*, 15 (1968).

[11] *J. Koblitz*, Informatik *16*, No. 5, p. 5 (1969).

[12] *K. Ch. v. Rothkirch-Trach*, Nachr. Dokumentation *17*, 169 (1966).

Organo-Eisenverbindungen
B-1970

14-354 **Ein stabiler Heptafulven-Komplex**

(Ehntholt, Daniel J.; Emerson, George F. und Kerber, Robert C.; J. Amer. Chem. Soc. 91 (1969) 26, 7547–48; Dep. of Chem., State Univ. of N. Y. at Stony Brook, Stony Brook, N. Y.; engl.)

S 7142
Q 0051

Der Ester (I) des aus 7-Carbäthoxy-cycloheptatrien mit $LiAlH_4$ in 90%iger Ausbeute gewonnenen 7-Hydroxymethyl-cycloheptatriens addiert das Na-Salz (II) unter Stickstoff in entgastem THF bei −70° unter Bildung des luftempfindlichen, flüssigen Fe-Komplexes (III) (Ausbeute 45%). Mit Tritylhexafluoroantimonat bildet dieser ein beständiges, dunkelrot kristallines Salz, das vermutlich die Struktur (IV) oder (V) besitzt. Ein spektraler Vergleich mit dem analog aus β-Brom-äthylbenzol und (II) über den Komplex (VI) dargestellten Salz (VII) bringt keine exakte Strukturaufklärung. –

I. Heidrich

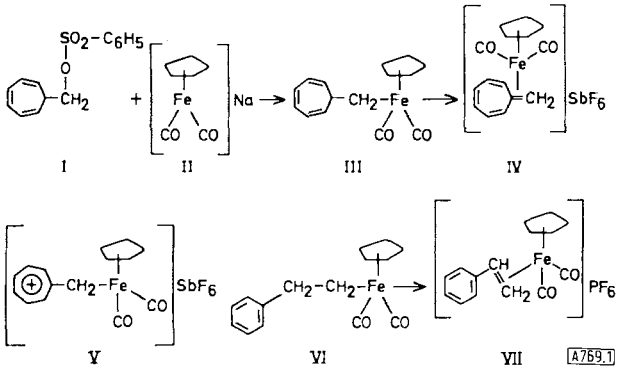


Fig. 1. Example of an easily readable abstract.

almost all information services use classification systems (UDC, DK [*], or their own) for the classification of the abstracts or titles they publish. According to its main content the information is filed in conformity with the system in the information service. The disadvantage of such a procedure is that articles containing several major points can be found only in one place. The abstract in Figure 1, for example, has several headings (S 7142 = organoiron compounds, isocyclic complexes, Q 0051 = seven-membered cycloaliphatic rings). Repetition of the same abstract is not possible on the grounds of cost. This shortcoming can be avoided by insertion of cross references in the other possible filing positions (*e.g.* in Chemical Abstracts) or by appending indexes, *e.g.* KWIC (Keyword in Context), keyword and compound indexes, to the journal issues. Keyword indexes with data relating to subject matter (properties, applications, *etc.*) as well as substance and compound classes, such as are found in the Chemischer Informationsdienst, are advantageous because the entries in the indexes come not only from the titles, as is the case with keyword indexes, but also from the text of the publication. With their alphabetically arranged keywords and additional context they are a valuable aid to finding specific information in the abstracts section [14]. In other words, the indexes are another form of information filed according to different principles.

To facilitate the use of the journal indexes "standardized" keywords [13], *i.e.* words taken from a concept list, are used instead of "free" keywords in the Chemi-

[*] UDC = Universal Decimal Classification; DK = Dezimalklassifikation.

[13] Nachr. Dokumentation *18*, 207 (1967).

[14] *W. Fricke, E. Kalex, F. Kretschmer,* and *M. Lüpnitz,* Informatik *16*, No. 4, p. 33 (1969).

ALPHA-NR. SCHLAGWORT Pho-Phy

P 3820.H PHOTOFLUORIERUNG
* FLUORIERUNG S.D.
* PHOTOHALOGENIERUNG S.D.
P 3850.P PHOTOGRAPHIE
P 3870.U PHOTOHALOGENIERUNG
* HALOGENIERUNG S.D.
* PHOTOBROMIERUNG S.D.
* PHOTOCHLORIERUNG S.D.
* PHOTOFLUORIERUNG S.D.
* PHOTOJODIERUNG S.D.
P 3910.J PHOTOHYDROBROMIERUNG
* HYDROBROMIERUNG S.D.
* PHOTOHYDROHALOGENIERUNG S.D.
P 3940.Q PHOTOHYDROCHLORIERUNG
* HYDROCHLORIERUNG S.D.
* PHOTOHYDROHALOGENIERUNG S.D.
P 3970.Y PHOTOHYDROFLUORIERUNG
* HYDROFLUORIERUNG S.D.
* PHOTOHYDROHALOGENIERUNG S.D.
P 4000.P PHOTOHYDROHALOGENIERUNG
* HYDROHALOGENIERUNG S.D.
* PHOTOHYDROBROMIERUNG S.D.
* PHOTOHYDROCHLORIERUNG S.D.
* PHOTOHYDROFLUORIERUNG S.D.
* PHOTOHYDROJODIERUNG S.D.
P 4040.Z PHOTOHYDROJODIERUNG
* HYDROJODIERUNG S.D.
A769.2 * PHOTOHYDROHALOGENIERUNG S.D.

Fig. 2. Section from the keyword list of the Chemischer Informationsdienst.

scher Informationsdienst (see Fig. 2). The author index is a further aid for those wishing to follow the progress of research teams. The indexes are produced by means of data processing machines at the same time as the abstract part of the journal. The advantage of this is that, once produced, the data tapes can be used in the development of further services (see Section 3.2).

2.3. Manageability (Format, Size)

The material issued by an information service should never be regarded as material for circulation. If it were it might either be passed on without being carefully looked at because of lack of time or it might fall into the hands of someone who keeps it to himself for a few months. In the first case the service would have failed in its aim to inform and stimulate, in the second it would no longer be up to date. For this reason the Chemischer Informationsdienst is intended to provide information for the individual chemist. The scientist should be free to mark the data he considers important, cut it out, and file it in his own card index.

This means, however, that care had to be taken over seemingly superficial things such as format when planning the new service since the material published by an information service, unlike a comprehensive documentation organ, has to be manageable if it is going to be read and used. In this respect, information services are like news magazines, which are also read anywhere and not merely at the desk. Not only to keep up to date but also to achieve a manageable size, therefore, it was decided that the Chemischer Informationsdienst should appear weekly; the result is a weekly output of 250–300 abstracts in the inorganic section and 350–400 in the organic section. Moreover, this system meets the demands of the users, the majority of whom prefer a weekly or fortnightly publication [8].

2.4. Relevance and Flexibility

Information services must be related to practice and hence also be flexible to the changing needs of their users. However, this is easier said than done. Because of their size, as well as on price grounds, the subscribers to the larger chemical abstracting journals, which are used both for searches and for keeping track of current developments, are establishments such as libraries, institutes, and companies. Most users have no direct access to the editorial staff of the abstracting journals, whereas this is important for the introduction of improvements into the abstracting service. Questionnaires distributed to determine the needs of the users unfortunately usually reach only the subscribers, who cannot be compared with the users. Therefore the Gesellschaft Deutscher Chemiker sent out questionnaires to its members. A successful move in the USA has been to call consumer forums which give rise to lively exchanges of ideas between the consumers and the information chemists.

It is particularly important for information service publications, whose circulations depend on the number of individual subscribers, to be relevant to current practice and to be tailored to meet the needs of the users. Hence when the Chemischer Informationsdienst was still in the planning stage its organizers profited by the industrial experience gained from the Fortschrittsbericht of Farbenfabriken Bayer AG and established the main policy for the new service in "hearings". One of the major outcomes of these planning conferences was that the users of an up-to-date chemical information service do not demand the kind of completeness necessary for a documentation system. On the contrary it is desirable, for the purposes of current awareness and for keeping an overall view of the stage knowledge has reached in the main branches of chemistry, that the less relevant publications should not be taken into account. *Bischoff*[14a] arrives at the same conclusion. He maintains that qualitative selection is necessary to cope with the avalanche of information. In his opinion the selective dissemination of information is a valuable help.

However, the introduction of the selection principle is certainly not without problems. A constant watch must be kept on its correct application by the readers of the Chemischer Informationsdienst. The scientists who make the selections bear a great responsibility. For this reason articles from fringe journals, the novelty value of which it is often difficult to judge, must be selected by experts from industry and research outside of the editorial teams.

Major journals which are well-known because of the quality of their articles and which fall within the field covered by the service are, however, fully evaluated. This is an additional aid to the subscriber because he no longer needs to look through these journals. An advisory board made up of university teachers and industrial chemists from various fields of research selects and classifies the journals in conjunction with the editorial staff. The members of this committee should be regarded as representatives of the users. They pass on to the board of the Chemischer Informationsdienst recommendations relating to the fields to be covered and the execution of the abstracts, the depth of analysis, *etc.* This ensures that the new service is relevant to current practice.

[14a] See ref. [2], p. 166.

3. Other Types of Information Services

3.1. Card Indexes, Microfilms

In addition to the type of service published in book form there are also services which take the form of microfilms or card indexes. Card indexes are the classic search medium. Both information and documentation are involved. The cards are filed according to salient features. If an article contains several salient points, the information is usually filed in several places. Since card index issues are being offered for the Chemischer Informationsdienst if the demand is sufficiently great, provisions were made to incorporate this feature of card indexes from the very beginning. Abstracts having several salient points receive a corresponding number of classification numbers. The subscriber can use this as a guide when building up his card index. The classification system with the classification numbers and their meanings is thus at his disposal. The services that offer their information on punched cards (edge-punched, notched, peephole cards), *e.g.* Documentation for Molecular Spectroscopy (DMS) are a modification of the classical card-index services. These services, however, are no longer pure information services.

Microfilm also fall outside the definition of information services given at the beginning of this article since they appear only after the journals of abstracts have been delivered and are used mainly for searches. It should be mentioned, however, that information services prepared with data processing machines (see Section 3.2) also use microfilm stores to supplement their computer answers (distribution of copies of abstracts instead of references)[15]. The microfilm service of the Chemischer Informationsdienst could also in principle meet such a requirement.

3.2. Selective Dissemination of Information

The user must himself sort out the information relevant to him from all the material supplied by the information services in printed or microfilm form. By so doing he is protected from becoming overspecialized and is from time to time stimulated by work in other fields, but it takes up more of his time. It is therefore understandable that information should be required that is tailored to meet the needs of the user[16]. There has recently been some discussion on whether field-oriented or mission-oriented information should be offered[17]. Suppliers of special services and special

[15] *H. J. Manecke*, Informatik *16*, No. 4, p. 46 (1969).
[16] *L. Vilentchuk*, Nachr. Dokumentation *16*, 94 (1965).
[17] *S. Adams* and *D. B. Baker*, Library Trends *1968*, 307.

card indexes have sought out and exploited this market (see Section 3.1, DMS). In this case too, however, economic factors set a lower limit for the number of subscribers.

There will therefore be no printed services that go any further toward meeting the needs of a few or just one individual, but such needs can be met by modern data processing techniques. The information meeting the requirements of the interested parties can be retrieved from magnetic tapes containing all kinds of data by means of data processing machines with suitable programs. The selective dissemination of information (SDI) by means of magnetic tapes has been discussed in the literature and has been successfully applied for some time. In the opinion of *Sage*, *Anderson*, and *Fitzwater* the selective dissemination of information is one of the most promising developments in the field of information [18] and *Brown* [19] believes that this method of communicating information will meet with increasing success.

In practice the magnetic tapes containing up-to-date information are checked against the user's search profile. As soon as the search term agrees with an entry on the information carrier, a high-speed printer types out the data. The information may consist merely of a reference number (*e.g.* abstract number) or of the literature reference for the appropriate work. The reference may be supplemented by the title of the work, keywords, *etc.* The answers are obtained by word analysis of the clear, uncoded text (*e.g.* titles) or by calling for keywords. Little work is involved in data input in the free word searches but the search programs are more arduous. On the other hand "structured" data, *i.e.* information that is arranged and categorized on input, has the advantage that it is easier to handle.

The data tape produced for the Chemischer Informationsdienst belongs to the second group. On it are stored the abstract particulars (year, part, issue, abstract number), the classification numbers given alongside the abstract, the title of the publication, the journal reference, the names of the authors, and the keywords with accompanying text in that order. The keywords are given in alphanumerical notation (letter + five-digit number) (see Fig. 2). The content of the accompanying text is roughly coded (*e.g.* 21 = preparation). As was mentioned earlier the keywords may be facts or classes of compounds. The issue indexes are also produced from this data tape. As will be obvious, however, it contains many more data, which are available for answering the inquiries of the participants in an SDI.

4. Cooperation in the Field of Information

The Chemischer Informationsdienst's data tape cannot give answers to inquiries for groups of compounds, partial structures, and reactions because of the way it is made up. This is a shortcoming that can be made good only by using the "structure tape" of the Internationale Dokumentationsgesellschaft für Chemie mbH (IDC). The IDC encodes the structural formulas and reaction schemes contained in the abstracts of the Chemischer Informationsdienst in accordance with the GREMAS system, and recently to a certain extent on a topological basis [20].

Originally, the structure tapes produced from these data were accessible only to the members of the IDC, but since April 1970 they have also been open to inquiries from university workers [21].

This is another step toward a national information system such as has been suggested by *Mathers*, *King*, and *Rea* [6] for the USA. These authors view the improvement of the existing information services and cooperation between them as the most practical solution. The cooperation between the editorial staff of the Farbenfabriken Bayer AG Fortschrittsbericht and the West-Berlin editors of the Chemischer Informationsdienst may be considered as the beginning of cooperation at a national level. Further signs of this can be seen in the existence of a working group for chemical documentation (Arbeitsgemeinschaft Chemie-Dokumentation) [22]. This working group deliberates on common development problems and thus helps to avoid unnecessary duplication and overlapping of work.

Even if such a national information system is set up it will in no way detract from the importance of cooperation with outside information or documentation systems. Furthermore, the work cited above [6] does not at all exclude the possibility of international cooperation. Indeed the superabundance of material makes such a thing urgently necessary.

With a view to the future, the Gesellschaft Deutscher Chemiker (GDCh) came to an agreement with the American Chemical Society in 1969. The terms of this agreement were that the GDCh should have at its disposal all the data tapes of the Chemical Abstracts Service (CAS) and that it should be empowered to use these tapes to develop special services [23].

Tapes from the following services are available for evaluation: Chemical Titles (CT), Chemical Biological Activities (CBAC), CA-Condensates (CAC), Polymer Science and Technology (POST), Basic Journal Abstracts (BJA), and other tapes which the CAS has not so far been distributing. Chemical Titles covers 130000 titles from 650 journals per year, and CBAC contains about 17000 abstracts from 550—600 journals per year. The compound numbers are contained on the data tape as well as the titles. CAC covers 250000 titles with keywords per year (the service therefore has the same coverage as the Chemical Abstracts Service), POST covers the work in the field of polymer chemistry (about 460 journals and appropriate patents), and BJA puts on tape the abstracts from 35 main journals. In this last case searches can be made for facts, compound names, and molecular formulas. Unlike the Chemischer Informationsdienst data tape, the CAS tapes are not structured. Tests on the CAS tapes have already been in progress for some years [24].

[18] *C. R. Sage, R. R. Anderson*, and *D. R. Fitzwater*, Amer. Documentation *16*, 185 (1965).

[19] *W. S. Brown*, Science (Washington) *158*, 1153 (1967).

[20] *M. A. Lobeck*, Angew. Chem. *82*, 598 (1970); Angew. Chem. internat. Edit. *9*, 576 (1970); *E. Meyer*, Angew. Chem. *82*, 605 (1970); Angew. Chem. internat. Edit. *9*, 583 (1970).

[21] Nachr. Chem. Techn. *18*, 156 (1970).

[22] Arbeitsgemeinschaft für Chemie-Dokumentation e.V., 6 Frankfurt/M., Varrentrappstrasse 40–42.

[23] Nachr. Chem. Techn. *17*, 325 (1969); Chem. Engng. News *47*, 22. Sept., p. 15 (1969).

[24] *A. K. Kent*, Svensk kem. Tidskr. *80*, 39 (1968); *J. Skov*, Nachr. Dokumentation *19*, 175 (1968); *M. J. Bloemeke* and *S. Treu*, J. chem. Documentation *9*, 155 (1969); *L. Bond, C. M. Bowman*, and *M. T. Brown*, *ibid.* *9*, 158 (1969).

Investigations are being carried out at present on a CA-Condensates test tape in the Development Division of Chemie-Information und -Dokumentation Berlin.

The evaluation of data tapes from foreign information services for information purposes in national centers has the advantage that it is easier to make contact with the users, and their requirements can be covered better. Furthermore, the experience they have accumulated in using the tapes is communicated to the producers of the data tapes *via* the national centers. The producers for their part take the suggestions into account in planning and development, so that the information services can be continually improved. The setting up of such a system should be advantageous to all chemists.

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Theoretical Aspects of Communication in Chemistry

By Robert Fugmann[*]

Nothing is more practical than theory
Ludwig Boltzman

Successful searching for publications on the basis of subject obeys rules whose relations to thermodynamics are unmistakable. As a collection of literature grows, the degree of order required increases, since the patience, time, and memory used by man to compensate for lack of order cannot keep pace. The high degrees of order that are necessary nowadays in scientific literature cannot be attained by traditional documentation methods. If modern techniques are used to improve communication, the conceptual basis of such a documentation method must be revised and adapted to suit the new possibilities. The conditions in chemistry are relatively favorable for the effective use of modern technical and conceptual methods, since the terminology has been developed further than in most other sciences.

1. Introduction

A factor essential to the progress of any piece of research is the closeness of communication with the scientific environment of the present and of the past. This communication is of direct practical value to any scientist or engineer if it provides him with experimental results that he no longer has to establish by his own time-consuming and costly experiments. Special investigations frequently even prove to be unnecessary, since the problem in hand has already been solved or brought close to solution.

Equally important is the heuristic role that has always been played by communication in science. In investigating unexplained phenomena observations by colleagues are as valuable as one's own findings, and the soundness of a hypothesis increases with the number of observations on which it is based. Furthermore, the more fully all subsequent experimental results are checked against this hypothesis (again largely a question of effective communication), the more rapidly and more reliably does the hypothesis develop into the final theory, *i.e.* the sooner one can form a new hypothesis with a greater explanatory value.

If one wished to obtain the epistemological raw material purely by one's own experiments and without the aid of communication, many generations would not be enough to complete the task in many cases. It is also not certain that the creative idea would emerge in any case after immersion in such an ocean of detailed work.

Communication is also involved when one more or less accidentally encounters new methods and results in other fields, after which these frequently prove to be extremely useful in one's own field. Many fields on the borderlines between physics, biology, and chemistry owe their relatively rapid development largely to interdisciplinary communication. It will be to the disadvantage of any research worker in the long run if he does not participate, or participates insufficiently, in this mutual give and take in science.

This is occasionally due to an individual way of working and a lack of willingness to communicate. However, other factors are always also involved, and they paradoxically result from the scientific work itself and the publication of its results. They become increasingly predominant with increasing intensity of

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the scientific work. It is obviously not enough that cognition and experience merely *exist*, printed in an exotic journal or presented at an exclusive lecture meeting. They must also be readily accessible to those who wish to advance knowledge or who require the published results for their own studies. Only then can they be useful in the heuristic or practical sense.

It is an accepted fact that people differ considerably in the extent to which they are inclined to consciously search for knowledge gained by others in order to utilize it, together with justified criticism, in their own situation. Thus, the efforts made by the individual scientist to look out for knowledge gained by others will vary between wide limits. Published knowledge is therefore all the less used the more troublesome the search for it is. This is all the more true in that the prospects of success in a search are often uncertain, whereas a result will undoubtedly be obtained in a reasonable time by one's own experiments.

A considerable discrepancy already exists between the actual outlay on research and development and the outlay that would be sufficient in case of effective communication. The resignation that is occasionally encountered in this connection is evident from the recommendation that a preliminary literature study may be dispensed with if the anticipated cost of a research project does not exceed 100000 dollars[1].

Various estimates have been made of the amount of unintentional duplication of work that results from lack of information about existing knowledge. The most reliable values for chemistry are probably around 30 %[2,3]. However, no one can guess how often new cognition in natural science has already failed to be reached merely because someone missed the vital link in the mosaic of facts, although it had already been published.

The present situation encountered in science is comparable with that of a manufacturing company which, while holding large stocks of its products, is faced with so much trouble in locating a specific article when an order is received that they rather repeat production than search through the existing stock. Eventual bankruptcy of such a company is by no means ascribable to faults in manufacturing techniques, for that is just the sector showing a tremendous productivity. Instead, the reason for failure is obviously to be sought in an entirely different sector that is nevertheless of equally vital importance.

The aim of the present article is to show the kind of obstacles that have stood in the way of fluent communication in science, and particularly in chemistry, and how these obstacles can be overcome with the greatest possible prospect of lasting success.

It is of secondary importance to these considerations whether the published knowledge is from journals or patent literature, has been published in a book, or was initially communicated orally. On the other hand, it makes a decisive difference whether or not one can *define* his information requirements, since only in the first case can the desired information be retrieved by a *directed* search. Otherwise it can be found only by *undirected* literature studies.

[1] *G. M. Corney*, Steel *152*, 20 (1963).
[2] *L. H. Flett*, Chem. Week *1960*, 75.
[3] *A. Neelameghan*, Library Sci. *5*, 264 (1968).

2. The Undirected Literature Study

It is inherent to science that no one can predict its progress in detail. Consequently, no one can specify in advance which future discoveries will be of particular interest to him. Only *after* hitting upon an innovation, *i.e. a posteriori*, can he decide from case to case and purely subjectively whether or not this is of interest to him. The discovery of penicillin or of the compounds of inert gases, the bonding of molecular nitrogen to organic molecules under physiological conditions, the surprising ability of saturated hydrocarbons to be protonated, and the accumulation of pure neutron matter in certain celestial bodies are only a few examples of subjects that might have interested any chemist. However, practically no one could have defined his interest in this direction *a priori*, *i.e.* before these phenomena were observed. It is only by regular undirected reading in the literature and by personal contact or by browsing in a library that one can keep abreast.

"What are the most favorable conditions for reaction A?" "What are the economic prospects for product B?" "What substituents reduce the toxicity of substance C?" These are also questions to which no documentation system can provide the answers. The questioner would be unable to decide *in advance* which of two reaction courses is the more favorable, if the apparatus requirements, the accessibility of auxiliary substances, the desired purity of the product, *etc.* have to be taken into account as well as the yield. Documentation can only help to uncover publications on these topics, and the questioner must then make a subjective judgement for himself.

3. The Directed Literature Study

The scientist's undirected literature study will provide him with information on a given topic at best from a certain time onward. The earlier literature had previously been disregarded by him. To include this literature in the search, reading must be confined to a very small part of all the previous literature, and this part must be selected in a *directed* manner.

The literature in its original state, *i.e.* in purely chronological order, is unsuitable for this purpose, since information relating to a topic is scattered in an almost completely random manner. One must therefore refer to literature prepared in some way in which the material of interest is more or less *localized*, either as itself or in the form of its representatives, *i.e.* the references. This prepared form of the literature may consist of monographs, handbooks, a well ordered library catalog, or an index. Alternatively, it is sufficient to localize the material of interest only when it is required, *e.g.* by selection procedures on a card index, a magnetic tape, *etc.* The preparation of literature in

this manner so that material on many subjects is localized or becomes localizable is the object of scientific documentation.

3.1. Terminological Requirements

Whatever the final form resulting from the preparation of literature in this manner, this preparation has usually been carried out by scientists *other* than those who will later use this aid for their directed literature studies. This is why the prospects of success in any directed literature study are strongly dependent on how far the terminology of a field has developed. They depend on how far it is terminologically possible for an author to express his ideas and experiences in the technical language, and how far the author's intended meaning can be grasped from this linguistic form of expression by a second expert. Terminological vagueness cannot be overcome even by an excessive employment of scientific personnel and technical aids in documentation.

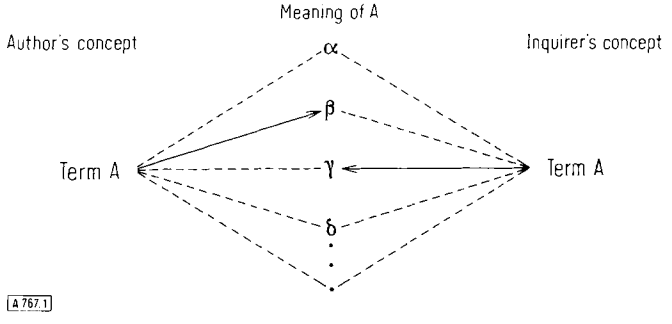


Fig. 1. Multiplicity of meanings of a term A.

To illustrate this, let us consider the unfortunate case of a term A with many different meanings α, β, γ, δ, *etc.* in common use. Two experts, *e.g.* the author and the inquirer, will therefore associate different concepts with the term A (Fig. 1).

One can *e.g.* easily encounter a dozen widely differing definitions for the term "corrosion", even when the medical and geological connotations are disregarded.

As an inquirer, the expert with the idea γ expects that the literature on the topic γ can be retrieved by means of the term A, *i.e.* in the simplest case under the subject heading A in an index. The word or words accidentally chosen by an author to describe this topic should not exert any influence on the assignment of the subject heading. However, the same requirement is valid for experts with the ideas α, β, δ, *etc.* They all expect the literature on their (different) ideas to be localized under the search term A.

The most that can be expected from a documentalist in this situation is that he will include *all* the concepts α, β, γ, δ, associated with a term A when they are recognizable in the text of a publication, and that he will make them all retrievable by the same search term A. Any inquirer, whichever idea he accepts, will then find literature references, many of which he will regard as ballast, since they correspond not to his own individual idea of the term A (*e.g.* γ), but to the other ideas α, β, δ, *etc.* This ballast inevitably increases in size with increasing heterogeneity of present and past terminology.

The situation in practice is less favorable still. It is impossible to establish all the ideas for each and every one of the numerous subject headings and to memorize them continually during literature analysis. Thus perhaps only the meanings α and β for the topic A will be considered, while all other meanings γ, δ, *etc.* are ignored. If these ideas occur in a publication, therefore, they will not be designated by the term A. This has a much more serious, though less obvious, consequence for many literature searchers than ballast, namely loss of relevant information.

If the *majority* of the terms in a certain field are terminologically vague, the maintenance of an intersubjective literature documentation based on joint work is an unrewarding task that can never be satisfactorily fulfilled. The only answer is for each worker to build up his own card index, in which he can use his own interpretations of the terms. Necessarily, he is then cut off from extensive communication with the literature in his field, since he can record at most only those publications that he has read himself.

The core of any chemical documentation system, *i.e.* substance concepts, is largely free from terminological difficulties of the type described. On the other hand, considerable vagueness exists in the terminology of reaction types. Even greater difficulties arise in borderline fields with engineering, biological, and other property concepts. A great deal of terminological work is required if communication in these fields is to be effective[*].

3.2. The Second Law of Thermodynamics in Documentation

In any directed literature study one expects the material on the topic of interest, at least insofar as it is definable, to be *localized* as well as possible in the part of the collection of publications to which the inquiry is addressed. For example, if the problem is to list the original literature on herbicidally active ureas, the collection should, so to speak, break down into two parts, in one of which the relevant material should be localized as completely as possible; this part should also be as free as possible from irrelevant material. The more complete this localization is, the surer the searcher can be that he will miss nothing relevant if he merely scans the localized part, and the less time it will take him to find the relevant material in this part (cf. Scheme 3 in Section 5.1).

The greater his uncertainty in this respect, the more he must rely on his memory – insofar as his time allows – in order to retrieve at least those cases which he himself has previously encountered in unforeseeable places.

Localization in this manner means nothing else but establishing order if order is defined as "meaningful proximity of the parts of a whole". The number of documentation systems that have been developed for this purpose is bewilderingly large. If on the other hand we accept the thermodynamic definition of order, it is relatively easy to obtain a general overview of these systems, and in particular to assess more reliably the very pronounced differences in their capabilities as well as their prospects for the future. *All these systems*

[*] Some terms from the documentation field are listed in Section 5.1, together with the meanings with which they are used here.

can be characterized by the degree of order that they can establish in the literature and by the extent to which they can be developed to obtain still higher degrees of order.

A collection of documents or references can exist in states with very different entropies[*], the state of least entropy and greatest order having the greatest working capability (*Erich Meyer*)[4]. Such a collection is productive in a very real sense, and performs useful work, so to speak, when this order provides an inquirer with practical or heuristic assistance in the form of an ordered collection of literature. Thus a documentation system with a high working capability will save much search time and effort of memory, both of which are always of only limited availability for a literature search. Moreover, a documentation of this kind will stimulate many scientists to undertake extensive literature studies.

3.2.1. Requirements as to the Degree of Order

Let us consider a case in which a medium degree of order prevails in or can be established in a collection of literature. Let us assume that 20 % of the references localized or capable of being localized for a given topic are relevant to the inquiry. It then makes an important difference whether there are two relevant references out of ten or 200 out of 1000. Purely because of lack of time, it will be necessary in the second case to content oneself with a few publications selected at random, and to tolerate loss of information.

If the references localized are to be scanned on the inquirer's behalf for relevant material by the documentalist, he will soon be overloaded by the amount of work that converges on him. This is true in particular if the collection is steadily growing. The number of searches with which the documentalist can cope steadily decreases, and he will be grateful for each search from which he is *exempted.* He is soon forced to sacrifice quality, and more and more often he has to restrict his search to *parts* of the collection ("the last few years are the most important").

If this work is left to the inquirer himself, on the other hand, the number of searches carried out will gradually dwindle to nothing, since this is, according to Mooers' law[6], the simplest way for the inquirer to avoid being overloaded by search work.

The result in either case is that the system will ultimately be discontinued, since the intellectual and technical outlay that would be required to keep it working would no longer be justifiable. Its working capability would thus have decreased in a very real sense, and would finally have fallen to zero.

If on the other hand *a higher degree of order* could have been established in the larger collection mentioned above, so that the 200 relevant references were localized among *e.g.* 300 instead of 1000, the information offered would be much easier to utilize, since it would generally be possible to read these 300 references instead of 1000 and "process" them intellectually.

It follows that the requirements as to order in a collection of literature increase with the growth of the collection. This is due to the limited and constant time available to man, the user of the system. Thus, if the growth of a collection of literature is regarded as a natural and even very desirable process, one must also recognize the need for a continuous increase in the order that prevails in this collection or that can be established in it.

It is even better to establish, as early as possible, such a degree of order that will be adequate to maintain the working capability of the collection for as long as possible in the future. For, to any given degree of order there corresponds a certain method of literature preparation and of localization in this collection (see Section 4). If this method were repeatedly changed to achieve increased order and to increase the working capability, the collection would become so heterogeneous over the years that it would no longer be possible to search through it reliably as a whole, since a different variant of the localization method would be required for each past period of literature processing.

Another factor that increases the demands as to order is the *frequency with which the collection is used to obtain information.* An ordered collection of literature naturally becomes more attractive to the inquirer as it grows. However, the time available to man for searching can be used up not only because of the increase in the time taken for each single search, but also because of the increase in the number of searches. This would lead to the same overloading even if the time required for each single search remained unchanged. Thus, as searches must be carried out with greater frequency, it becomes more important to counteract the increasing search work by a corresponding increase in order.

The degree to which the future of a literature documentation is assured is seen when the tendency toward specialization in science begins to affect the kind of inquiries addressed to the collection. In the example given above, we had to find 200 references that were relevant to a given topic. If this inquiry were repeated in the same form 20 years later, the result might be 2000 relevant references. A topic on which the literature volume is moderate today may grow extensively in only a few years. For instance, the needs of the steroid chemist in earlier times would have been satisfied if every relevant publication had been posted under the subject heading "steroid". Nowadays, on the other hand, it is normal that inquiries in the steroid field specify the precise positions of certain substituents on the ring skeleton, the exact positions of double bonds, the configurations and conformations at carbon atoms, *etc.* These inquiries can now be answered only if the documentalists of many years ago had the foresight to devise, test, and use sufficiently detailed methods in literature processing. Similarly, it is still necessary today to make *provisions for future*

[*] In this discussion "entropy" is always to be understood in the thermodynamic sense, and not in the sense in which it is used in information theory[5].

[4] *Erich Meyer*: Grundfragen der Patentdokumentation. VDI-Verlag, Düsseldorf 1960, p. 207.

[5] Cf. *W. Meyer-Eppler*: Grundlagen und Anwendung der Informationstheorie. Springer-Verlag, Berlin 1969, p. 78.

[6] *C. N. Mooers*, Amer. Documentation *11*, 204 (1960).

specializations and to record such details *now* that will be used as search conditions only in the distant future.

Thus it is an essential criterion for the future usefulness of a literature and patent documentation system that it should at any time possess a remarkable reserve of inquiry specificity. In other words, provision must always be made for degrees of order that will be utilized only in the future, and which would always appear excessive when measured against present-day requirements.

3.2.2. The Price of Order

Any increase in the degree of order such as is necessitated by the three factors mentioned (growth of the store, increasing frequency of searches, tendency toward higher specificity) is inseparably bound with an increase in cost. As a postulate of thermodynamics, increases in order never occur spontaneously, but must be enforced by a supply of energy. Otherwise we would have a perpetual motion of the second kind. The amount of energy that must be supplied inevitably increases with the degree of order that is desired.

In documentation, the energy that must be supplied to establish order is mainly intellectual work. Those concepts and connections of concepts on the basis of which the literature is later to be ordered must be selected from the publications to be stored. These facts must then be brought into a form that can be predicted in future searches, to ensure that the inquiry can be phrased adequately.

In addition to this work, it is often necessary to write an abstract that presents the essentials of a publication lucidly, and to this are often added programming costs and the cost of the machines used.

The higher the degree of order that is desired in a collection of literature the greater is, for thermodynamic reasons, the cost of these operations. For example, if it is desirable to be able to localize literature not only on specific compounds, but also on certain methods for the preparation of these compounds, possibly under certain operating conditions, then all concepts relating to synthetic chemistry and to chemical engineering must also be selected from the respective literature, translated into a suitable form, and stored.

In the short-term view, therefore, it will always appear that a very pronounced decrease in the cost of literature processing could be achieved by a small decrease in order, although such a measure is necessarily accompanied by an increase in the work of searching. In doing so, however, the future prospects of the system would be reduced, since the result would be a lower degree of order and hence a cut in the reserves on which the system will very soon have to call. However, one should not bemoan the surprisingly high cost of a documentation system with a guaranteed future, since the steadily increasing use of a growing system will more than justify the cost, provided that the system retains its working capability.

One of the peculiarities in the documentation field is that the working capability of a literature collection can be very easily decreased, and that the consequences of such a change are extremely serious. By merely continuing a procedure that was initially entirely satisfactory one can steadily devalue the whole outcome of the procedure. This decrease in value even affects the work that was done earlier by this procedure and that adequately satisfied the requirements at that time, since the collection was then much smaller, since search frequency was low, and since inquiries of the more general kind still predominated.

If the decrease in the working capability finally brings the documentation system to a halt, the fruits of all the documentation work carried out in past years must be written off as valueless. Apart from the system's use in former years the situation is then the same as if no literature documentation had been carried out at all. This means a serious loss of time, work, and results.

The requirements as to order, and hence the minimum cost, are much smaller for systems that will always remain small. This situation is found in fields in which the literature quickly becomes obsolete or uninteresting for some other reason.

A similar situation prevails when it is intended to select from current publications only those in which the user is most likely to find material of interest. Facilities of this kind have been available for a long time for journal and patent literature. Rough grouping is adequate for this purpose, since the part of the collection that is to be scanned by the user is, relatively speaking, very small. It includes only the recent publications from the last issue of an information bulletin of the "current awareness" type.

It would be wrong, however, to think that groupings or indexes based on such very general topics need only be cumulated mechanically in order to establish cheaply a large collection of literature for retrospective retrieval purposes. Since such a cumulation process is not associated with a second and deeper analysis of the literature, the degree of order in the cumulated collection is no greater than that in the original collections. Such a collection would very soon lose its working capability, and would thus become valueless for searches of the retrospective type.

A method that is often considered for the wide field of patent documentation is also merely cumulative. It involves the separate development of viable special documentations for the various fields, which is not excessively difficult or expensive. It has been suggested that a comprehensive documentation for the field as a whole could then be obtained by purely assembling these subsidiary systems. Again, the order in this cumulated system can never be greater than that of the individual parts. However, the order requirements for any one of these parts would be much less rigorous; the order in the cumulated system will also be correspondingly low, whereas the requirements here are very much higher. Accordingly, cumulation in this manner leads not to an integrated system for the field as a whole, but to chaos.

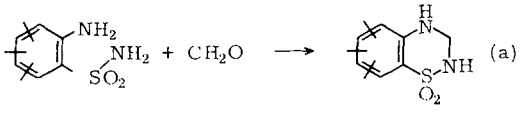
3.3. The Nature of the Order that Can Be Required

We have considered in an abstract manner the degree of order that is desirable or necessary if a literature collection is to remain capable of working. The degree of order is a measure of the extent to which irrelevant publications will be found in the localized part of the ordered literature collection (ballast), and of how many relevant publications of the collection are absent from this part (loss of relevant information). We have not yet considered the question of the conditions that a publication must satisfy in order to rank as relevant to the inquirer's topic.

The inquirer can expect to find the literature in an ordered state such as he has in mind only on one condition: He must be able to define the nature of this order. It has already been shown in Section 2 that those literature problems that cannot be adequately defined fall entirely in the field of the undirected literature study.

Experience has shown, however, that most chemical searches in practice fall in a broad border area between directed and undirected literature studies. The inquirer is entirely unaware of this problem if he is accustomed to carrying out the search himself. With the modest means available to him (usually conventional indexes) he cannot narrow his particular field of interest adequately. He therefore has to scan much more literature than is relevant to his problem. After having digested the scanned publications, it is easy for him to decide intuitively and subjectively whether the additional concepts, for which he had no suitable subject headings in his search, are also satisfied. To do this, there is no need to decide on the nature of these additional concepts *a priori*.

If a literature study of this nature is delegated, it is an essential part of the documentalist's duty to clarify, by discussion with the inquirer, which parts of his inquiry are to be regarded as defining the problem and which are intended merely as examples. In an inquiry for literature on the reaction (a), for example, it could emerge from such a



(a)

discussion that the inquirer is interested not only in formaldehyde itself, but also in its derivatives (acetals, 1,1-halogeno ethers, *etc.*) and in formaldehyde generators (hexamethylenetetramine, methanol-dichromate, formic acid by disproportionation, oxalic acid likewise, *etc.*). Even reactions involving "low aliphatic aldehydes" in general, as well as their generators and derivatives (enols, epoxides, *etc.*), may be of possible interest. The formulation given by the inquirer could even be open to objection in respect of the starting material indicated. It would fail to retrieve *e.g.* the ring closure reactions of the acylated amino compound or of acylamino sulfonyl chlorides, in which replacement of halogen by an amino group and ring closure take place in a single step. The definable object of the search would thus merely be "ring closure to form the 1,2,4-thiadiazine derivative", and the documents found in this way would then have to be checked *a posteriori*, preferably by the inquirer himself, to see whether they satisfy the entire aim of his search.

Even when everything that cannot be defined *a priori* has been eliminated from an inquiry, the decision regarding the relevance of localized references is still occasionally problematic. Judgement of relevance is at present a highly controversial topic in documentation literature, and several criteria have already been proposed [7], in some cases even with graded evaluations. However, a rough division into relevant and non-relevant publications is sufficient for our purposes. To illustrate this, let us consider the inquiry: "Obtaining α-amino acids by fermentative processes with microorganisms".

An inquirer can expect a documentation system to localize all the publications, as far as they are contained in the collection, in which

a) the desired concepts occur with equal or higher specificity,

b) the concepts are connected in the desired manner, so that they occur in the desired context.

[7] Cf. *S. E. Robertson*, J. Documentation *25*, 93 (1969).

The words that an author happened to choose to express his results or ideas should be of no influence. Moreover, the subject of interest need not even have been referred to expressly by the author. For example, in a process that proceeds "aerobically", it is unnecessary to mention that microorganisms are involved. If amino acids are obtained in a "fermenter", a common type of apparatus for this process, the participation of microorganisms is again implied with sufficient clarity. The formation of amino acids is indicated by a report on the total hydrolysis of proteins or on the determination of the hydrolysis products with the aid of typical amino acid reagents, *etc.*

On the basis of all these criteria, the following topics would be relevant:

1. "Treatment of filtrates from the cultures of *Acetobacter suboxidans* to isolate L-glutamic acid as the sodium salt".

2. "A sugar-decomposing microorganism is grown in a culture medium with a source of nitrogen, and the amino acids formed are isolated with the aid of ion exchangers".

3. "Biotechnical production of diaminopimelic acid by *E. coli* in submersed and aerobic cultures".

4. "Increased formation of free amino acids, particularly glutamic acid, in the aerobic degradation of wheat straw".

5. "Production of L-amino acids from keto acids in the presence of L-glutamic acid as a catalyst with the aid of a multienzyme system from *Cl. butylicum* with the addition of extracts from *E. coli*".

The following topics would not be relevant according to the above criteria:

6. "Formation of α-ketoglutaric acid by *Aerobacter aerogenes* in a culture medium containing glutamic acid".

7. "Formation of acids in sausage fillings after infection with the microorganism *Lactobacillus plantarum*".

8. "Determination of amino acids, particularly glutamic acid, by cultivation of a *Pseudomonas* mutant that requires glutamic acid on a deficient culture medium".

Should a general topic of the type 7 be of interest as well as the specific topic, the inquiry would have to be formulated in a more general manner at the outset. However, the inquirer must be protected in some way against excessive generality, and the best solution is to draw the line where the stored publication becomes more general than the inquiry. Otherwise the position of the dividing line with respect to non-relevant responses could not at all be defined reliably.

In special patent searches, however, the situation may be completely reversed. In a search to establish the patent situation regarding a certain subject, for which an application is intended, one is interested in all more general claims that cover this subject. Subjects that are more specific than the subject of the intended application, on the other hand, are of minor interest. They must be covered primarily in a search for novelty.

3.4. Distortion of an Inquiry

Every user of a documentation system should realize that localizing all relevant publications in a collection, approximately without loss and without ballast, is an ideal case of extremely high order. A documentation system can approximate to this ideal case only insofar as the means are available in the form of adequately qualified personnel and technical aids. However, the user must also accept that some of his expectations could prove to be generally incapable of fulfillment, since he is unable to define these expectations.

On the other hand, the documentalist is well advised to pay the greatest conceivable attention to the requirements that *can* be satisfied. The surest way of taking practical requirements into account is to carry out an extended analysis of the needs of future users and to try to ensure the localization or localizability of the literature relevant to inquiries of the types recognized, in accordance with the above criteria.

In particular, it would be a serious misunderstanding of the task of documentation if the inquirer's expectations regarding his general inquiry concepts were not fulfilled. To find literature on "amino acids" in a certain context, it should not be necessary for the inquirer to list all conceivable *specific* members of this group, or to enumerate all (!) conceivable species of microorganisms that might occur in the desired context. It must be left to the documentalist and his system to include these concepts unasked, so that an inquiry for a generic concept will be satisfied not only by a stored concept on the same specificity level, but also by all more specific subconcepts of this generic concept. If a system does not allow the localization on this basis so that the inquirer or documentalist is forced to list all more specific concepts as alternatives, the result is usually *falsification* or *distortion* of the original topic, since the selection of the more specific concepts to which one is forced to commit oneself will usually be incomplete. In no circumstances can he then expect the satisfactory localization of the literature in which he is interested. The best result that can be obtained after such a distortion of the topic by the enforced specificity is precise localization on the basis of the distorted topic, and this will necessarily be associated with loss in respect to the original form of the inquiry.

If forced to use more specific concepts, one will naturally include mainly those for which the probability of being found in the literature is greatest. They may, for example, still be remembered from earlier literature studies. Glutamic acid will thus be favored in comparison with an aminostearic acid, *etc.* The frequently given advice, however, that the inquiry should be confined to the "correct" subconcepts is worthless in this general form, since it presupposes knowledge of what one wishes to learn, *i.e.* of the existing literature on this topic and of the contents of the store. A listing of subconcepts for retrieval would be easy to make *a posteriori*, *i.e.* after examination of the entire store. In retrieval, however, the same judgement must be made *a priori*.

Distortion of the original inquiry again occurs if instead of a concept of the inquiry such as "amino acid" or "microorganisms" only a more *generic* term ("aliphatic carboxylic acids", "primary aliphatic amines" or "plant life forms", "organisms") is available for localization, the distortion in this case being due to enforced generalization. The inevitable result is that the publications localized will include ballast in an amount that depends on the degree of distortion. The causes are again purely conceptual in nature, and even the most effective mechanized localization technique can do nothing to alter the situation.

The above discussion leads us to the postulate that for substantially every scientific inquiry topic, insofar as it is definable, there should be an extremely precise formulation under which the relevant literature is localized (index) or can be localized (mechanized systems). To fulfill this postulate these undistorted formulations should be able to be chosen just as specifically and generically as the inquiry topic itself. This means that a very great number of these "inquiry terms", as we shall now call them, should be available in a documentation system. The greater the number of meaningful inquiry terms and the greater their differentiation, the greater is the likelihood of finding an inquiry term that corresponds exactly to the inquiry topic; this is a fundamental necessity for localization with the minimum loss and ballast.

It sometimes becomes necessary to resort to concepts bearing no systematic relationship at all to the theme of the inquirer. If a search is made, *e.g.* for production routes for a particular class of compounds, a search for supposed authors of relevant documents means a considerable distortion of the original search idea. Ballast and loss will be correspondingly large. — Similar conditions apply when one bases his literature search on the citations given by authors. These citations naturally refer to conceptually highly diverse publications which rarely form a meaningful class with regard to the specific idea of the inquirer, since the work of any one author is mostly made up of diverse statements that are the subjects of his citations. Nor can any author even approach completeness in his citation of all the pertinent previous work conducted by other chemists that is likely to be of interest to an inquirer with his own individual viewpoint.

As to the number of inquiry terms available, and in general the extent to which distortion of the inquiry topic can be avoided, great differences are found in the present-day methods of practical chemical documentation. These methods therefore differ greatly in the degree of order that can be brought into the literature with their help.

4. Practical Methods for Directed Literature Studies

The discussion of these documentation methods is easiest if they are divided into three groups:

1. purely intellectual localization,
2. purely mechanized localization,
3. combined intellectual and mechanized localization.

Intellectual and purely mechanized localization methods are distinct opposites in scientific documentation, with characteristic advantages and shortcomings. Neither of these methods can lead to high degrees of order if used in isolation. Their specific defects can, however, be overcome by a suitable combination of the two methods, and combinations of this type form the basis of the most successful documentation systems today.

4.1. Purely Intellectual Localization

In the purely intellectual localization of literature, any publication that falls in the respective subject field is usually examined by a documentalist to establish

which important concepts and topics are expressed or implied.

To do this a publication need not satisfy any special conditions or standards, except that it must be easily understandable to any expert. It is no obstacle in intellectual localization if the publication is in a common foreign language, nor does it present any serious difficulties if the author uses trade names, scientific nomenclature, or names chosen by himself and not agreeing with any standards for structures and reactions. When the documentalist encounters unfamiliar terms or novel concepts, he turns to a reference work, or confers with colleagues. Concepts that are merely implied are also recognized and denoted by appropriate subject headings. Thus, irrespective of the formulations that the author happened to choose, in intellectual localization a very pertinent picture of the author's ideas is obtained. This is in sharp contrast to the purely mechanized localization discussed later. This picture, however, is an essential prerequisite for reliable localization of the literature on a topic in question.

The documentalist also bears in mind a substantially preset vocabulary of inquiry terms for generic concepts and topics of which it can be said that there is some probability of their being used in inquiries. In the simplest case this is the vocabulary of subject headings for generic concepts that is characteristic of subject indexes.

If it is found that a publication is relevant to one or more of these subject headings, they are assigned to this publication[8]. This completes the most important step for the intellectual localization of the literature, *e.g.*, under the subject headings of an index or of a conventional card index or on the concept cards of a peek-a-boo card index.

4.1.1. Lack of Order in the Vocabulary of Inquiry Terms

The difficulties inherent in this technique are illustrated by the structure shown in Scheme 1. Let us assume that literature regarding the carbonic acid derivatives of aminobutylbenzenesulfonic acids is being searched for. In order to find the pertinent subject heading, or at least approximately pertinent subject headings, in an index, one has to have a complete overview of the whole vocabulary; for, an appropriate subject heading may occur in almost any alphabetical position in the vocabulary. Frequently, an approximately pertinent term will not be found at all. When it is to be memorized as reliably as is required in a search, a vocabulary should contain no more than one to two thousand subject headings. If this limit is exceeded it becomes unlikely that the documentalist will reliably remember the appropriate term and actually use it both during literature analysis and during searching.

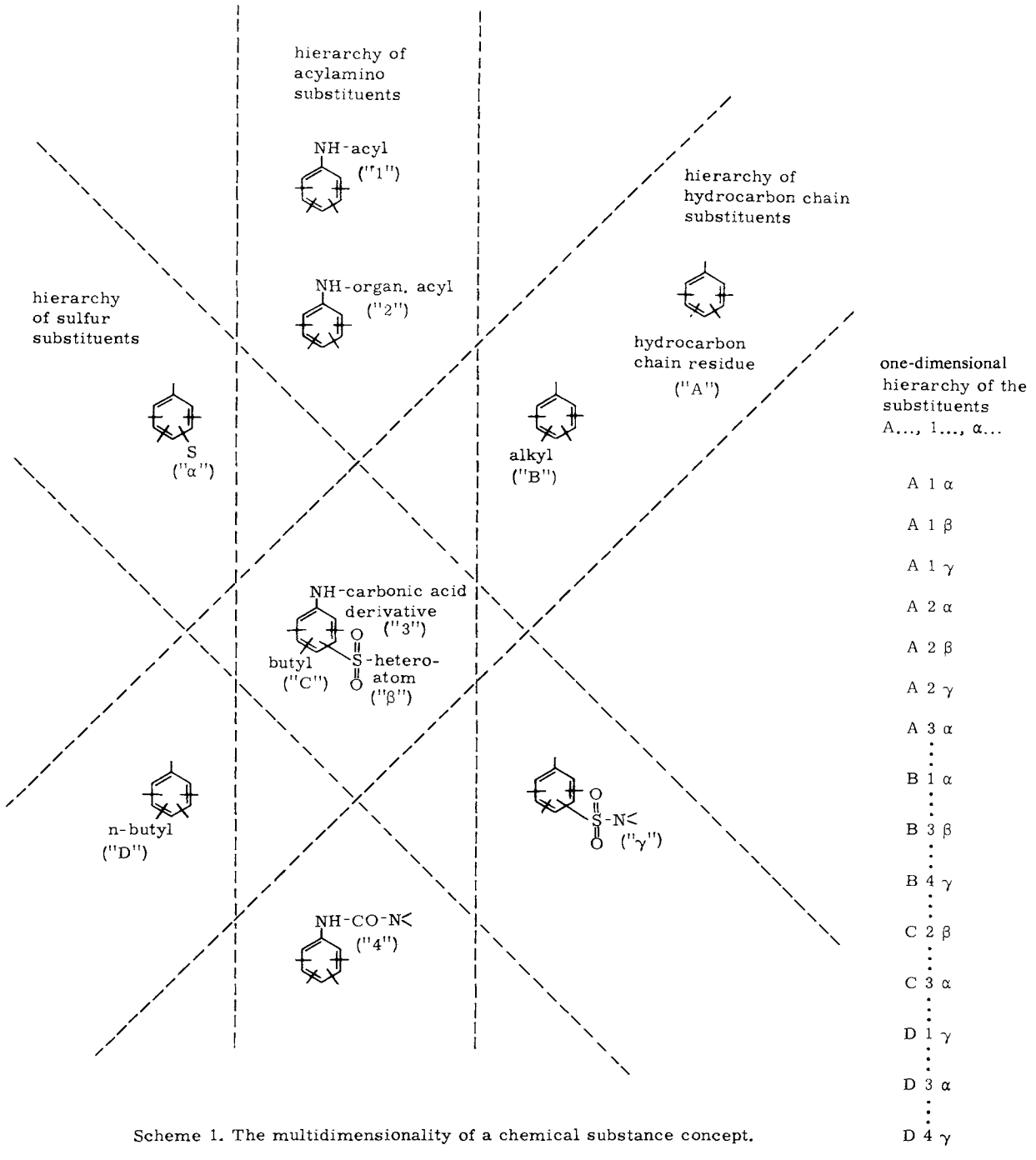
[8] *C. L. Bernier*, Amer. Documentation *16*, 323 (1965); cf. *J. Koblitz*: Schlagwortgebung in Information und Dokumentation. VEB Bibliographisches Institut, Leipzig 1968.

Many present-day subject indexes give the impression of an extremely large and highly differentiated vocabulary for generic concepts. The fact that *e.g.* no more than a dozen articles are cited under the subject heading "diene synthesis" in an annual index of world literature, however, shows just how unreliable intellectual localization with such a vocabulary is in practice.

Thus, the problem of order is met on another level: If order is to prevail in a collection of publications, then an order should be established before in the vocabulary of subject headings. One should not have to rely on memory and patient searching if an optimum choice of subject headings is to be made. Instead, the subject headings that come into question for this choice must be brought together at a predictable place in this vocabulary, as completely as possible and mixed with only a minimum number of nonpertinent subject headings. If this order is not established the vocabulary must be restricted to far too small a size if it is to be capable of functioning. This is a serious obstacle to the localization of the literature with the aid of this vocabulary for an undistorted representation of an inquiry theme will only rarely be possible. Thus a high degree of disorder, *i.e.* ballast and loss, will mostly remain after purely intellectual localization, owing to the lack of order in the vocabulary.

The basic reason for the lack of order in the literature after purely intellectual localization lies in the impossibility of achieving a sufficiently high order of technical terms with the aid of the conventional kind of index, which is usually the outcome of this kind of localization. The aim to express hierarchical relationships between terms by spatial proximity can only be accomplished for a single dimension. Hierarchical relationships between terms, however, normally extend over many dimensions. For instance, it is possible to proceed from the central concept in Scheme 1 in a variety of dimensions and to arrive at a related concept, depending upon whether one moves in the hierarchy of the hydrocarbon chain, of the acylamino group, or of the sulfur substituent. Just this simple example gives $3\times4\times4 = 48$ substance concepts if the vacancies in this scheme are considered occupied by further dimensional intersections.

If one were forced to arrange these interrelated substance concepts as a linear series, as indicated in abbreviated form on the right-hand side of the scheme, it would be possible to base such an arrangement on only one dimension as a primary ordering principle, *e.g.* the dimension of the hydrocarbon chain. Such a list would begin with all representatives having the generic concept "hydrocarbon chain" ("A"), combined with variants from the other dimensions. Then would follow all representatives bearing an "alkyl" ("B") substituent. The list would close with all substance concepts containing the *n*-butyl substituent. No objections could be raised regarding the order in the dimension of the hydrocarbon chain. However, the concepts from the acylamino (*e.g.* "1") and the sulfur dimension are scattered throughout the list. In practice they are scattered much more randomly than in the



Scheme 1. The multidimensionality of a chemical substance concept.

example, which has only three, equally short and completely occupied, dimensions.

Whichever of the many possible dimensions is chosen, relationships existing in the remaining neglected dimensions will always be hidden. If a question is then aimed at a concept from one of the neglected dimensions, the inquirer is faced with an almost completely chaotic vocabulary.

One-dimensional arrangement of concepts not only impairs the overview of the vocabulary but is also responsible for the complete lack of any natural filing position for a large number of concepts. For, if neither the author nor the inquirer makes any statement in the preferred dimension ("ring-substituted carbamylamino sulfonamides" — no mention of alkyl substituents) it is always necessary arbitrarily to choose a statement in the preferred dimension in order to be able to express the respective concept with the aid of the one-dimensional vocabulary. This amounts to distortion of the original concept.

4.1.2. Localization in a Single Dimension

The immediate consequence of a linearly ordered vocabulary is that the literature itself can also be ordered only in a single preferred dimension. This need not be detrimental so long as only literature for a single subject heading is searched for, *e.g.* only for "ureas", for "sulfonamides", or for "herbicides". In a search for a combination of subject headings however, such as "ureas containing sulfonamide groups as herbicides", all the more specific subject headings given under "ureas" must be examined to see whether they contain any that refer to a herbicidal effect, or an analogous search is to be made under "herbicides".

If this process proves too time-consuming, the documentalist can introduce a new subject heading into the vocabulary, corresponding to the "compounded" concept ("urea herbicides"). In such a subject heading the constituent elementary concepts are contained in a "precoordinated" form. During literature analysis the documentalist must always remember these compounded concepts and assign the respective subject headings to any relevant literature that he may encounter.

This possibility is subject to natural limits from two sides. Firstly, the formation of a highly precoordinated subject heading is justifiable only if it is already in common use. Otherwise hardly any requester will use this subject heading in his literature searches. It would therefore be pointless to coin an artificial subject heading "urea herbicide" and introduce it into the vocabulary. It would also be asking too much of the documentalist to expect him to keep such unusual terms constantly in mind during his analysis of the literature.

Even if common terms already exist for such highly compounded concepts, however, there still remains the inherent disadvantage of practically any vocabulary of precoordinated subject headings. Even when it is as large as is still acceptable from the working psychological point of view it can never approach the desired comprehensiveness. For example, if one formed precoordinated subject headings merely for all practically important binary combinations of the substance-property type, the resulting vocabulary would already be much too large to be reliably memorized for the practical analysis of the literature. — An equally serious disadvantage is that the relations between the subject headings remain latent. Thus one would also have "pyrimidine herbicides", "carbamate herbicides", *etc.*, and with an inquiry for "herbicides in general" in a certain context, one would be faced with an almost completely unordered vocabulary.

The one-dimensional character of the subject index is however not only the cause of an incomplete vocabulary of inquiry terms, but also of an incomplete localization of documents under each subject heading, even though this is not very obvious. This leads to loss, for it is unreasonable and also impracticable to post *all* relevant documents under the pertinent subject heading. For example, there would be so many structures to be listed under "ureas" that a (linear!) list of this kind would no longer permit a specific inquiry, *e.g.* for "sulfonated phenylureas", because of its size and inherent disorder. It is therefore necessary, in order to preserve the practical usefulness in the case of such a broad subject heading, to drastically reduce the number of relevant citations. It is therefore usual in a subject index to make a selection from among the references for most of the subject headings and to cite only the most typical publications for a subject heading. For example, in a common annual index of world chemical literature, it has been found that as many as 30 % of all publications on phenothiazines were not listed under the appropriate subject heading [9]. However, this type of loss in subject indexes is not immediately obvious, and is therefore not widely known.

Thus, the documentalist responsible for compiling a subject heading vocabulary for a conventional index has the choice of using mainly elementary concepts or giving preference to compounded concepts. Subject headings for elementary concepts allow localization for a greater number of very general topics, but lead to large quantities of ballast in more specific inquiries. With a preponderance of precoordinated inquiry terms, on the other hand, no localization will be possible for many topics, owing to the necessarily large proportion of gaps in such a vocabulary.

[9] *B. Loev*, J. chem. Documentation *1*, 27 (1961).

4.1.3. Subdivision of Concepts According to the Kind of Index

The subject index is characterized by its subject headings for generic concepts, *i.e.* for concepts that can be further specified by the addition of a further conceptual characteristic. "Carbamylaminoalkylbenzenesulfonic acids", for example, can be further specified by the length of the alkyl chain, its branching, its configuration, *etc.* Depending on the kind of characteristics that are added to a generic concept of this nature, the sequence in which they are added, and their number involved, a generic concept can be the origin of many hierarchies of various lengths for more specific concepts.

These characteristics for further subdivision must be chosen with great care. It would be of little value, for instance, to subdivide the phenylureas according to their heats of combustion, their diffusion rates under standard conditions, or the structure of their crystal lattices. The resulting substance class concepts would be totally unsuitable for the documentation needs of a synthetic chemist. Molecular weight and elemental composition are also of minor importance from this point of view, since these characteristics can differ very widely within a meaningful class of substances. In a search for a generic concept, no inquirer from the field of synthetic organic chemistry would be inclined to commit himself in respect of such unimportant characteristics. Thus, if it is desired to store generic concepts (particularly classes of compounds) and to use them in searching, the respective *essential* characteristics of the objects must be determined and chosen for subdivision ("canon of relevance" [10]).

The situation is entirely different for the individual concepts, in which the progressive specification of the generic concepts has reached a limit. Every conceivable characteristic of the concept, whether important or unimportant has been evolved and determined [11]. 2-Carbamylamino-5-*n*-butylbenzenesulfonamide cannot be specified further by any substance characteristic. Even its heat of combustion, molecular weight, and elemental composition are fixed, both for storage and for inquiry. In these circumstances one has complete freedom in the choice of a characteristic for the arrangement of the individual concepts, be it essential or purely formal. Given this freedom of choice, it is preferable to select a characteristic that is as simple as possible to handle, *e.g.* the elemental composition in the form of the molecular formula. Applying these characteristics stepwise in an arbitrarily established sequence (carbon, hydrogen, nitrogen content, *etc.*) one always arrives at only one hierarchy in which each individual concept necessarily finds its place.

Whenever it is necessary to display a single hierarchy of concepts such as would result from subdivision on

[10] *S. R. Ranganathan*: Prolegomena to Library Classification. Asia Publishing House, London 1967, p. 146.

[11] *v. Freytag-Löringhoff*: Logik – ihr System und ihr Verhältnis zur Logistik. Kohlhammer-Verlag, Stuttgart 1955, p. 27.

the basis of a single characteristic, the linear structure of a conventional index is an entirely adequate medium. For individual concepts, there is accordingly no need to use multidimensional techniques, which are much more expensive, and whose capabilities would not be even approximately fully utilized.

Authors may also be looked upon as individual concepts. A single characteristic of the person, *e.g.* his name or the instant of his birth, is again satisfactory as an ordering principle both for filing and for retrieval.

In our experience, however, the individual concept plays a very much smaller part in the literature interests of the scientist than would appear from the use of author and formula indexes. In most cases where a literature search is carried out on the basis of an individual structural formula or an author's name, distortion of the actual topic of the inquiry has already occurred. Really, the inquirer is interested in a whole class of substances, in which, *e.g.*, the length of the alkyl chain can vary, and not in one single individual compound. The structural formula with which the literature search is started is usually intended as an example rather than as a definition of the topic of the inquiry. The factors that lead the inquirer to use the individual concept are the ease of use of formula and author indices, as well as the difficulty and uncertainty of finding a generic subject heading in the subject index that fits the topic of the inquiry. This is why too much value is often placed on documentation systems and notations that are only designed for individual compounds.

Though indexes, because of their one-dimensionality, can only present the literature in very modest degrees of order, they are nevertheless of great value to the chemist. They allow undirected literature studies in which there is no need to specify the object of the search in too much detail, and the chemist can decide subjectively and *a posteriori* what is of interest to him. If the index is used for this purpose, the lower order will not prove a serious disadvantage. The information available in this way covers a much wider area in any case than when one reads only a few special journals. Indexes will therefore still hold their place in the future alongside the large mechanized stores.

4.2. Purely Mechanized Localization

The deficiencies inherent in the purely intellectual localization method result in the necessity of having to separate relevant from non-relevant literature by (renewed) expert surveillance. Time and cost required for this has steadily increased with the volume of literature and with the number of references under a given subject heading. On the other hand, the time available to each scientist for literature work has by no means increased. The possibility of compensating intellectually for the disorder that remains after purely intellectual localization has therefore steadily decreased, relatively speaking. For this reason, all mechanized methods that allow the localization of literature *without* intellectual examination of many publications merit great interest.

The general practice in every sphere today is to try to use machines whenever demands on time or reliability are beyond human capabilities. Computers have found wide-spread use even for those processes that were formerly left entirely to the human mind. The credit for the occasionally astonishing results has been given almost exclusively to the machines, though man who gave the machine its instructions can claim at least an equal share of success. The programmer must first analyze the process in a depth that is otherwise rarely necessary, and this is sometimes a high-ranking scientific task. If despite this analysis the machine encounters a situation that the programmer failed to foresee, it finds no instruction, and is unable to solve the problem at hand. *It is important to our discussion, though seemingly trivial, that processes can be programmed and left to the computer only if the parameters which exert an influence on this process are foreseeable by man.*

4.2.1. Poor Predictability of Storage Terms

In documentation, the retrieval of publications from a store also involves a large number of operations, which one wishes to execute as rapidly and as reliably as possible. It has been found in purely intellectual localization that the need for a human expert to read every publication to be stored creates a serious bottleneck. One is therefore inclined to try the use of machines for this purpose. In a typical example of purely mechanized localization, the texts are transferred letter by letter into the memory of a computer without prior standardization or interpretation by man. In such a store the machine can also find any desired word or part of a word in any part of the text, purely mechanically.

The problem that faces scientific documentation, however, is not the retrieval of publications in which the inquirer's *verbal formulation* occurs, but of those publications whose *subjects are sufficiently closely related* to the topic of the inquiry [12]. If this search is to be carried out by a computer, it must be given precise instructions as to which particular formulations in the stored publications are to be regarded as relevant to the topic of the inquiry. These instructions must be continuously effective as the machine searches through the store and compares the stored formulations with the inquiry term. If exact or sufficiently close agreement is found between the "storage term" of a publication and the inquiry term, the publication is regarded as pertinent. Its text or bibliographical data are then printed out in a list or fixed in some other way. This completes the purely mechanized localization.

We shall use the expression "storage term" for any formulation of a stored topic, provided that this formulation serves for the mechanized localization of publications. It is of no importance whether it is in clear text or in a code of some kind.

It is always easy for an expert to recognize which concepts are expressed or implied by an author, including their context, in a given text. This is the process always involved in purely intellectual localiza-

[12] *C. L. Bernier*, J. chem. Documentation *2*, 117 (1962).

tion and intelligent reading. The judgment required here may be described as *a posteriori*, *i.e.* the decision as to the meaning of a formulation is taken only *after* this formulation has been presented.

The main task to be fulfilled in using our common language is to represent scientific facts in as lively and precise a manner as possible. It provides us with much freedom for choice of expression and development of personal style. However, such a language is extremely unsuitable as a basis for the purely mechanized retrieval of relevant literature, since here the relation between a particular mode of expression and what is meant by this expression cannot be decided *a posteriori*, as it normally is in scientific communication. On the contrary, concepts and their context are given and it is necessary to judge *a priori*, without seeing relevant publications, what modes of expression could conceivably have been used for this concept. All these formulations must be assumed to occur in the store, and must therefore be specified in the inquiry term, since this is part of the instructions that the machine requires in order to check the stored publications for pertinence.

As is well known, it is far easier to describe an event with hindsight than to predict it. Any rational and valid prediction requires that the course of the event follows a known pattern. The event of phrasing scientific concepts in the words of our colloquial and technical language is no exception to this rule. However, we know of no set of principles which are strictly obeyed by man in expressing ideas in his language and which would therefore permit the prediction of the words used. Indeed, should there be such a set of principles then we are at present still very far from knowing them. Purely statistical regularities in the use of language by authors have been established, but their shortcomings are apparent[13], for they are invalid for the isolated case of an individual publication and give no guidance, for example, of how an author might have expressed himself when formulating his first patent application. In scientific documentation, however, we always have to deal with the isolated case.

The *a priori* character of such a determination of an inquiry term is not altered by the fact that publications already exist which could give guidance about the storage terms that have already occurred for the concept of the inquiry and consequently are to be taken into consideration in establishing the inquiry term. The main point is that these publications are unknown to the inquirer and that he does not know of anyone whom he can or will ask about them.

If however an inquirer has previously read the publications which he is now searching and can remember in detail the linguistic formulation then the *a posteriori* route to the formulation of the inquiry term is open to him. One must remember, however, that the fraction of the literature which the scientist happens to cover today in the course of his own reading is becoming smaller and smaller. Still much smaller is the fraction which he remembers so precisely in all details as is demanded in the purely mechanized localization. Consequently, only a very small fraction of documents relevant to his inquiry can be retrieved reliably in this way.

The conceptual problems involved in purely mechanized localization can be readily imagined from the list of topics given earlier for the "production of α-amino acids by fermentative processes with microorganisms". There is no general rule according to which a search mechanism that operates purely formally could recognize which of the stored topics listed there are relevant to the inquiry topic and which are not. It will always be easy to devise examples, or to find them in the literature, for which such a rule fails, however many refinements one makes to it.

The situation is not much better even in inquiries for structures alone, though the names are easier to deduce here because of the rules of nomenclature. An attempt has been made, for example, to find literature on Schiff bases that are mentioned in a certain context[14]. For the structural part of the inquiry it was thought sufficient to search for the character sequence "imin" or "Schiff base" or "azomethin". It is indeed difficult to add appreciably to this search instruction by mere prediction of other possible names.

Such an *a priori* definition of the inquiry term inevitably means that a number of names of compounds will be omitted, partly because though perfectly familiar, they can never be completely memorized, and partly because they are quite unforeseeable (*e.g.* "anil", "hydrobenzamide", "benzylidene...amine", "azallyl compounds", *etc.*). This results in a loss of relevant information. Practically the only way in which this loss can be discovered is by parallel searches with more effective systems and tedious comparison of the results. However, this has been done only in very rare cases. Thus the shortcomings remain unrecognized for a long time, and the first assessment of the effectiveness of a fully mechanized system is usually much too high.

It is much easier to assess the ballast in this method, since this becomes evident in every localization operation[15]. In this case it results from words such as "*imino* ether", "e*limin*ation reaction", "ketone *imines*", and "ethylen*imine*", as well as from trivial names such as "capaur*imine*". Equally unwanted is the retrieval of all imines that are not substituted on the nitrogen by carbon.

A literature search based exclusively on *names* of structures and partial structures will often be unsuccessful simply because no names are given for many published structural formulas. This holds *e.g.* for all patent claims that are formulated in a general fashion.

The root of these failures is that in purely mechanized localization no distinction is made between a word and its meaning. When one wishes to find a *concept*, one merely searches in the stored publications for the *words* that might have been used by chance to express this concept. In this respect the same confusion that arose in the early literature of logic, before a distinction was made between object language and metalanguage, now recurs in documentation[16]. If on the other hand we try to compensate for this by means of the requirement that all other conceivable formulations should be sought, in addition to that chosen by the inquirer, we are again presupposing what we wish to know. We are presupposing the knowledge of the relevant publications in the store with all the details of their formulation.

The tacit postulate of the predictability of the storage terms, which is the ultimate basis of purely mechanized localization, is thus illfounded. It is not surprising

[13] Cf. *M. E. Lesk*, Amer. Documentation *20*, 27 (1969).

[14] *Kallner*, Lecture on May 21, 1969 at the University of Köln.

[15] *D. S. Colombo* and *J. E. Rush*, J. chem. Documentation *9*, 47 (1969).

[16] Cf. *W. Stegmüller*: Wissenschaftliche Erklärung und Begründung. Springer-Verlag, Berlin 1969, p. 30.

that the degrees of order attainable in this way have so far always been rather poor, *i.e.* localization has always been subject to considerable loss and ballast. However, even this can represent an improvement on the prevailing situation. Moreover, it cannot be denied that intellectual localization is sometimes far from perfect, particularly when hindered by the limited possibilities of a one-dimensional method. In such cases purely mechanized localization is sometimes quite capable of competing. This is so in particular if the machine search is based on an extremely careful language analysis [17, 18].

What are the prospects of further development of the mechanized method to such a point that man can adequately be replaced by the computer in literature analysis? The above arguments have shown the utopian demands that would have to be made on the machine (and on the people that must program it!) to achieve this. The computer would have to make a skilled assessment of any text in the store, in order to decide whether or not it is relevant to the inquiry. But is it really possible to *foresee* all the many situations, and to cover them in a machine algorithm, in which the human agent must interpret an author's implications? It is only thus, for example, that one will be able to find the starting materials if an author has merely given the final product and the respective preparation reaction. Only thus can one find a method of control for a pathogenic parasite if the author has described only the control of a typical intermediate host for this parasite because he could leave the reader to draw the obvious conclusion from this.

It would be of little value to science if the effectiveness of scientific documentation was decreased as a result of the uncritical adoption of purely mechanized documentation methods. Efforts are being made everywhere to provide research with increasingly effective tools, and with good reason. Should these principles not apply in scientific documentation?

Anyone who is very well aware of the drawbacks of purely mechanized localization, but nevertheless recommends its use in the practical large-scale documentation of chemical journal and patent literature, must have underestimated the degree of order that must be attainable in such a store now or in the near future if it is to remain capable of working. This route inevitably leads to a dead end [19, 20].

Thus if high demands are made on the order in a literature collection, special efforts must be made to render the storage terms predictable. We shall see in Section 4.3.1 what form these measures can take.

[17] *G. Salton*, Proc. 19th Annual Conference of the Assoc. for Computing Machinery, Philadelphia 1964.

[18] *J. O'Connor*, J. Assoc. Computing Machinery *12*, 490 (1965).

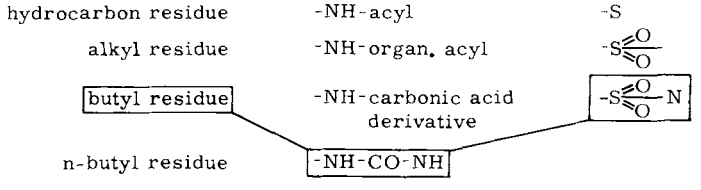
[19] *M. Woitschach*, Nachr. Dokumentation *17*, 74 (1966).

[20] *R. Fugmann*, Nachr. Dokumentation *17*, 79 (1966).

4.2.2. Multidimensional Localization

As one drawback of the purely intellectual localization we recognized that the subject index is always in a one-dimensional order only and that accordingly the literature is localized in only a single dimension. Should one wish to display the multidimensional conceptual relationships given in Scheme 1 without distortion then one obviously must avail oneself of a likewise multidimensional method of representation.

In most chemical substance concepts one can distinguish – on grounds of definition alone – a series of conceptual units which should be available to the inquirer either as an *isolated* unit or in *combination* with any other unit. Frequently, these units also occur as isolated generic concepts in the literature to be stored ("ureas", "sulfonamides", *etc.*). Many of these units are so closely interrelated that they can be placed in one and the same hierarchy of concepts. Each hierarchy now corresponds to one of the dimensions into which a compounded concept has to be split if it is to be represented in all its dimensions. The example from Scheme 1 would result in a picture of the following type (Scheme 2).



Scheme 2. Hierarchically arranged three-dimensional list of elementary concepts for the example from Scheme 1.

The most appropriate inquiry term for a given topic is then found very reliably and easily by selecting the appropriate elementary concept from the respective hierarchy, and combining it with an elementary concept that can be freely selected from another hierarchy. Scheme 2, for example, shows the representation of carbamylaminobutylbenzenesulfonamide by "postcoordination" of the respective elementary concepts (by connecting lines). Very many inquiry terms can be formed by this postcoordination of elementary concepts.

From this scheme the inquiry terms for any combination which is compounded of a smaller number of dimensions can also be taken. The *storage* of compounded concepts is similarly facilitated if one splits them into the same dimensions.

In spite of the large volume of inquiry terms covered such a vocabulary always remains comprehensible. The number of elementary concepts from which the most complicated inquiry terms can be compounded, remains small and easily memorizable.

The analysis of compounded concepts into simpler concepts is a well-known and well-established philosophical principle. Any scientific system is ultimately founded on this analytical approach. A procedure of this type can, furthermore, be based on axioms and on fundamental principles of classification theory. One then speaks of an analytic-synthetic

classification, the development of which has been mainly due to *Ranganathan* and his Indian school[21,22].

This resolution of a compounded concept into its constituent elementary concepts affords the prerequisites for the localization according to each single elementary concept and particularly according to every desired coordination of them. To this end, each of these concepts is represented on a suitable carrier, *e.g.* on a concept card of a peek-a-boo card index, by a typical pattern of holes or magnetic spots on punched cards or on magnetic tape *etc.* Then, by means of a suitable technique, those publications can purely mechanically be localized, which fulfill *all* dimensions of the inquiry. For instance, all documents in a store can be localized, which contain the desired concepts "urea" *and* "alkylbenzene" *and* "halogenobenzene" *and* "herbicidal activity". Publications in which only one of these concepts or only up to three of them are contained are excluded, contrary to the one-dimensional localization. Hence, in the mechanized multidimensional localization a much higher degree of order is achievable.

4.3. Combined Intellectual and Mechanized Localization

If we draw up a balance of the specific advantages and weaknesses of the two localization methods, we find the picture shown in Table 1.

Table 1. Capabilities of three localization methods. The superiority of a method is indicated by +.

Feature / Localization method	Recognition of what is meant	Possibility of obtaining suitable inquiry terms by coordination	Reading time required after localization	Predictability of the storage terms
Purely intellectual	+	–	– [a]	+ [b]
Purely mechanized	–	+ [c]	+	–
Combined	+	+ [c]	+	+

[a] Much time is required to sort out the relevant material among the ballast.

[b] The predictability is achieved by the translation into a preestablished vocabulary of subject headings.

[c] By postcoordination.

It is clear that the two methods complement each other well, and should be capable of being combined in such a way that their advantages are retained while their specific disadvantages are cancelled out. In such a combined conception (line 3 in Table 1), the purely intellectual method would have to be used in the analysis of the publications to be stored. The author's ideas are now recognized, irrespective of whether they have been expressed explicitly in words or in pictures or whether they are merely implied. Everything that might be the subject of a later inquiry is selected for storage, as far as the technical and economic possibilities allow.

A further important intellectual contribution is that the form of these facts in the store is made predictable. This can be done by the use of subject headings in clear text, either formed particularly for this purpose or even taken from the original text under certain conditions, to represent the essential concepts and their context. These designations are stored in the most suitable form depending on the technical facilities available. These storage terms must be recognizable in this form by the respective mechanical aids, and can therefore be used for mechanized localization of the publications characterized in this way, either singly or in postcoordination.

Several attempts have also been made to arrive at a combined intellectual-mechanized method of localization by transferring the subject headings of a conventional index onto mechanically searchable carriers. However, one must always consider how many concessions had to be made regarding the conceptual soundness of the subject headings when they were intended for an index and how unreliable their assignment to publications is. This is particularly true with regard to the high degree of precoordination which materializes in these subject headings. If they are incorporated uncritically into a technique which is completely capable of conceptual postcoordination the efficiency of the mechanized technique would be far from fully exploited. *There is no subject heading vocabulary that is equally suitable for working both with a conventional index and with a mechanized system.*

4.3.1. Methods of Making the Storage Terms Predictable

From the methodical viewpoint of documentation, one can differentiate between achieving predictability of the storage terms for concepts themselves or of the particular connections in which the concepts occur in the context of a publication.

There are often good arguments both for treating a given idea as a single compounded concept ("urea herbicide") and for regarding it as being compounded of separate elementary concepts ("urea derivative", "herbicidal activity"). Once it has been decided for a given field which categories of concepts are to be capable of being used for the localization of literature ("substances", "reactions", "properties", *etc.*), this at the same time provides a guide as to what is to be regarded as a compounded concept and how far compounded concepts must be broken down. According to this guide all those concepts must be resolved which contain concepts from more than one category or dimension. Otherwise one would tolerate that a certain concept from one category would be scattered throughout the system of concepts, depending on the other concepts with which it happened to be compounded. — To combine the elementary concepts to form the compounded concepts required by inquirers is then the task of postcoordination.

4.3.2. Predictability of Storage Terms for Concepts

In order to make the storage term for an elementary concept predictable the original text of the publication can no longer be fed directly into the computer without supervision, as it is in the fully mechanized

[21] Cf. *S. R. Ranganathan*, Library Sci. *6*, 193 (1969).

[22] Cf. *A. Neelameghan*, Herald Library Sci. *8*, 96 (1969).

method. Instead, a "thesaurus"[23] is compiled and kept up to date to show the various expressions that have already occurred for a given concept in the stored publications. Before phrasing an inquiry term, one ascertains beforehand which expressions for the inquiry concepts have so far been incorporated into the store. These are all formulated as alternative search conditions in an appropriately comprehensive inquiry term ("manipulated grouping"[24]).

The effectiveness of this method is greatest when the store is still relatively small, *i.e.* when the number of different terms that have occurred for a given concept and related concepts is not yet too large. However, in the course of time more and more storage terms will have to be taken into consideration for an inquiry term. Furthermore, owing to the tendency that soon arises to make inquiries more and more specific, the number of concepts for which this step is necessary in each inquiry also increases. The work of establishing and handling all these alternatives can easily grow to a magnitude that is unacceptable both for man and for machine.

The problem cannot be solved in the long run by fixing all the alternatives for an inquiry concept once and for all and giving them to the machine in advance as a fixed instruction, so that all the alternatives for a given inquiry concept are automatically considered. Taking into account and searching for a very large number of alternatives can mean an excessive cost in machine time, particularly when the number of alternative terms per inquiry concept reaches orders of magnitude of more than a thousand.

On the other hand, this method has the advantage that a store suitable for searches is available very quickly, and there is no need to wait for the tedious construction of a system of concepts, since this system can be built up independently of and parallel to the storage. In doing so one can thus be guided by the practical requirements encountered in current storage and in searching.

A further step toward improved predictability of the storage terms is to use only one single term for the storage of a given concept, all other expressions with the same meaning (synonyms) being replaced by this standard term[25].

For this purpose, all texts may be scanned mechanically before final storage to establish whether they contain any synonyms that must be eliminated. The machine is instructed to replace such terms by the standard form. If it encounters terms for which it has no instructions, a corresponding message is printed out, and the documentalist can then provide the appropriate further instructions. – Difficulties arise in this method from the fact that there are terms that can have entirely different meanings, depending on the context in which they occur; examples of such terms are cell, oil, and plasma ("homonyms"). These would therefore have to be converted into *different* standard terms, depending on the context.

Furthermore, there is always some doubt regarding the reliable recognition of the author's ideas, since intellectual analysis of the text, particularly regarding context, is carried out only in the emergency cases notified by the machine. Many an implication that could be readily gleaned by reading between the lines is thus lost.

The only escape from this difficulty is that one entirely dispenses with feeding an original text into the store word for word without any intellectual interpretation. Instead, an expert must be introduced into the documentation process at this point. Only he can decide everything that is stated and implied in the author's words and pictures, so that the implied concepts can also be expressly added to a publication and thus made retrievable. – On this occasion he could easily standardize the expressions for concepts to be stored. This conversion of the expressions encountered into a pre-established, controlled, and hence predictable form is nothing other than the traditional "coding", which is still the most widely used method of preparing scientific publications for storage, and is by no means an antiquated procedure, but is an extremely important step if one wishes to attain high degrees of order[26].

The amount of work involved in coding can be reduced considerably by employing machines. One need only write out a clear text word and put it on tape. Then the machine replaces this (or other words having the same meaning) by a notation according to previous instructions[25,27,28]. The progress that is always associated with such a standardization of storage terms, whether carried out purely mechanically or intellectually, is unmistakable. It means that only one storage term for each concept need be taken into consideration in phrasing the inquiry term, at least as far as *individual concepts* are concerned, such as a single compound or one specific reaction.

The special position of individual concepts becomes clear if one recalls the relevance rule of Section 3.3. For an inquiry containing the concept α, all publications are relevant in which α itself or any more specific concept occurs for which α is a generic concept. The reason for the simplicity of the situation with an individual concept is that it has no more specific concept below it in the hierarchy concepts, which would have to be considered in a search. If on the other hand an inquiry is made for a generic concept *e.g.* for "herbicide", provision must be made for the localization of literature on more specific concepts such as "selective herbicide", "contact herbicide", and "soil herbicide". All these more specific concepts, that fall under this generic concept must therefore be used as alternative search conditions in the inquiry term. The fact that after standardization only one storage term is required for each of these more specific concepts (*e.g.* only "soil herbicide" and not also the synonym "root herbicide") already greatly simplifies the phrasing of the inquiry term. Considerable problems can nevertheless arise if the number of more specific concepts to be considered is large.

[23] *D. Soergel*: Klassifikationssysteme und Thesauri. Deutsche Gesellschaft für Dokumentation, Frankfurt/M. 1969.

[24] *R. Fugmann*, Nachr. Dokumentation *13*, 120 (1962).

[25] *M. Scheele*, Naturwissenschaften *52*, 1 (1965).

[26] Cf. also: National Acad. of Sciences, National Research Council, Washington, D. C., Publication 1150: Survey of Chemical Notation Systems; Publication 1278; *D. E. H. Frear*: European Nonconventional Notation Systems; *F. A. Tate*, Annu. Rev. Information Sci. Technol. *1967*, 285.

[27] *Ernst Meyer*, J. chem. Documentation *9*, 112 (1969).

[28] *H. Behmenburg* and *M. Glos*, Nachr. Dokumentation *12*, 146 (1961).

In a situation such as that prevailing in chemistry, where one generic concept ("urea derivative") has an immense number of more specific concepts ("halogenophenylurea", "halogenoalkylphenylurea", "polyhalogenodialkylsulfaminocarbanilide", *etc.*), any attempt to make even an approximately complete list of all such specific concepts and to handle them by machine at a reasonable cost as alternative search conditions is doomed to failure. There is only one reliable way to achieve order of the kind and degree that are expected by the inquirer: the hierarchical relationships between the concepts must be expressed so clearly in their controlled storage terms that these relationships are recognizable even by a machine when it encounters these terms as it scans the store. This can readily be achieved by storing all urea derivatives with a term in which a certain character sequence, *e.g.* "PD" always occurs, irrespective of the other details of the structure of the molecule. In other words, "PD" is fixed as a mandatory notation of *all* urea derivatives.

If all structures have been stored in the form of "systematic notations" of this type, it is easy to formulate an inquiry term for "urea derivatives" (*e.g.* in conjunction with a certain herbicidal activity). The machine is instructed to search the stored molecular structure notations for the character sequence "PD". The relevant publications are localized without ballast and without loss. With this method it is no longer necessary to know or to guess which specific urea structures are present in the store.

This principle can be made even more effective if it is agreed that all "carbonic acid derivatives", which as a generic concept includes all urea derivatives, will be denoted by the fixed character "P". An inquiry containing this generic concept will then necessarily result in the retrieval of all stored guanidines, carbodiimides, isocyanates, ureas, isoureas, *etc.* if the character sequences "PA", "PB", "PC", "PD", "PE", *etc.* have been assigned to these types of compounds ("mechanized group formation [24, 29]).

The changeover to systematic notations is also necessary in the case of biological concepts as soon as a significant number of these concepts has been collected in the store [25, 30].

4.3.3. Predictability of Storage Terms for Connections Between Concepts

The measures described so far are still not enough to satisfy the requirements of very large literature collections in which searches are frequent. It is certainly possible with their help at least to make the storage terms for a concept and for a family of concepts predictable, so that a search instruction can now be reliably phrased for these concepts.

[29] Cf. also *R. Fugmann, W. Braun,* and *W. Vaupel,* Angew. Chem. *73,* 745 (1961).

[30] Cf. Chemical-Biological Coordination Center, National Research Council, Washington, D. C. (1950): A Method of Coding Chemicals for Correlation and Classification, Biology Code.

However, they do not help us to predict the many ways of expressing the *particular context* in which the concepts occur in the stored publication. Accordingly, mechanized searching for concepts in a particular context still remains unsatisfactory. If the problem of an inquirer is actually concerned with the context of concepts, he must therefore tolerate a great deal of loss and ballast. Much research has recently been undertaken on this topic [31].

The techniques of mechanized localization differ extremely widely in their ability to express context in storage and to include contextual search conditions in the inquiry term. With simple manual punched cards, one cannot expect much more than a single level of concept coordination and a very simple connection logic of concepts. Computers, on the other hand, together with highly advanced programming, enable many details of context and connection logic to be represented during storage, and to be used in the inquiry term [32–37].

4.3.4. Distinguishing Different Levels of Concept Coordination

It is interesting to examine more closely the publications that could be localized by the simple post-coordination of the inquiry concepts "urea derivative", "alkylbenzene", "halogenobenzene", and "herbicidal activity". Though all the publications localized would satisfy the condition that they contain all the concepts mentioned, there is no guarantee that it is in fact the urea derivative that has the desired herbicidal activity. A publication may be concerned with herbicidally active pyrimidines that have been synthesized from ureas, and the other structural conditions may be satisfied in another context, *e.g.* in the solvent, in the structures of precursors, in the substances of a peripheral reaction *etc.* These publications then formally satisfy the search conditions in the inquiry term, though they are not relevant in the true sense. This can only be avoided if the storage term shows the various *levels of coordination* as they occur in a publication. At least, structural concepts relating to one and the same compound must be presented very closely coordinated in the storage term. Otherwise, the degree of order in the localized literature cannot be very high. For the same reason, it is desirable not

[31] Cf. *J. M. Perreault,* Proceedings of the International Symposium on Relational Factors in Classification. Information Storage and Retrieval *3,* 177 (1967).

[32] *E. Marten*: Haystaq: A Mechanized System for Searching Chemical Information. National Bureau of Standards, Washington, D. C., Technical Note 264, Sept. 1965.

[33] *J. Frome* and *P. T. O'Day,* J. chem. Documentation *2,* 248 (1962).

[34] *R. Fugmann,* Classification Research, Munksgaard, Copenhagen, *1965,* 341.

[35] *P. A. D. De Maine, K. Kloss,* and *B. A. Marron*: The Solid System. National Bureau of Standards, Washington, D. C., Technical Note 413, Aug. 1967.

[36] *G. Salton,* Commun. Amer. Assoc. Computing Machinery *1962,* 103.

[37] *R. Fugmann, H. Nickelsen, I. Nickelsen,* and *J. H. Winter,* Angew. Chem. *82,* 611 (1970); Angew. Chem. internat. Edit. *9,* 589 (1970).

merely to mention *properties of substances* in the storage term but also to assign them exactly to the respective substances.

The particularly close coordination that exists between the *components of a mixture* should also be shown. An inquirer will occasionally be interested only in publications that expressly describe the use of two substances *as a mixture*, *e.g.* in a pharmaceutical preparation. Publications in which these substances are mentioned only in other connections, *e.g.* in a comparison of their activities, are then of no interest. In many cases a substance is of interest only in connection with a certain other component as a stabilizer, solubilizing agent, additive to increase activity or to decrease side effects, *etc.*

If one wishes information on the preparation of a class of substances from a certain other class by successive reaction steps, then it is desirable to preserve the close coordination of all substances that *belong to the same sequence of reactions* but not to different, mutually independent reactions, which may all be described in the same publication. It is also desirable to show the time sequence of the reaction steps and substances, and to be able to specify this in the inquiry term. Ballast must otherwise be expected in the form of publications in which the reverse reaction sequence is described.

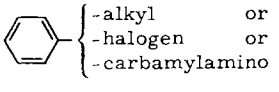
If the preparation of a certain *class of substances by a certain type of reaction* is wanted, then simple coordination can lead to ballast in which the class of substances and the reaction type are certainly described, but independently of each other and in different context.

Different coordination levels can even be recognized within a molecular structure. They are reflected in the requirement that the alkyl, halogeno, and carbamylamino groups be *substituents on the same benzene ring*, and not on different benzene rings that might be present in a stored molecular structure. Furthermore, this one benzene ring should carry only one of each of the substituents named, and there should be no other substituents on this ring, *etc.*

4.3.5. Connection Logic of Concepts

To find literature on the therapeutic use of a particular combination preparation, an inquiry might specify *e.g.* the concepts "penicillin" and "tetracycline" in the logical relation of conjunction. All publications in which only *either* penicillin *or* tetracycline is described, *i.e.* in which they both occur in disjunction, are then of no interest.

Similarly, a formula of the type



such as often occurs in patent literature should not be localized in response to an inquiry according to which *all three* substituents are to be present on the same benzene ring.

There are also much more complicated cases of multi-level logic, particularly in the patent literature of the macromolecular field. Copolymerization of substance A may be required, together with the substance B or with a mixture that consists either of the components C and D or of the substance E, to which either F or G may be added. If the details of the connection logic were ignored here, one would have to expect literature to be localized along with an immense proportion of ballast. The simple condition that the substances A, B, *etc.* should merely occur in a publication is not sufficient for a precise enough localization, since the literature in this field is rather monotonous with regard to the substances used, and the emphasis is placed on their typical coordination in the documents.

It was mentioned in Section 3.2.1 that as a literature store grows and as the proliferation of knowledge progresses, the inquiries to the store become increasingly specific. This specification of the inquiry is effected by the addition of further, restricting search concepts, which may be of a positive or *negative kind.*

It is quite meaningful to submit an inquiry for herbicides that are *not* of the urea or pyrimidine types. Herbicidally active arylated ureas having any substituents on the phenyl residue except sulfonic acid or alkyl substituents, may be of interest, *e.g.* because this group has already been exhaustively studied.

Publications in which the "forbidden" concepts occur in any other, possibly purely peripheral context should naturally not be rejected with an inquiry of this type. A publication in which the forbidden urea or pyrimidine structure in fact occurs may nevertheless be relevant to the first of the above inquiries, if these structures are mentioned only incidentally, *e.g.* as standard preparations for comparison of action.

Similarly, generally excluding any alkyl groups attached to rings in the structure would be a serious distortion of the inquiry if one wished to exclude only alkyl groups bound to *one particular* phenyl residue. It is also important that a negation in the inquiry should not lead to the rejection of stored publications in which a forbidden concept indeed occurs, but belongs to a group of alternative concepts. For, this alternative concept can be thought of as being replaced by another alternative concept, "innocuous" for the requirements of the inquirer.

It is thus permissible to express negations in an inquiry term only if their effect can be restricted precisely to those parts of a publication at which the inquiry is aimed. This again calls for a rigorous distinction between various coordinative levels and appropriate indication of disjunctive connections in the storage term. Otherwise concealed distortion of the subject to be stored will result. If these precautions are not taken in compiling the store, there may later be a serious limitation of the possibilities for the phrasing of highly specific inquiries, with the result that the future usefulness of the documentation system is endangered.

With the introduction of multidimensional techniques (punched cards, computer systems) conceptual post-coordination has found a wide field of application. Despite all its advantages (see Section 4.2.2), however, its success has for the most part remained far behind expectation. In the mere resolution of *several* compounded concepts of a publication or inquiry into their constituent elementary concepts, a completely structureless conglomerate of elementary concepts arises. Every desired coordination of elementary concepts can now be read out from such a conglomerate, and not only just those which correspond exactly to the original compounded concepts. Hence, if the manner in which elementary concepts are connected is not represented by a special method in

the storage and inquiry term considerable distortion of the original information occurs.

Strictly speaking, complete predictability of the storage terms for concepts and for concept connections can be achieved only by translation of the author's ideas into a new, *artificial language*. This language must be tailored to suit primarily the needs of retrieval, and not so much those of conveyance of ideas and experience, like a natural language. To serve that purpose the artificial language must have a large vocabulary, and this must have an extremely systematic structure, so that the choice of an appropriate term does not make excessive demands on memory and patience in searching for it. The artificial language, for the sake of high fidelity, must also have a very expressive "grammar" to enable the connections of concepts to be displayed as they occur in the document or as they are required in the inquiry [38].

If one considers scientific documentation from this angle, it is easy to estimate whether a documentation system can meet the requirements in a large-scale documentation scheme. If it does not involve any kind of artificial language and if no provisions are taken to ensure predictability of the storage terms, the future prospects of the system must be rated as poor. The same is true of a documentation system based on a kind of artificial language that is not sufficiently expressive. A vocabulary of only a few thousand terms, possibly with no highly developed possibility of representing relationships and connections between concepts is not an adequate basis. Many plans for large-scale documentation schemes in science are being discussed and even started at present before it has been ascertained that the method envisaged will be adequate from a conceptual viewpoint to cope with the requirements that will soon arise. The mere provision of computers is no guarantee by itself that a method will be effective.

4.4. Topological Documentation Methods

Let us turn again to the statement that rigorous post-coordination leads to extremely high demands with regard to fidelity of representation of the connections between concepts. This is the basic reason why an almost self-evident treatment of chemical structural formulas is only now being belatedly introduced. Chemical substance concepts are more suitable for an analytical treatment than any other scientific concepts. They are built up not only in a figurative sense but also materially from elementary concepts, *i.e.* the atoms themselves.

However, the consistent breakdown into atomic elementary concepts has so far been hindered by the lack of a method of preserving the connections of the atoms in a structure, and in particular of a method that can also be used in the inquiry term for a class of substances, and which is therefore effective during localization. Without such a tool a thorough analysis of compounded concepts would have been useless, as was pointed out in Section 4.3.

What is needed is an inquiry term that covers not only the atoms themselves *but also their connections* as desired by the inquirer. For lack of sufficiently effective methods, it has been necessary in the past to be content with a rather superficial analysis of the structural concepts which ceases at highly precoordinated concepts such as "ureas", "pyrimidines", *etc.*

A structural formula may be regarded mathematically as a "graph", *i.e.* as an abstract system of "nodes" and "edges". The nodes may be taken to denote atoms, and the edges are interpreted as bonds between the atoms. The mathematical laws that govern such topological systems can now be used to allow the complete description and storage of a structural formula as a graph, and also to retrieve it by using a graph as the inquiry term. In particular, any partial structure consisting of atoms and their connections, *e.g.* the urea or the pyrimidine grouping, can be detected mechanically in a topologically stored structure [39–41].

Since topological storage in principle preserves all the details of a structural formula, it is possible, if necessary, to search even for partial structures that have never before been thought important, for which no suitable inquiry term would be available in any other system, and for which no suitable name has even been given as yet. For example, there are no difficulties in a topological system for the reliable localization of biuret or triuret structures, or of any other urea derivative still more compounded and irrespective of how this structure is built into a larger molecule.

In the literature and in inquiries, one occasionally also encounters substance concepts that cannot be represented by a certain sequence of atoms and bonds ("unsaturated aliphatic amino acid derivatives", "alicyclic diketones", *etc.*) without distortion. A structure concept of this type cannot be treated purely topologically. A solution to this problem can be achieved by parallel use of a second, non-topological system specifically designed for the storing and searching of such generic concepts. Both systems interact in such a way that all topologically encoded structural formulas are transformed mechanically into the generalized representation of the second system [39]. There they are then available for a non-topological search together with those generic concepts which had to be entered by a direct route into the second system. Such a search can be carried out in a most economical manner. Only those few publications which had responded to the preceding search in the second system need now be subjected to the expensive topological search.

In inquiries for molecular structures such a combined system works practically without loss or ballast. It is

[38] Cf. *S. R. Ranganathan*, Library Sci. *5*, 296 (1968).

[39] *Ernst Meyer*, Angew. Chem. *82*, 605 (1970); Angew. Chem. internat. Edit. *9*, 583 (1970).

[40] *D. P. Leiter, H. L. Morgan*, and *R. E. Stobough*, J. chem. Documentation *5*, 238 (1965).

[41] *D. J. Gluck*, J. chem. Documentation *5*, 43 (1965).

largely unaffected by the growth of the store, the increase in the frequency of searches, and increased specificity of the inquiries. Accordingly, it can work unchanged for many years, and so leads to a homogeneous store in which searches are easy. It is not surprising however, in view of the thermodynamic arguments presented earlier, that the cost of such advanced ordering facilities is considerable.

In the topological documentation of structural formulas, we meet the analytic-synthetic principle in an extremely advanced form. The concept analysis has been pursued down to the ultimate meaningful units, the atomic elementary concepts. The manner in which these concepts are (literally "synthetically") connected to one another in the molecule is represented exactly. Using an extremely small and hence easily memorizable vocabulary of about a hundred elementary concepts, the chemical elements themselves, we have available an unlimited number of (predictable) storage terms and an equally large number of inquiry terms. Despite this large number, there is no difficulty in finding the appropriate term in every case, since there is no need to look it up in a large index. It is simply formed by postcoordination in accordance with each particular case of storage or inquiry.

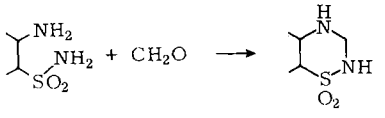
4.5. Documentation of Reaction Types

Other concepts in which the ground is equally well prepared for the analytic-synthetic documentation principles are reaction types. The common names for reaction types ("Hofmann degradation", "diene synthesis" ,"beta oxidation", "Krebs cycle", *etc.*) appear from this standpoint as terms for highly compounded concepts. As long as the only documentation techniques available were printed indexes and reference works, the only route open was *via* highly precoordinated terms. The usefulness of such aids, within their natural limits, is undeniable, as is the case with the likewise one-dimensional subject and formula indexes.

As in the case of pure structural chemical concepts, however, a nonanalytic approach of this type does not display the relationships between concepts. This is a serious obstacle to a generic inquiry for reaction types. For example, ring closures that were carried out with a certain component are scattered randomly over such a vocabulary of precoordinated reaction concepts, and it is practically impossible to bring them all together, however much memory and patience one can devote to the task. Moreover, storage by a method of this kind must also be very incomplete. Not only is such a vocabulary too large and too difficult to memorize, but it is also incomplete insofar as no generally accepted names exist for the vast majority of reaction types, and particularly for all new reaction types. Furthermore, names of this type are mostly quite insufficiently defined.

Ideas differ widely *e.g.* as to which synthetic variants should be included under Friedel-Crafts reactions. While one chemist believes that the use of the typical catalysts in a reaction is enough to make it a Friedel-Crafts reaction, another imposes conditions with respect to the reactants *etc.*

On the other hand, this difficulty can be overcome by resolving reaction concepts in the same way as the structural-chemical concepts[29,34,42,43]. To do this one establishes certain criteria according to which it is decided which parts of a molecule are actually involved in a reaction. Each of these parts is described in its states before and after the reaction, and in this way one obtains elementary concepts of the reaction-chemical type. In the reaction



for example, the carbon of the formaldehyde would be considered to be involved in the reaction. Another characteristic of this reaction would be the thiadiazine ring formed. This reaction could therefore be written as follows:

1. Formaldehyde → CH_2 of heterocycle
2. – → thiadiazine ring formed
3. $C-NH_2$ → C–NH as members of a heterocycle.

The same vocabulary as is used in structure documentation can be used to name the parts of molecules that are involved in the reaction. The only difference is that the parts of the molecule encoded are to be interpreted as participants in a reaction, and that the particular kind of connection between these elementary concepts must be represented.

All types of reactions can be completely described for storage and inquiry by enumerating the constituent reaction-chemical elementary concepts and by representing their connections with one another. As in the case of structure documentation, a relatively small vocabulary of elementary concepts is sufficient for this purpose.

It is easy to see that the complete specification of all starting materials, intermediates, and final products can by no means replace reaction documentation of the kind described. For example, if one tried to find alkylations of aromatic systems by reaction with the olefinic double bond of another component, it is not sufficient merely to demand both classes of compounds to be mentioned as reactants in a publication. For, these conditions are already fulfilled if the reactants did not react *with each other* but *with any other reactant* also mentioned in the same document. Even if they reacted with each other, the desired attachment of the carbon chain to the aromatic ring need not necessarily have taken place. According to the inquiry, other reactive groups present in the reactants must not be excluded, and just these may have reacted with each other in various ways. All this would lead to immense ballast.

Success in the documentation of other fields similar to that achieved in pure chemistry will be possible only by abandoning the present precoordinating thinking in favor of the analytic-synthetic approach,

[42] *H. J. Ziegler*, J. chem. Documentation *6*, 81 (1966).

[43] *G. E. Vleduts*, Information Storage and Retrieval *1*, 117 (1963).

with the simultaneous use of a highly advanced technique for the representation of the relationships and contextual and logical connections between concepts in storage and in inquiries.

If this approach is not yet very widespread in the field of reaction chemistry, it is even less so for concepts from neighboring fields such as "corrosion", "zone melting", "fluidized bed drying", *etc.* Chemists in these fields must come to accept that the creation of a new technical or scientific expression carries with it a duty to define the concept meant, or at least to describe it in detail.

5. Concluding Remarks

No efforts and costs have been spared in the attempts to improve our experimental capabilities in chemistry and in the natural sciences. The most effective techniques imaginable have been developed and used, partly even to a degree that is beyond the powers of single countries and has led to international alliances. For centuries it has been a matter of course that man need not content himself with the effectiveness of his natural sense organs for the *observation* of phenomena. In all our attempts to *interpret* and understand these phenomena, however, we are still seriously handicapped by the lack of methods that have been developed to a comparable degree of perfection and that have a similar superiority over the natural *mental* aids that man has available for research work.

Cognition in natural science means ingeniously ordered experience. To trace out a hitherto hidden law of nature, one gathers together as much published material as possible that might be related to this topic. Today this is still largely a matter of patience and memory, as well as luck in finding relevant material. This information, supplemented by our own experiments, is scanned for analogies in order to find clues to the conjectured relations. Imagination and scientific intuition must tell us what can be hypothetically postulated as analogy, *i.e.* as conformity in the essentials. However, the facts must then be reordered in the light of the new hypothesis in order to separate those that support the hypothesis from those that oppose it and to weight the two sides against each other. Any falsification of the hypothesis leads to a new modification that explains the facts better, and new material has then to be collected once more and ordered in accordance with new ideas. Since the possibilities for the ordering of scientific facts in accordance with any point of view are still at such a backward stage of development, we are constantly operating at the limits of our patience and memory. Thus we are still far from having exhausted the possibilities offered by effective communication with contemporary and with long-established knowledge.

It is important to realize that the freezing of communication is *not* fundamentally due to the mere mass of published knowledge and its continuous growth. If this were so, there would be no remedy. The true cause is the lack of order that science has tolerated among its own results from the very beginning. The effects of this disorder have become increasingly disturbing with the continuous growth of our knowledge, since they cannot be counteracted by a continuous increase in the patience and memory devoted to searches.

Any resignation to the communication problem, such as is sometimes encountered nowadays, is therefore unjustified. On the contrary, this problem presents science itself a task of paramount importance [44]. The efficiency of research and development work must be prevented from lagging even further behind the expectations to which we are entitled in view of the outlay in labor and in experimental aids.

However, this is a problem that cannot be solved by natural scientific thinking alone. If one wishes to achieve more than a provisional result of limited working capability, important principles from philosophy must be followed. Close contacts exist in particular with mathematics, logic, and epistemology, and extensive studies have been carried out on this aspect in recent years. It is fortunate that the technical aids that are necessary to satisfy the requirements of theory have now become available in the form of computers. Thus the time seems mature, from both the theoretical and the technical standpoints, for a breakthrough to fundamentally new, more effective communication methods.

We look forward to the time when the results of philosophy for the first time begin to exert a direct influence on the efficiency of research in natural science, and first of all in chemistry, since the basic conditions for fluent communication are best satisfied here as far as terminology and concept formation are concerned.

5.1. Meanings of the Terms Used

Order:

State characterized by the meaningful proximity of the parts of a whole.

If the "whole" is a collection of publications or their representatives (abstracts, references, referred to in the following as "documents") or a collection of terms for concepts, the user of such a collection must specify what type of arrangement of these objects is "meaningful" for his present search or future searches.

In this case "proximity" means

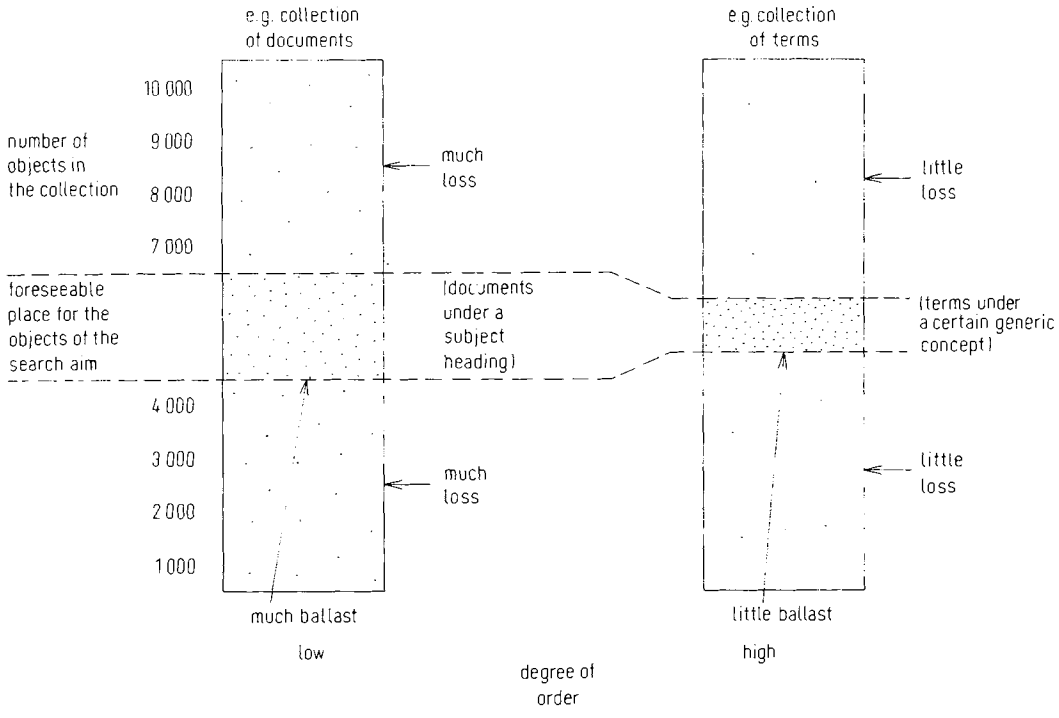
a) that a maximum number of objects corresponding to the search aim should be collected at a foreseeable place and

b) that a minimum number of objects not corresponding to the search aim should be collected at the foreseeable place.

Ballast:

Documents or terms that are found at the foreseeable place after localization, though they do not correspond to the search aim.

[44] Cf. Report of The Presidents' Science Advisory Committee USA, The White House, Jan. 1963: Science, Government and Information. Supplement No. 12 to the Nachr. Dokumentation.



Scheme 3. The rectangles represent the size of a collection of objects. Each point denotes an object corresponding to the search aim. The space between the points represents a complementary number of objects not corresponding to the search aim.

Loss:

Documents or terms that are not found at the foreseeable place after localization, though they do correspond to the search aim.

Degree of order:

Measure of the extent to which a meaningful proximity has been established by localization, *i.e.* the extent to which ballast and loss have been avoided at the foreseeable place.

Relevance:

A document is relevant ("corresponding to the search aim")

a) if it contains all the concepts of the search aim in the same or higher specificity, and

b) if it contains the concepts of the search aim in the desired connection with the tolerance indicated in (a).

The occurrence of the required concepts and connections in the document must be capable of being clearly recognized by an expert in this field, irrespective of the mode of expression chosen by the author.

Inquiry term:

The entire formulation of an inquiry that is used for the localization of documents.

Storage term:

The entire formulation of a stored document with which the inquiry term is mechanically compared, and which can be used in the mechanized localization of this document.

Subject heading:

Inquiry term assigned mentally or physically to a document to be stored during the intellectual relevance check, irrespective of whether or not it occurs in the document itself. A subject heading characterizes the place at which the relevant documents are localized.

Localize, localization:

Establishing order in a collection of objects. — The foreseeable place where *e.g.* the documents corresponding to the search aim (relevant documents) are collected may be a place for the physical collection of the documents themselves, a place for listing the representatives of the publications (*e.g.* under the subject heading in an index), or a collection of documents prepared on particular demand and corresponding to a user's search aim.

Intellectual localization of documents:

Localizing of documents purely by expert examination.

Intellectual localization results in the assignment of characterizing subject headings to the documents or in the assignment of documents to their characterizing subject headings.

Purely mechanized localization of documents:

Localization of documents without any expert examination of these documents, purely on the basis of search instructions established in advance.

Combined intellectual and mechanized localization of documents:

Intellectual localization followed by localization purely on the basis of search instructions established in advance, without further expert examination of the documents that have already been localized intellectually.

Search:

Localization of documents relevant to an *a priori* stated search aim or relevant to a search aim which the inquirer has modified *a posteriori*, *i.e.* after examination of documents.

Category:

Most generic concept, for which there is no broader concept in the subject field that would be meaningful in an inquiry.

Elementary concept:

Concept formed by logical subdivision of a single category.

Compounded concept:

Concept formed by synthesis from several elementary concepts. It contains the sum of the characteristics of the elementary concepts.

Precoordination:

Coordination of at least two elementary concepts to form a compounded concept *before* the localization is carried out.

Localization is carried out only for those compounded concepts for which these coordinations have been formed in advance.

Postcoordination:

Coordination of at least two elementary concepts to form a compounded concept *after* the localization for the elementary concepts has been carried out.

Postcoordination allows localization of relevant documents with regard to all concepts that can be formed by coordination of elementary concepts, without (further) expert examination of the respective documents.

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Use of the IDC System

By Martin A. Lobeck [*]

The documentation system operated by the IDC Internationale Dokumentationsgesellschaft für Chemie mbH uses electronic data processing methods. It allows the storage and retrieval of structures, reactions, and nonstructural keyword information. Structures and reactions are coded as terms of a faceted classification, while keywords are stored in clear text. 900000 formulas from patent and journal publications, including many Markush formulas, have now been stored on magnetic tape. Searches in this store are carried out with IDC programs, which require an average computer time of less than 1 minute per inquiry (CPU time). The structure terms can be produced by computer from topological records. The field covered at present is low molecular weight organic chemistry, though extension to macromolecular chemistry is feasible, and is in fact planned.

1. Introduction

The IDC (Internationale Dokumentationsgesellschaft für Chemie mbH, Frankfurt) has undertaken to encode chemical publications (journals and patents) to make them amenable to searches by the methods of electronic data processing. The first field chosen for attack was low molecular weight organic chemistry, since this is the field in which it is most difficult to answer the kind of questions about partial structures that are frequently asked in practice. In the IDC system, therefore, structural formulas of organic substances are stored in such a way as to allow searches for partial structures, as well as for reactions of organic substances with organic and inorganic reactants and for other keywords.

2. Development of the IDC System

2.1. Coding of Structures

The development of the system started in the 1950's at Farbwerke Hoechst. *Fugmann* and his coworkers found that the methods of structure coding in existence at that time were unsatisfactory for searches in large files. The system conceived and used at Hoechst was soon adopted by the Farbenfabriken Bayer and by the Badische Anilin- und Soda-Fabrik, who also introduced improvements and new ideas. The IDC was founded only in 1967, and its membership now consists of 13 chemical companies.

When the society was founded, there were already more than 400000 records stored on magnetic tape, and this number has now more than doubled. To each record there corresponds one or more related structural formulas coded by the GREMAS method [1].

2.1.1. Triplet Terms

The GREMAS system is based on a faceted classification. Each carbon atom in an organic compound is described by at least one term consisting of three letters and known as a triplet term.

The first letter of the triplet term, which is called the generic letter, tells us something about the number of hetero bonds in which the C atom in question is involved, and usually also with what atoms. Any bond that does not lead to a hydrogen atom or to another C atom is regarded as a hetero bond.

It can be seen from Figure 1 that *e.g.* the generic letter for amines is B, that for halogeno compounds is H, and the first

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[1] Generic REtrieval with MAgnetic tape Storage.

Genus B:	Amines	*e.g.*
BA.	primary	CH_3-NH_2
BB.	secondary	$(CH_3)_2NH$
BC.	tertiary	$(CH_3)_3N$
BD.	quaternary	$(CH_3)_4N^{\oplus}$

Genus H:	halogen compounds	*e.g.*
HA.	fluorine	C_6H_5-F
HB.	chlorine	C_6H_5-Cl
HC.	bromine	C_6H_5-Br
HD.	iodine	C_6H_5-I

Genus R:	unsubstituted chain C atoms	*e.g.*
RA.	saturated	CH_3-CH_3
RB.	olefinic	$CH_2=CH_2$
RC.	acetylenic	$CH\equiv CH$

Fig. 1. Examples of genus and species.

letter of the triplet term when the C atom is not linked to a hetero atom is R.

The second letter of the term, *i.e.* the species, qualifies the information embodied in the first term. Thus in the genus B, the letter A in the second place denotes a primary amine, B a secondary amine, C a tertiary amine, and so on. In the genus H, the second letters A, B, C, *etc.* denote fluorine, chlorine, bromine, *etc.*, and in the genus R they indicate whether or not the C atom is involved in double or triple bonds.

The last letter of the triplet term, the subspecies, indicates the environment of the C atom in question, *e.g.* whether it is situated in or on a heterocycle, an aromatic compound, or a chain with or without double bonds (Fig. 2).

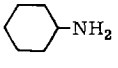
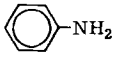
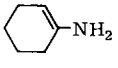
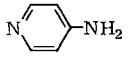
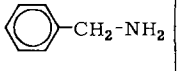
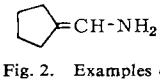
BA.	Primary amines
$CH_3-CH_2-NH_2$	BAA
$CH_2=CH-NH_2$	BAF
$CH\equiv C-NH_2$	BAM
	BAQ
	BAR
	BAT
	BAS
	BAD
	BAH

Fig. 2. Examples of subspecies.

Well over 3000 triplet terms are defined by combination of letters; the result is a very fine network, which should represent the structure very satisfactorily. These terms were in fact accepted as a complete structure at first, but it was soon found that the percentage of false drops in many inquiries was still quite considerable.

2.1.2. Zone Terms

Zone terms of variable length (Y terms) were therefore introduced to show *e.g.* what substituents are present on a ring or chain, whether there are double or triple bonds present and how many, and in the case of aromatic compounds, whether substitution is *ortho*, *meta*, or *para*.

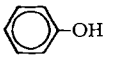
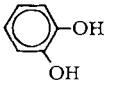
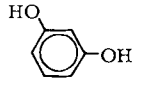
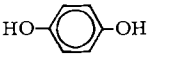
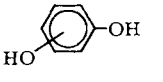
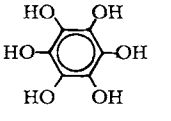
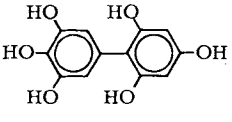
	Triplet terms	Zone terms
	SFA EAR	YT E---
	SAF EAR	YT EE2–
	SAF EAR	YT EE3–
	SFA EAR	YT EE4–
	SAF EAR	YT EE1–
	SAF EAR	ZT EEEEEE----
	SAF EAR	ZT EEEØTØ----- and ZT ETEØEØ---

Fig. 3. Zone terms can distinguish structures having the same triplet terms.

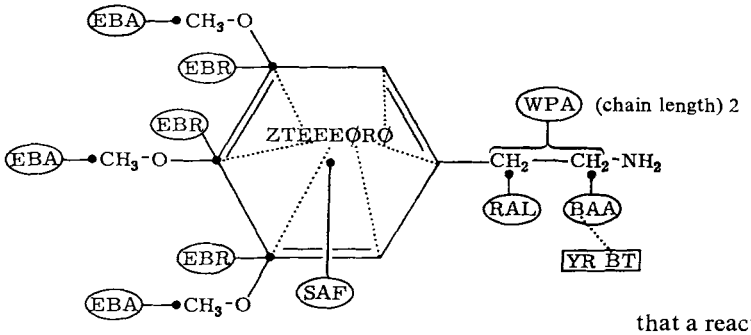
For aromatic compounds with more than two substituents, it was even made possible to specify how all six positions were occupied (Z terms). In the zone terms, the substituents are indicated merely by the generic letter, *i.e.* not very precisely.

As can be seen in Figure 3, different zone terms are obtained for compounds having exactly the same triplet terms, and the structures can therefore be distinguished.

2.2. Example of Structure Coding

This example of the complete coding of a compound will also be used later to illustrate retrieval.

It can be seen that a triplet term has been assigned to each C atom in Figure 4. In the final listing, terms that occur more than once are listed only once. The ether linkage is considered on the one hand from the alkyl side and on the other from the phenyl side, and gives



BAA EBA EBR RAL SAF WPA
YRBT --
ZTEEEØRØ ----

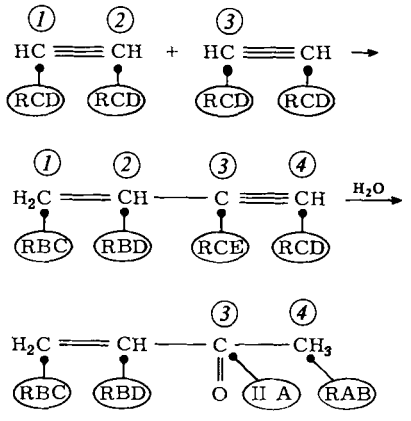
Fig. 4. Complete coding of a structural formula.

the terms EBA and EBR. SAF denotes the benzene ring, or more precisely, each of its C atoms. RAL indicates the aromatically substituted CH_2 with no hetero ligands, and BAA the NH_2-substituted CH_2.

A term WPA is added for a chain length of two C atoms, and it also shows that there are many triplet terms that have not been discussed here, including terms for substitution and condensation data in heterocycles and carbocycles, terms that indicate pharmacological or microbiological activity of the structure in question, and others that contain information about spectroscopic or analytical properties.

2.3. Reaction Coding

Reactions are coded with the aid of the triplet terms of each reacting carbon atom. The first three places of a twelve-place term are occupied by @ DR to indicate



@ DR RCD RBC - - 1
/ DR RCD RBD Z L 2
/ DR RCD RCE Z L 3
1 2 3 4 5 6 7 8 9 10 11 12 *1st step*

@ DR RCE I I A - - 3
/ DR RCD R A B - - 4
1 2 3 4 5 6 7 8 9 10 11 12 *2nd step*

Fig. 5. Coding a reaction with prefix (1—3), initial term (4—6), final term (7—9), reaction conditions (10—11), and numbering of the C atoms (12).

that a reaction code will follow. The triplet term of the C atom *before* the reaction is then given followed by that *after* the reaction. Special features, such as ring closure or cleavage, or chain lengthening (ZL), are coded in places 10 to 11, and the carbon atom may be numbered in place 12 so that it can be recognized again if further reaction steps are described in the same article. The search can then be carried out over several steps in retrieval.

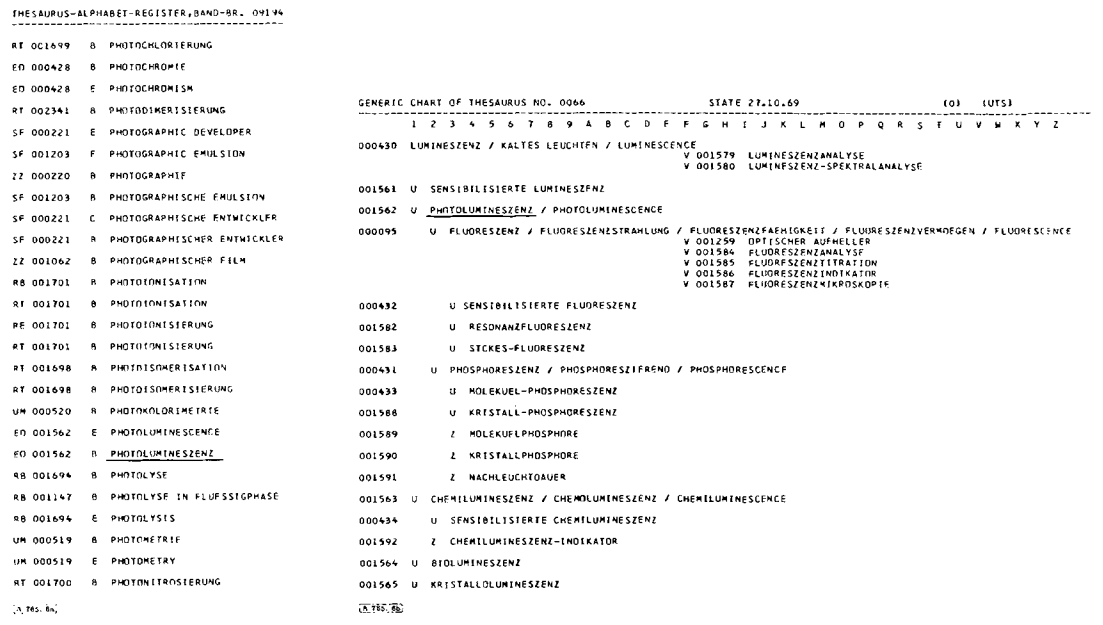
Since the reaction terms must be sought with special programs, "short reaction terms" are always formed. These are a simplified coding of the reaction, which is stored at the same time during the coding of the end products, and which is 2RB, 2RC, and 3ZL, or 2II and 2RA here. These reaction terms can then be retrieved like any other triplet terms. In many cases these are sufficient, and they often make it unnecessary to use the actual reaction retrieval program.

2.4. Nonstructural Concepts

Frequently occurring keywords are given triplet terms of their own, as was mentioned earlier, while other concepts are stored in clear text, as are inorganic reactants. The coder has been given a completely free choice of words in the case of concepts, so that new ones need not be expressed in terms laid down before these concepts existed. Because of this, however, very intensive checking is necessary, since each new concept must be examined, and relations with other concepts, *e.g.* belonging, part-to-whole relation, hierarchic relations (wider concepts, narrower concepts), or synonymity, are established. A definition or explanation of the concept is formulated, and the collection of terms is periodically printed out as a thesaurus, in which all the concepts (Fig. 6a) are transferred from an alphabetic register to the appropriate concept fields, from which all the relations can be seen (Fig. 6b).

2.5. Storage

In the IDC system, all the formulas to be stored are encoded, and the terms are recorded, together with the facts, on punched cards or tapes. Facts and inorganic reactants, as well as the reaction terms, are given different prefixes, which are checked during subsequent searches and prevent searching in locations that definitely do not contain information of the desired nature. The structures are not all encoded by human operators; this is necessary only for structures that



THESAURUS-ALPHABET-REGISTER, BAND-BR. 09146

RT 001699 B PHOTOCHLORIERUNG
ED 000428 B PHOTOCHROMIE
ED 000428 E PHOTOCHROMISM
RT 002341 B PHOTODIMERISIERUNG
SF 000221 E PHOTOGRAPHIC DEVELOPER
SF 001203 F PHOTOGRAPHIC EMULSION
ZZ 000220 B PHOTOGRAPHIE
SF 001203 B PHOTOGRAPHISCHE EMULSION
SF 000221 C PHOTOGRAPHISCHE ENTWICKLER
SF 000221 B PHOTOGRAPHISCHER ENTWICKLER
ZZ 001062 B PHOTOGRAPHISCHER FILM
RB 001701 B PHOTOIONISATION
RT 001701 B PHOTOIONISATION
RE 001701 B PHOTOIONISIERUNG
RT 001701 B PHOTOIONISIERUNG
RT 001698 B PHOTOISOMERISATION
RT 001698 B PHOTOISOMERISIERUNG
UM 000520 B PHOTOKOLORIMETRIE
ED 001562 E PHOTOLUMINESCENCE
ED 001562 B PHOTOLUMINESZENZ
RB 001694 B PHOTOLYSE
RB 001147 B PHOTOLYSE IN FLUESSIGPHASE
RB 001694 E PHOTOLYSIS
UM 000519 B PHOTOMETRIE
UM 000519 E PHOTOMETRY
RT 001700 B PHOTONITROSIERUNG

(A 765, 8a)

GENERIC CHART OF THESAURUS NO. 0066 STATE 27.10.69 (0) (UTS)

1 2 3 4 5 6 7 8 9 A B C D E F G H I J K L M O P Q R S E U V W X Y Z

000430 LUMINESZENZ / KALTES LEUCHTEN / LUMINESCENCE
V 001579 LUMINESZENZANALYSE
V 001580 LUMINESZENZ-SPEKTRALANALYSE
001561 U SENSIBILISIERTE LUMINESZENZ
001562 U PHOTOLUMINESZENZ / PHOTOLUMINESCENCE
000095 U FLUORESZENZ / FLUORESZENZSTRAHLUNG / FLUORESZENZFAEHIGKEIT / FLUORESZENZVERMOEGEN / FLUORESCENCE
V 001259 OPTISCHER AUFHELLER
V 001584 FLUORESZENZANALYSE
V 001585 FLUORESZENZTITRATION
V 001586 FLUORESZENZINDIKATOR
V 001587 FLUORESZENZMIKROSKOPIE
000432 U SENSIBILISIERTE FLUORESZENZ
001582 U RESONANZFLUORESZENZ
001583 U STOKES-FLUORESZENZ
000431 U PHOSPHORESZENZ / PHOSPHORESZIFREND / PHOSPHORESCENCE
000433 U MOLEKUEL-PHOSPHORESZENZ
001588 U KRISTALL-PHOSPHORESZENZ
001589 Z MOLEKUELPHOSPHORE
001590 Z KRISTALLPHOSPHORE
001591 Z NACHLEUCHTDAUER
001563 U CHEMILUMINESZENZ / CHEMOLUMINESZENZ / CHEMILUMINESCENCE
000434 U SENSIBILISIERTE CHEMILUMINESZENZ
001592 Z CHEMILUMINESZENZ-INDIKATOR
001564 U BIOLUMINESZENZ
001565 U KRISTALLOLUMINESZENZ

(A 765, 8b)

Fig. 6. Thesaurus print-out. Example: *photoluminescence* (a) in the alphabetic index and (b) in the hierarchic concept field.

exceed the capacity of the formula reading machine, which records the formulas mechanically and topologically. The structure terms are then formed from the topological record by a computer program [2].

After repeated checking, the information recorded on punched cards or tapes is stored on a supplementary tape that is separate from the "structure tape". Each structure has a separate record, which contains all the necessary bibliographical data, *e.g.* a document number of the publication in question. Separate searches in the structure tape and in the supplementary tape can then be correlated by means of the record number and the document number.

For each document the coder adds one or more field letters, by which the publication is roughly classified; for example, B denotes organic chemistry in general, D is pharmaceutical chemistry, and E is pest control.

This field letter can be included in the inquiry to reduce the number of answers in the case of substances that occur with a high frequency.

These notes on storage are not complete, but should be sufficient to enable the reader to understand the following inquiry formulations.

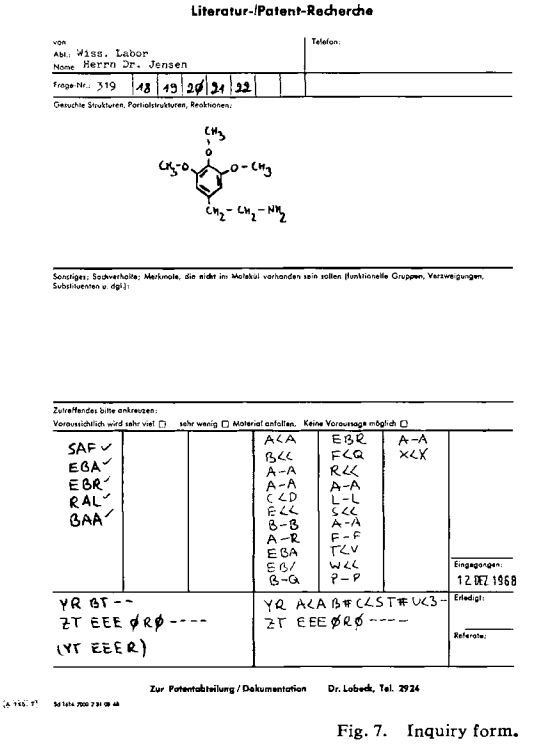
3. Retrieval

3.1. Organization

On entering our company, each chemist receives inquiry forms as shown in Figure 7. The main points about retrieval possibilities are presented in a brief note. The forms give the chemist's department and name, as well as a three-place inquirer number. The chemist draws the required structure and notes any further conditions, and the form is submitted to the Documentation Section.

[2] *E. Meyer*, Angew. Chem. *82*, 605 (1970); Angew. Chem. internat. Edit. *9*, 583 (1970).

Following the three-place inquirer number, a running tally of the inquiries by this chemist is indicated in the input by a two-place number. Consequently, all inquiries, computer lists, *etc.* for a given chemist will be found together on the storage shelves.



Literatur-/Patent-Recherche

von Telefon:
Abt.: Wiss. Labor
Name Herrn Dr. Jensen
Frage-Nr.: 319 18 19 20 21 22
Gesuchte Strukturen, Partialstrukturen, Reaktionen:

Sonstiges: Sachverhalte; Merkmale, die nicht im Molekül vorhanden sein sollen (funktionelle Gruppen, Verzweigungen, Substituenten u. dgl.):

Zutreffendes bitte ankreuzen:
Voraussichtlich wird sehr viel ☐ sehr wenig ☐ Material anfallen. Keine Voraussage möglich ☐

SAF ✓
EGA ✓
EBR ✓
RAL ✓
BAA ✓

ACA BCC A-A A-A C-D E-C B-B A-R EBA EB/ B-Q
EBR FCQ RCC A-A L-L S-C A-A F-F TCV WCC P-P
A-A XCX

Eingegangen: 12.DEZ.1968
Erledigt:
Referate:

YR BT - -
ZT EEE ØRØ - - - -
(YT EEER)

YQ ACABFCCSTFUC3 -
ZT EEEØRØ - - - -

Zur Patentabteilung / Dokumentation Dr. Lobeck, Tel. 2924

Fig. 7. Inquiry form.

3.2. Coding of Inquiries

For each inquiry, the structure in question is coded on the form as outlined above, together with other encodable criteria, such as particular preparation methods.

At first sight it appears a good idea to use the same terms as search conditions as were used for the storage of the compound. This is in fact possible, and yields

all records involving the formula in question; unfortunately, however, a very large proportion of false drops is usually also obtained. The search principle corresponds exactly to the procedure used with peek-a-boo cards. It is clear, therefore, that with this method only minimal requirements can be queried in a record; all required terms *must* be present, but there may be others too. One therefore obtains not only the desired structures, but also more complicated ones. Matters can be improved only if it is possible to forbid all unwanted terms. Obvious as this may seem, it is rare for such a facility to be provided in documentation systems unless they use electronic data processing equipment.

In view of the large number of triplet terms, all the terms to be forbidden cannot be listed individually. The usual method of formulation in the IDC system will be illustrated by a model search for the structure encoded in Figure 4.

If we start with the structure terms entered at the bottom left of the inquiry form (Fig. 7), these must be arranged in strict alphabetical order in formulating the inquiry. This need for alphanumerical arrangement could be avoided by the use of a simple sorting program. Such a program is in fact used in the storage of structures, but not in the inquiry. The reason for this is that the forbidden terms are also included here, and it is logical to run through the possible genera (first letter of the term) to see whether any term in this genus is required. If the answer *e.g.* for genus A is no, this genus can be forbidden by the simple formulation A < A. The program allows the extension of this system to entire ranges; thus H < L means that the record must not contain a triplet term with the genus H, I, J, K, or L.

The requirement that a given term must be present in the record is formulated by giving the term itself, *e.g.* BAS for a primary amino group attached to a heterocycle. If the requirement is more general, one may specify a range from which at least one term must be present. The "any" symbol *, for which any character in the record may stand, is used.

Thus the requirement H**, which means that there must be at least one halogen atom somewhere in the molecule, will result in the retrieval of all stored terms that begin with H. The "any" symbol may be qualified, *i.e.* restricted. Thus in H** B—C R—S, the second term B—C qualifies the first asterisk, and R—S qualifies the second; the inquiry calls for halogen (H) which must be either chlorine (B) or bromine (C), and which must be attached to an aromatic (R) or heterocyclic (S) ring. Other compounds containing halogen, such as iodobenzene (HDR) or chloroethane (HBA) do not fall within the required range, and are not retrieved. Fluorochlorobenzenes (HAR HBR), on the other hand, are retrieved, since HBR is called for.

If it is desired to prevent this, both requirements and exclusions must be specified within a genus. This leads to an "only" condition; H << B—C R—S is the same requirement as before, except that all H terms outside the specified range are expressly excluded. There are also pure exclusion terms. H // B—C R—S is the exact negation of the corresponding term with**. A < C means that all terms begining with A, B, or C are excluded. If we now consider the example in Figure 4, we see that the genus A must not be present, but B is required in BAA (and only there). The formulation is therefore A < A B << A—A A—A. The other formulations are read in the same manner. To make it easier to understand, the search has been carried out in various versions in part of the IDC file (Figure 8). If only the triplet terms required by the structure are

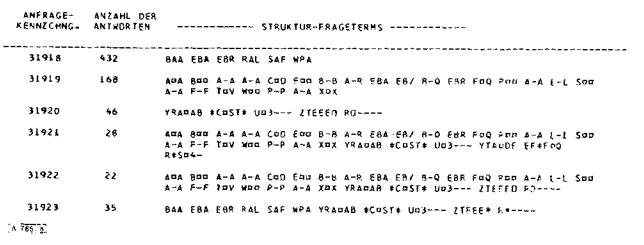


Fig. 8. Number of answers for various formulations of an inquiry. (□ is equivalent to <)

used, the search yields more than 400 answers. If we now add the exclusion of all other triplet terms, the number of answers is reduced to less than half. Using Y and Z terms alone, without triplet terms, one obtains 46 answers. The usual formulation is shown in inquiries 31921 and 31922. In these cases the Y or Z terms are called for in addition to the triplet terms, and 28 or 22 answers are obtained.

We have assumed so far that the structure being sought is given in full. This is by no means the most common type of inquiry, since it is easy to find such a compound from indexes. The problem assumes a different complexion if only partial structures are specified in the inquiry. If in our model case, for example, *any* further substitution of the benzene ring is allowed, no terms can now be excluded. We are therefore left with the triplet terms required and the appropriately modified zone terms. This leads to 34 answers.

Between these two extremes (*i.e.* complete data on the one hand and a partial structure with unrestricted substitution on the other), there are many intermediate stages that can be taken into account in various ways during formulation. Since the system was designed by chemists, chemically similar groups also have similar triplet terms, which can be easily requested together in an abbreviated notation, and which can equally well be excluded.

During the coding of patent claims, it is common to encounter Markush formulas, *i.e.* structures in which a parent structure may be substituted in one or more positions with various and often numerous alternative substituents. In the storage of such formulas, the alternative fragments are stored in specially labeled locations, so that the structure is not blocked by exclusions in the inquiry. Thus if a compound may have either a chlorine or a hydroxyl substituent in one position, this compound should be retrieved in a search for the chlorinated compound, even if OH is forbidden. Alternative groups may also be indicated by a special symbol in the inquiry, and several alternatives are again possible. The ability to include alternatives in the inquiry is not essential for a successful search. A structure in which one position can have three alternative substituents can be found by three individual inquiries. On the other hand, if it has three positions with six possible substituents on each, it is much easier to formulate a single inquiry instead of $6^3 = 216$. In many other systems, however, searches for Markush formulas are very tiresome tasks.

In searches for reactions, the inquiries may again be very special, or they may be general; structural conditions will usually also be known and included in the inquiry. Though the programs for structure searches and reaction searches are executed separately, the results can be correlated afterwards.

Bibliographic data on the encoded publication itself cannot be retrieved directly, since they are not included in the record. For example, one cannot carry out a search for authors. However, there are concordance volumes in the patent field that give the patent number against the abstract. With the aid of these volumes and other data sources that give more detailed information against the patent numbers, it is possible, *e.g.* to prevent one's own patents from being retrieved in the search.

The inquiries coded on the inquiry forms are recorded on punched cards, and the search is carried out with an IBM/360-50 computer.

3.3. Checks for Errors

All inquiries are first checked for formal errors by a diagnostic routine. The inquiries are listed with their number and the codes, and if a discrepancy is found, such as failure to follow the alphabetic sequence, an appropriate error description is printed out.

Punched cards having an inquiry number for which an error description has been received are removed from the batch by the operator, and the diagnostic routine is repeated for the remaining cards. The list of these inquiries, which is now free from errors, is used for this machine run. The computer time required for the diagnostic routine is about 2 to 5 seconds.

3.4. Sequential Scanning

The actual search begins immediately after the diagnostic routine. The entire file is scanned sequentially. At first sight, this procedure seems time consuming. It is even more surprising to find that the time taken for a single inquiry is only about 90 seconds, and that the time is usually reduced by about half, and often to as little as 20 seconds, when several searches are carried out simultaneously. The time given here is the CPU time, *i.e.* the time during which the central processing unit is in use, which is the basis of cost calculations.

3.5. Screening

High searching speed would, however, be impossible if every term of every record were actually checked. It is made possible by "screening" a technique introduced by *Ernst Mayer*, as a result of which the formerly very time-consuming and hence expensive mechanical search has become a relatively cheap routine.

In screening, each record is preceded in the store by a machine word of 32 bits. One bit in this word is reserved for each possible generic letter from A to X; thus if *e.g.* the genus C occurs in the record, an entry is made in the third bit in the screen word, which is reserved for C, by a special program during the storage operation. In the preparation of the inquiry, a bit is inserted in an inquiry screen word (also mechanically) for each *forbidden* genus. The screen words in the inquiry and in the store are then compared at the beginning of the search in a very fast machine operation (Fig. 9).

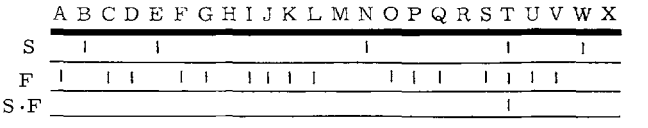


Fig. 9. Screening. In the first screen word, the genus letter of the record S (*i.e.* B, E, N, T, W, in this case) is compared with the genera that are *forbidden* in the inquiry (*i.e.* A, C, D, F, G, I—L, O—Q, S, T, U, V). The logic product S · F of the two sets must be zero. This is not so in the example, since the record contains T, which is forbidden in the inquiry.

If any place is occupied in both, the record contains a genus that is expressly forbidden. This record consequently need not be checked further; the computer jumps over it and tests the screen word of the next record. In addition to this screen word there are also four others, which check combinations of the first and second or of the second and third letters of required triplet terms. Even with the first screen word alone, however, an average of 99% of all the records in the store can be rejected without further checking.

3.6. Output

The answers found by the computer are temporarily stored on a magnetic tape, sorted according to inquiry numbers, and then printed out in a list. Assistants in the Documentation Section then find the corresponding abstracts, and copy them or enlarge them from microfilm. The copied abstracts are examined by documentation officers and sorted into relevant and false drops. The requesting chemist receives both, mainly because even irrelevant compounds are structurally similar to one another and to the compound sought, and *could* therefore be of interest. The computer list remains in the Documentation Section, and is shelved, as are the inquiry punched cards.

If the number of answers is greater than 200, it is usual to ask the requester whether he wants so many answers, or whether he can narrow the inquiry. It is possible, but not very meaningful, to give an average number of answers. This is clear when one considers that there are many searches for structures that are to be claimed as new in patents. In such cases the requester hopes for, and usually receives, the answer "No records". On the other hand, the Documentation Section tries to avoid very large numbers of answers, so that the majority of inquiries yield 0–100 abstracts.

3.7. Updating of Files, Standing Queries

Roughly every three weeks, the IDC supplies new material for filing on magnetic tape, which is simply appended to the existing file, owing to the sequential arrangement. However, the new material is first submitted to all the standing queries in hand.

This type of standing instruction may be regarded as a form of selective dissemination of information. A standing query is frequently made broader than the original query to the existing material. We always have about 60–70 standing queries in hand.

4. Critical Data for a Documentation System

Besides a knowledge of coding, the course of searches, and the search possibilities in a system, other points of great interest are:

1. Coverage (what publications are encoded?)
2. Depth of analysis (how precise? Is every compound named encoded?)
3. Proportion of false drops and the closely related question of the danger of missing relevant documents
4. Frequency of error in encoding
5. Time taken (a) for storage, (b) for encoding inquiries, (c) for machine searches
6. Costs of (a) storage, (b) searches.

These points will be briefly discussed below.

4.1. Coverage and Depth of Analysis

It is common knowledge that all documentation systems yield too little relevant material. The IDC has encoded practically no material earlier than 1959. Moreover, the sources used for coding do not cover the relevant literature fully, though coverage of patents is better.

The sources used at present are:

a) The Farbenfabriken Bayer Progress Report ("Fortschrittsbericht"), which covers about 600 journals.

b) The Chemical Information Service ("Chemischer Informationsdienst"); prior to 1970 the rapid abstracts service of Chemisches Zentralblatt ("Schnellreferate des Chemischen Zentralblatts") was used.

c) The patent report (Patentschnellbericht) published by the Badische Anilin- und Soda-Fabrik, Farbwerke Hoechst, and Farbenfabriken Bayer.

This contains abstracts by the Patent Documentation Group (PDG) of new chemical patents from Belgium, France, the United Kingdom, the Netherlands, Austria, the German Federal Republic, the German Democratic Republic, the Soviet Union, the USA, and Japan. Corresponding patents published later in other countries are not reabstracted but can be searched with special lists.

In the case of the Chemical Information Service, the coding is based on the original publication instead of on the abstract. All compounds named are encoded for all sources (with a few exceptions, such as very common solvents, which no one wishes as an answer to a search).

4.2. False Drops

The proportion of false drops in the IDC system is strongly dependent on the compound being sought. Only a few reasonably dependable rules can be given:

1. The more complicated the structure, the smaller will be the absolute number of false drops.
2. The more general the formulation of the structure, the greater will be the number of false drops, since the number of terms that can be forbidden decreases.

Systematic false drops are sometimes unavoidable. For example, it is often impossible to separate isomers; thus 3-octanol cannot be distinguished from 1-, 2-, or 4-octanol. Moreover, when chain lengths are given, it is not possible to indicate which of several chains is meant. The degree of saturation cannot be given precisely for many heterocycles. An immediate improvement results if topological searching is possible.

Since nearly all formulas will in future be filed by IDC in form of a topological matrix, from which triplet and zone terms can be produced by computer, topological searching will be available in these cases as a means of fine selection. This mutual complementation of the two methods is a decisive factor to us for future planning in the Documentation Section, since it means that earlier and future files can both be questioned by the same methods. The future usefulness of the file is assured by the possibility of topological searching, and despite the enormous data files to be expected, the Documentation Section need neither give up nor start from the beginning again.

4.3. Misses and Error Frequency

The reverse of the false drop problem, *i.e.* the loss of items that have been filed, is found with any ordinary card index arranged according to subject. The loss rate usually increases at first with the size of the index and then falls off again to zero, since the card index has become so large that it is no longer used. This danger is small in the IDC system. Misses result almost exclusively from errors in coding and punching. Punching errors are usually detected at an early stage by quadruple punching. Many typing errors and coding errors can be detected by specific error inquiries (*e.g.* for non-existent terms or combinations of terms). The residual error is not accurately known, but is probably less than 1% of the *terms*. This does not mean, however, that the corresponding *compounds* are untraceable.

Coding and punching errors can also occur in the inquiry. Moreover, the information officer has to know

all the formulations that were used in the system at earlier stages. Some coding possibilities did not exist during the first few years, and many questions must therefore be asked differently in different parts of the file.

4.4. Time Taken

Delays in *storage* were formerly quite appreciable at times. However, the backlog has now been almost completely cleared. For 1970, IDC expects a delay of 8–10 weeks between receipt of the abstracts and delivery of the magnetic tape with the coding to members.

The time taken to *encode an inquiry* varies. It may be a matter of minutes, but it may also be half an hour if the inquiry is difficult to reconcile with the faceted classifications. Inquiries involving substitution data of the type "0 to 2 OH groups and 0 to 3 halogen atoms in the molecule" are nearly always time-consuming.

The *search time* per inquiry has already been reported as 20–90 seconds. The programs written in assembler language require core storage for 54 K bytes. Since only 12 K of these are occupied by the actual search program, smaller core memories may be used, though the operation is then not quite so fast.

The time taken for subsequent treatment naturally depends on the number of answers. In general, however, the chemist receives copies of the abstracts within 24 hours of submitting the inquiry.

Thorough familiarization is necessary in order to acquire a precise knowledge of the sophisticated search technique. However, the system is logical and well thought out, so that an intelligent technician can master it with 4 to 8 weeks' training.

4.5. Costs

The search costs depend on the computer used and on the accounting system of the computer center. The CPU times given should provide an adequate indication to anyone interested; however, the search costs are small in relation to the membership subscription to the IDC. Each member at present pays about 1000 DM per annum per chemist, this subscription being based on a minimum of 50 chemists. Subscription fees are reduced if a member desires searches of the literature or the patents section only, and naturally also decrease as the membership increases. Members with no computer of their own can have searches carried out at the IDC.

5. Outlook

The IDC system provides a search method that, though not very cheap, is reliable and has an assured future. Coding of inquiries is convenient and flexible. The scope will be extended in the near future to include macromolecular chemistry, a further step toward the still distant goal of complete and rapid documentation of the chemical literature of the world.

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Versatile Computer Techniques for Searching by Structural Formulas, Partial Structures, and Classes of Compounds[1]

By Ernst Meyer[*]

The principles of the topological encoding of formulas and machine searching are briefly described. These methods have been developed to the point where it is now possible to carry out a computer search for a given structural fragment without the risk of false drops. It is also possible to carry out searches whose requirements, while well-defined and readily used by chemists, cannot be represented exclusively by element symbols and chemical bonds.

1. Introduction

One of the most important tasks of any information system for organic chemistry is the retrieval of structural formulas and of classes of substances characterized by a common structural unit. Up to now this has generally involved the use of fragmentation codes, in which a selection of structural characteristics is encoded as predetermined code symbols, which can then be searched for singly or in combination. The principal advantage of such systems is the ease of searching. The disadvantages are the intellectual effort required for indexing and above all the restriction to a limited number of predetermined characteristics. If a search is to be run on substances with structural fragments for which there is no actual code symbol, it is necessary to

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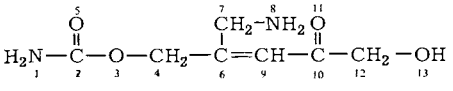
[1] The work was supported in part by the IDC Internationale Dokumentationsgesellschaft für Chemie mbH, Frankfurt.

falsify the question and run the risk of false drops in the answer. This can often be very tedious, and renders pointless many searches that would otherwise be of interest.

2. The Topological Method

The topological method is a new procedure made possible by the introduction of computers. It was suggested by *Mooers* [2] in 1951 for the documentation of structural formulas, and has the advantage that under this system it is possible to search for any structural fragment without the risk of false drops, even if the significance of such a fragment was not appreciated at the time of indexing. The following example shows the basic principles (Fig. 1): To index a compound, its

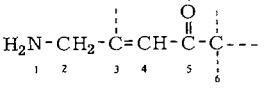
File structure:



1	N	1–2.
2	C	1–1, 1–3, ②–5.
3	O	1–2, 1–4.
4	C	1–3, 1–6.
5	O	②–2.
6	C	1–4, 1–7, ②–9.
7	C	1–6, 1–8.
8	N	1–7.
9	C	②–6, 1–10.
10	C	1–9, ②–11, 1–12.
11	O	②–10.
12	C	1–10, 1–13.
13	O	1–12.

Bond types:
1 = Single bond
②= Double bond

Search structure:



1	N	1–2.
2	C	1–1, 1–3.
3	C	1–2. ②–4, ...
4	C	②–3, 1–5.
5	C	1–4, 1–6, ②–7.
6	C	1–5, ...
7	O	②–5.

Match: search structure: 1 2 3 4 5 6 7
file structure: 8 7 6 9 10 12 11

Fig. 1. Topological structural formula coding (simplified example). Above is a stored formula, and below is shown the required structural fragment both as formula and code.

formula is encoded by assigning a number to each atom other than hydrogen; the order in which these numbers are assigned does not matter. Each atom is then coded (on a separate line), the code consisting of the symbol for the element and the numbers of its "ligands" (neighboring atoms). Each ligand number is prefixed by a code number for the type of bond with which the ligand is connected to the atom in question. In this way we derive a connectivity matrix that may appear at first glance to be heavily influenced by the chance sequence in which the atoms were numbered, but which nevertheless can be used to reconstruct uniquely the original structural formula.

The structure for which a search is being run can be encoded in similar fashion. It is highly unlikely that the numbers assigned to the atoms in the search structure will coincide with those in the corresponding stored structure which answers the question, but the computer can "recognize" equivalent structures. In Figure 1, this is done as follows: Atom No. 1 in the search structure is nitrogen, and the first nitrogen atom in the file structure is also numbered 1. Both have only one ligand, attached by a single bond, and in both cases this is carbon. If we continue the comparison, however, a difference appears: Atom No. 2 of the search structure should have only two single bonded ligands, but No. 2 of the file structure has three. No. 2 (and consequently also No. 1) thus does not meet the requirements of the question. The computer therefore supposes that the next nitrogen atom of the stored structure (No. 8) might correspond to No. 1 of the search structure. For this to be so, its ligand (No. 7) must correspond to No. 2 of the search structure. Both are carbon atoms with two singly-bonded ligands. The next atom of the search structure (No. 3) would then have to correspond to the (still unchecked) ligand of atom No. 7 of the file structure, *i.e.* No. 6. Both are carbons, and the atom of the file structure – as required – has at least one singly and one doubly-bonded ligand. The latter, No. 9, would then have to correspond to atom No. 4 of the search structure (see the comparison in Fig. 1). This process is continued to give a list of possibly matching assigned atom numbers. At branching points it is possible that several atoms of the file structure will have to be considered as possible matches for one atom of the search structure, and these are carefully noted. If the further search shows discrepancies, the computer program jumps back to the last branching point and follows an alternative path. This is repeated until the required structure (or structural fragment) has been found, or until all possible paths have been exhausted.

The Chemical Abstracts Service [3] programmed a similar topological search system [4] at about the same time as ours. It should be mentioned that there are other methods for topological structure comparisons [5], but the iterative search described has the advantage of simulating largely the thought process of a chemist comparing structures, and for this reason it could be extended to meet more complex requirements. Thus, from the beginning we have provided for the indexing of Markush formulas (*i.e.* formulas with one or more positions capable of having several alternative substituents), and have devised a search program that will retrieve these formulas without the need for them to be resolved into all their possible individual compounds; otherwise, in patent documentation too much storage space would be required. We were also able to take into consideration defined rings with substituents at undefined locations.

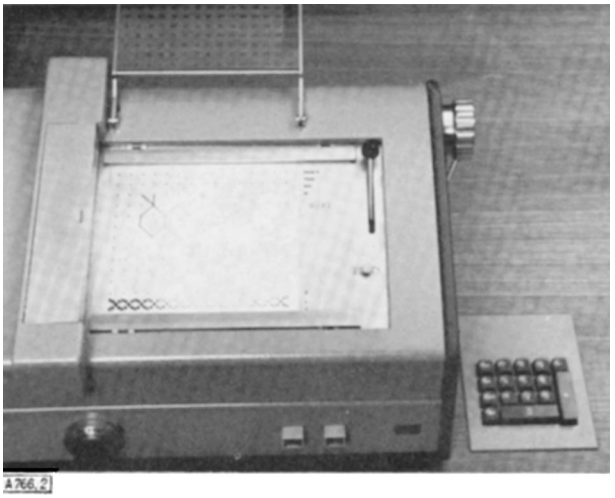
The topological method has two disadvantages: firstly, the indexing would involve a lot of writing and there would be a high risk of error if the connectivity matrices were to be

[2] *C. N. Mooers*, Zator techn. Bull. *59*, 1 (1951).

[3] We are grateful to members of the Chemical Abstracts Service (CAS) in particular Mrs. *Myrna Krakiwsky*, for stimulating discussions within the framework of our exchange of information.

[4] *W. E. Cossum, M. L. Krakiwsky*, and *M. F. Lynch*, Amer. chem. Soc. Meeting, Philadelphia, Pa., April 1964.

[5] *G. Salton* and *E. W. Sussenguth jr.*, ADI Annual Meeting 1963, Short Papers, Part 2, p. 143; Scientific Report No. ISR-6 to The National Science Foundation, Harvard University, April 1964.



A766.2

Fig. 2. Formula reader. The structure is drawn on a transparent grid sheet, which is placed in a slide and scanned by twelve photocells; a punched paper tape is produced which can be processed further by the computer.

prepared manually; secondly, it would take far too much machine time to check all the structural formulas of a large file in this way. We have described elsewhere[6] how we overcame these difficulties. For encoding we built a special the computer, the topological formulation also generates a coding by *Fugmann*'s GREMAS system[9] (an approved and extremely efficient fragmentation code), and this is further processed to give a particularly machine-oriented (and therefore quickly searchable) superimposition code[10]. Only the formulas that pass these two preselection stages — and they represent only a very small portion of the file — need be subjected to a topological search, assuming that the GREMAS search was not sufficient. The machine costs for this are rarely significant.

The topological method has yet another limitation; it does not make it possible to search for structural fragments which, although clearly defined, cannot be represented as structures consisting of a definite number of atoms and bonds, for example "carboxylic acid derivatives" or "alkyl", "alkynyl", "cycloalkyl", "heterocyclic" or "aryl" fragments. This type of question occurs relatively frequently, because the chemist is accustomed to think in these terms and because, for example, he formulates his patent claims in this manner. For this reason we have built into our search programs the possibility of searching for a large number of such fragments, and also of connecting them with well-defined partial structures. We attacked this problem in two ways: In the first place, we used

Parameter-Nr. (Adresse)	Elementsymbol	Bindungswert	Ringwert	Zahl d. H-Atome	Zahl d. Liganden	offene Bindungen (Ladung)	Heteroorientierung	Komplex-Bindungen	Flags	1. Ligand		2. Ligand		3. Ligand		4. Ligand		5. Ligand		6. Ligand		Ringzugehörigkeiten			
										Bindgs.-Typ	Nr.	Bindgs.-Typ	Nr.	Bindgs.-Typ	Nr.	Bindgs.-Typ	Nr.	Bindgs.-Typ	Nr.	Bindgs.-Typ	Nr.	Nr.	Nr.	Nr.	Nr.
	a	b	c	d	e	f	g	h	i	k	l	m	n	o	p	q	r	s	t	u	v	w	x	y	z
HAUPTMATRIX MAT																									
MAT	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
1	5	1	5	1	2	0	0	0	29	3	2	3	3	0	0	0	0	0	0	0	0	19	0	0	0
2	5	1	5	1	2	0	0	0	40	3	1	3	4	0	0	0	0	0	0	0	0	19	0	0	0
3	5	1	5	1	2	0	0	0	42	3	1	3	5	0	0	0	0	0	0	0	0	19	0	0	0
4	5	1	5	1	2	0	0	0	52	3	2	3	6	0	0	0	0	0	0	0	0	19	0	0	0
5	5	1	5	1	2	0	0	0	54	3	3	3	6	0	0	0	0	0	0	0	0	19	0	0	0
6	5	1	5	0	3	0	1	0	65	3	5	3	4	0	7	0	0	0	0	0	0	19	0	0	0
7	7	0	0	1	2	0	0	0	77	0	6	0	8	0	0	0	0	0	0	0	0	0	0	0	0
8	7	1	0	0	2	0	0	0	89	0	7	4	9	0	0	0	0	0	0	0	0	0	0	0	0
9	5	1	0	1	2	0	2	0	101	4	9	0	10	0	0	0	0	0	0	0	0	0	0	0	0
10	5	1	5	0	3	0	0	0	113	0	9	3	11	3	12	0	0	0	0	0	0	20	0	0	0
11	5	1	5	1	2	0	0	0	124	3	10	3	13	0	0	0	0	0	0	0	0	20	0	0	0
12	5	1	5	1	2	0	0	0	126	3	10	3	14	0	0	0	0	0	0	0	0	20	0	0	0
13	5	1	5	1	2	0	0	0	136	3	11	3	15	0	0	0	0	0	0	0	0	20	0	0	0
14	5	1	5	1	2	0	0	0	138	3	12	3	15	0	0	0	0	0	0	0	0	20	0	0	0
15	5	1	5	0	3	0	1	0	149	3	14	3	13	0	16	0	0	0	0	0	0	20	0	0	0
16	7	2	0	0	3	0	0	0	161	4	17	0	15	4	18	0	0	0	0	0	0	0	0	0	0
17	6	1	0	0	1	0	0	0	162	4	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	6	1	0	0	1	0	0	0	160	4	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0
19	4	3	5	0	0	0	6	0	41	0	0	0	0	0	0	0	0	0	0	0	21	0	0	0	0
20	4	3	5	0	0	0	6	0	125	0	0	0	0	0	0	0	0	0	0	0	22	0	0	0	0
21	160	19	1	2	4	6	5	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
22	160	20	10	11	13	15	14	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

A766.3

Fig. 3. Topological connectivity matrix with redundant data ("Main matrix"), as used in core storage for the production of the GREMAS code and for searching. "Flags" denote the previous dot numbers on the grid sheet, *inter alia* for easier reconstruction of the formulas.

"formula reader"[7] (Fig. 2), in which the structures drawn on grid sheets are scanned by photocells, which convert the information into a form acceptable to the computer.

We overcame the searching difficulty by developing a two stage preselection system[8]. When the structures are fed into the connectivity matrix to generate a number of "redundant" data. For this purpose we allotted special lines which represent a ring rather than an

[6] *E. Meyer*, Angew. Chem. *77*, 340 (1965); Angew. Chem. internat. Edit. *4*, 347 (1965).

[7] *E. Meyer*, Nachr. Dokumentation *13*, 144 (1962).

[8] *E. Meyer*, J. chem. Documentation *9*, 109 (1969).

[9] *R. Fugmann*, Proc. IUPAC Congr., München 1959, p. 331; Classification Research. Munksgaard, Copenhagen 1965, p. 341; *W. Braun, R. Fugmann*, and *W. Vaupel*, Angew. Chem. *73*, 745 (1961); Nachr. Dokumentation *14*, 179 (1963).

[10] *E. Meyer*, Proc. FID/IFIP Joint Conference, Rom 1967, p. 280.

atom[11] (from now on we shall refer to both these concepts by the more generalized term "parameter"). For each parameter we retained a number of characteristic data in our "main matrix", *i.e.* in the expanded connectivity matrix (Fig. 3). For this we made use of concepts like "ring value", "bonding value", "degree of hetero orientation", and also the number of ring members, the attached hydrogen atoms or other ligands, the charges, *etc*; we entered these into the main matrix, thus making them rapidly accessible for searching.

For example, the ring value indicates the type of ring to which an atom belongs (heterocyclic, aromatic, or other carbocyclic). The bond value shows the number of double and/or triple bonds in which the atom is involved, irrespective of the neighboring atoms to which they lead; this information is particularly valuable in cases of tautomerism. The degree of hetero orientation, which is based on the GREMAS coding, indicates the number of bonds that are not part of a ring and lead to hetero atoms. Special columns are used to record the numbers of the rings to which the atom concerned belongs or with which the ring concerned is condensed. In addition to this, in ring parameters a reference address leads to a counting up of the ring members. Furthermore, we may distinguish eight types of bonds: single, sesqui, double, and triple bonds, either in chains or in rings.

Code	Significance	
$A	Anything, not *H*	
$B	Hetero atom	
$C	Nonmetallic hetero atom	
$D	Metallic hetero atom	
$I	Nonaromatic ring	in store "Position undetermined"
$J	Aromatic ring	in store "Position undetermined"
$K	Hydrocarbon residue, general	
$L	Alkyl	unsubstituted
$M	Cycloalkyl	unsubstituted
$N	Aryl residue	unsubstituted
$O	Isocyclic residue	unsubstituted
$P	Alkenyl (position of double bond unimportant)	
$Q	Alkynyl (position of triple bond unimportant)	
$R	Unsaturated hydrocarbon chain (position unimportant)	
$S	Hetero- or ring-substituted alkyl	
$Z	Ring closure	
HL	Any halogen	

Bond values (completely additive)

0	Only single bonds
1	One (possibly delocalized) double bond
2	Two double bonds (etc. additive)
6	One triple bond

Fig. 4. List of pseudo-element symbols and bond values used in topological searches. The computer follows this direction and checks whether any fragments other than those given occupy this position.

Secondly, in addition to this, we introduced a number of pseudo-element symbols (Fig. 4), for coding questions; their effect in searching is to call up the appropriate subroutines, which test for definite requirements laid down in the program. For example, the subroutine for "alkenyl" will search in the direction given and will check whether the structure stored there has only carbon (and hydrogen) atoms and has (at least) one double bond in a chain together with single bonds in a chain. By building in further such subroutines we can, if required, introduce any other search concept that is well-defined but not structurally describable.

[11] This enables general questions to be put concerning ring structures, such as the number of members, number and type of multiple bonds, number of substituents and/or condensed rings, *etc*.

3. Examples of Applications

A high flexibility in asking questions inevitably complicates the coding of the enquiry. We have used a set schedule in an attempt to keep the question input as simple as possible, reducing the risk of error and simplifying checking; apart from this, the computer checks the question for formal errors and internal inconsistencies. In order to demonstrate just how many ways there are of putting a question to the system, we are going to describe the process of encoding the question in more detail. It begins, as in the case of formula input, with the drawing of the structural fragments required to be present (or absent) and a numbering of atoms (except for hydrogen) and rings (Figs. 5 and 6).

The sequence of numbering is quite arbitrary, but it is possible to save much computer time by following certain rules; for example, it is preferable to start with the least common hetero atom and then to number in the direction of some other uncommon characteristic. As has already been indicated, it is possible to put a number of partial structure requirements linked by the logical operators AND, OR, and NOT to the same formula on the same question form (Fig. 7); for this it is possible to ask for the identity (overlapping) or nonidentity of individual atoms in different subquestions (col. 20–22) and also to require or prohibit that individual atoms should belong to given ring parameters (col. 23–25). In addition to this, several inquiries can be combined into one (col. 5); it is then required that the inquiry structures should occur in the same document, *e.g.* in a starting material and in an end product.

The question form is filled in by first placing a "1" in column 11 (logic operator); further subquestions start in this column with a number corresponding to their logic. In columns 12 and 13 is entered the number of the atom or ring to be described, in this case "01", and in columns 15–16 the symbol for the element or pseudoelement. Further characteristics for this parameter are entered into the appropriate columns of the same line.

The last four double columns cannot be used for the moment, since up to the present our program has not taken these characteristics (complex bondings, reactions, chirality, and mass) into account. Most of the columns describing properties of the parameter have a logic (L) column prefixed to them; this indicates whether the property in question is required or prohibited, or whether it is to be greater than, less than, or equal to a given value.

In the case of the following atoms it is assumed – provided that there is no entry in column 11 – that they are bonded to the atom immediately preceding them, and the type of bond is indicated in columns 17–19. If more than one type of bond is permitted, then their code numbers are added together and the sum is en-

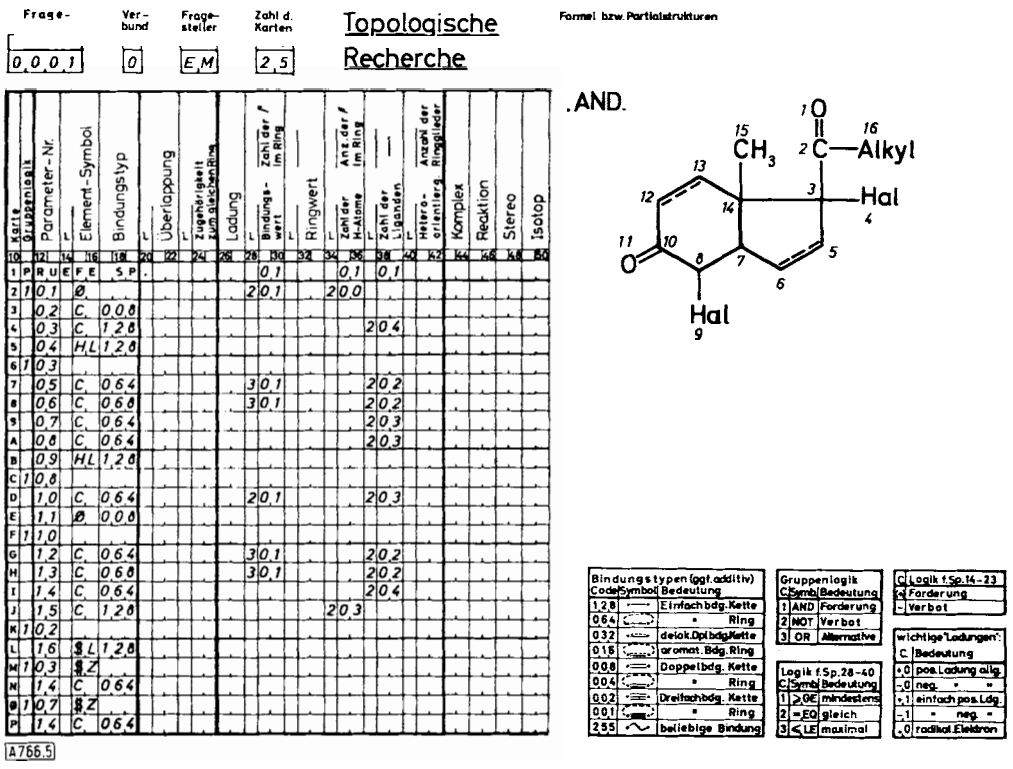


Fig. 5. **Sample question: the type of compound required is shown in the formula.** At the points marked the ring may have double bonds but no substituents, and no further rings may be condensed with it.

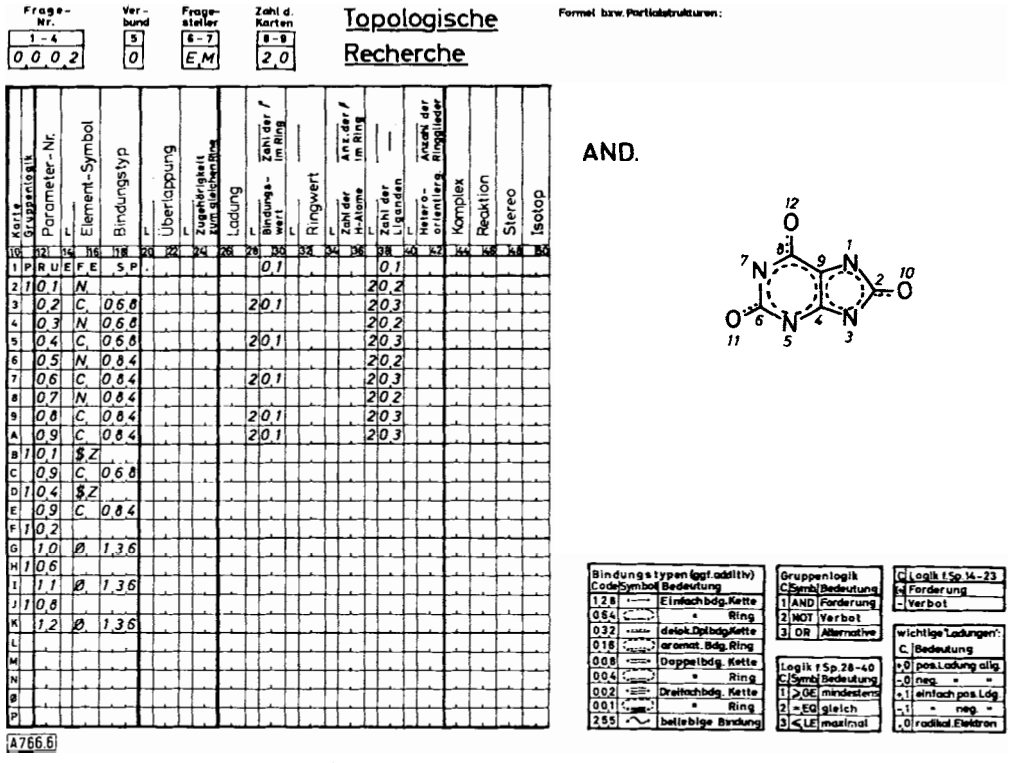


Fig. 6. Sample question: search for all the tautomeric formulas of uric acid and its esters.

tered into the computer memory. (The fact that the code numbers are all in powers of two will make it at once obvious to the expert that we are working with bit strings and masks, and thus the use of alternatives does not require any additional machine time.) If a continuous chain of atoms has been coded in this way and we then want to jump back to a branching point from which a side chain is next to be encoded, then we must first of all enter a "1" in column 11 of a new line and then repeat the number of the branching point in columns 12–13; the rest of this line is empty. Ring closures are coded in a similar way, but here the symbol "$Z" is entered in the element symbol column, and in the following line are given the atom number of the ring closure partner, its element symbol, and the type of bond required for ring closure.

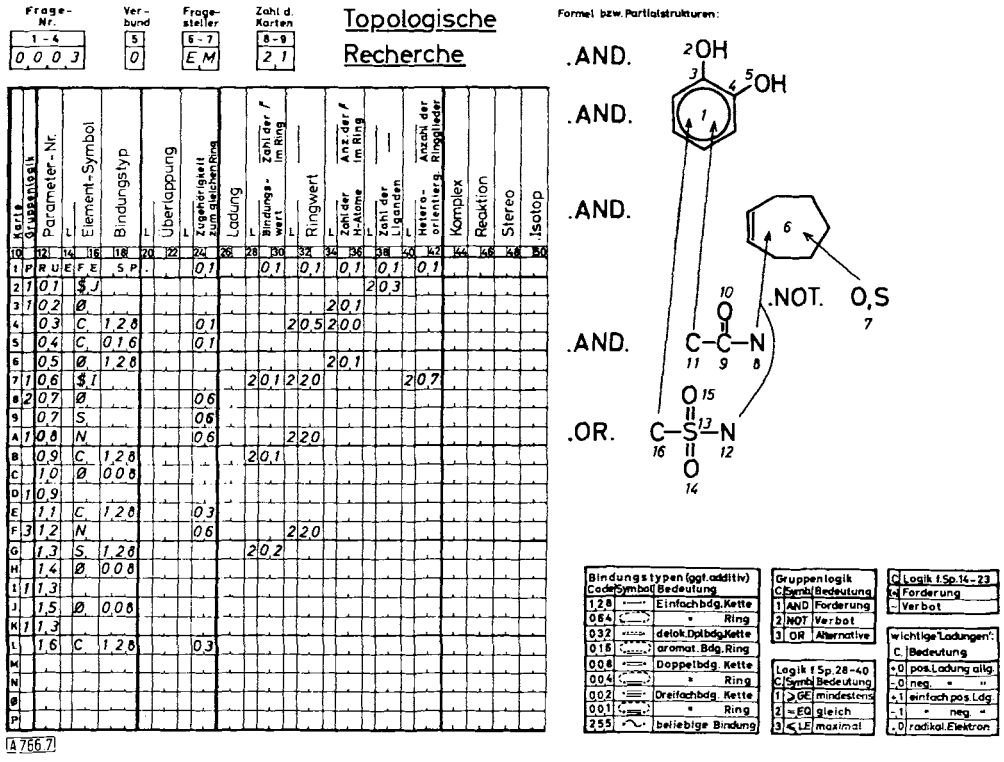
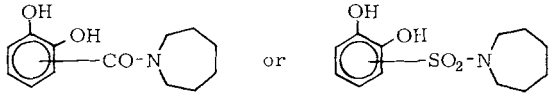


Fig. 7. Sample question: a search for all compounds having the formula



in which the pyrocatechol ring has no other substituents or rings condensed with it, and the seven-membered heterocycle has one double bond but does not contain either oxygen or sulfur.

The "overlap" column is used when a parameter of a given partial structure is to be identical (or nonidentical) with a parameter from a previous partial structure; the number of the earlier one is entered here (in the second partial structure the atom or ring would be given a new number). In the same way, the number of a previously quoted ring or ring atom is entered into columns 24–25 if the atom which is being encoded is to belong (or not to belong) to the same ring. Some of the columns have different significances when ring parameters and not atom parameters are involved; if required, it is possible to enter the number of double bonds in the "bonding value" column, the number of triple bonds in the ring in place of the number of hydrogen atoms, and the number of ring members in place of the hetero orientation. This permits question formulations of the type "Heterocycle with at least seven members and not more than two double bonds". (The maximal ring that can be stored as a ring parameter is a nine-membered one; larger rings can only be searched for as chains with ring closure.)

As already mentioned, alternative formulations can be coded as partial structures in their own right with the appropriate logic operators. If the only alternative requirements are individual atoms or pseudoelements the coding is even simpler; they are given the same atom number and are thus entered in successive lines of the question form (Fig. 7, rows 8 and 9).

Redundant data, *i.e.* those that can be derived from the rest of the question coding, do not need to be entered. Nevertheless, it is often expedient to do so, since then under certain circumstances the computer will discover more quickly that it is on a false track; this can save computer time but it should be remembered that an increase in the number of redundant data also leads to an increase in the danger of erroneous question coding.

For the simpler type of enquiry there is no need for all the columns of the question form to be used. In order to exclude these requirements from the question and thus to save computer time, we have introduced a "column vector". In the first line of the form an "01" is entered into each column to be used; the others are not checked. If one form is not sufficient for a question, others can be attached to it; in each continuation sheet the first line is struck out. Figures 5–7 show the coding for three sample questions, which illustrates some important search requirements and the way in which they are encoded. There is no space in the present article to describe further possibilities or details.

Once the form has been filled out and checked, the information it contains is transferred to punched cards, each line of the form being punched on a separate card. These cards, together with a list (on tape or disk) of the formula numbers that have passed the preselection steps, are fed into the computer with the search program and are then compared by the machine with the tape of topological data. In order to save reading time, the latter tape contains the main matrices in a greatly abbreviated form. The redundant data are still

explicity given, but the overwhelming number of zero elements of the matrices are suppressed by simple routines; it does not require a great deal of computing time to blow them up again in the core storage. The computer prints out the answers either in the form of literature references or as abstract numbers; in most cases we copy the abstracts and send them to the inquirer. If required, the structural formula can also be reconstructed from the main matrix by computer, and can be printed out. This may be done even during input for checking purposes; however, the commercial high-speed printers currently used are not very good at printing out formulas.

4. Conclusions

The computer programs for the searches described have been written for the IBM 360 (OS) and have been tested out [12] – with the exception of the four question modes mentioned previously. These too are being written. "Complex" is intended for searches for co-ordinate bonds and also for significant hydrogen bridges. "Reaction" will be used when studying a series of reactions to specify an atom that has reacted or will react. "Stereo" will use a system suggested by *Petrarca, Lynch,* and *Rush* [13] to check whether a given atom has the required chirality or *cis/trans* position. (The real prerequisite for the practical application of the technique is an economic method of input; programs for achieving this with the aid of our formula reader have already been written for the IBM 7090, but they have not yet been rewritten for use on the 360.) Finally, "Isotope" will be used for compounds labeled in certain positions.

We hope that this documentation system will be a useful tool, particularly for the preparative chemist. Not only will he be able to get answers to his questions from chemical data banks more rapidly and certainly than before, but also the possibility of putting questions in a large variety of new ways should enrich and stimulate chemical research, provided that these possibilities are recognized and put to use. This should make it possible to plan the work more logically, and above all it should reduce the danger of unwittingly duplicating previous work.

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Translated by Express Translation Service, London

[12] The topological input and processing programs (IBM System 360) were written by Herr *Peter Schilling* who contributed a number of interesting ideas.

[13] *A. E. Petrarca, M. F. Lynch,* and *J. E. Rush,* J. chem. Documentation *7*, 154 (1967).

TOSAR – A Topological Method for the Representation of Synthetic and Analytical Relations of Concepts

By Robert Fugmann, Herbert Nickelsen, Ingeborg Nickelsen, and Jakob H. Winter [*]

In mechanized systems used for searching in literature stores there is a steadily growing necessity not only to be able to formulate concepts as a search condition but also the characteristic connections under which these concepts appear in the inquiry. In this way the precision of the mechanized literature search is considerably increased. TOSAR has been developed in order to improve computerized literature searching in this respect.

1. Introduction

With the steady growth of chemical literature, increasing importance is being attached to all methods that allow the retrieval of relevant publications in response to a scientific or technical inquiry. Conventional indexes are quite helpful only if the inquiry is confined to a single concept, and only if the index contains a keyword for this topic. With increasing specialization in science and technology, however, it becomes increasingly difficult to express the subject of a question by a single concept, *e.g.* by a structural formula. A search for terephthalic acid derivatives or for propylene alone would nowadays result in the retrieval of more literature than anyone could afford to examine, unless he intended to write a monograph on this subject and was prepared to spend several months on the task, including the literature searches.

Normally the requester would be much more interested in being directed to literature on *e.g.* processes for the

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oligomerization of propylene to form hexenes and higher olefins with a certain organoaluminum catalyst, with re-utilization of unreacted propylene for the continuous elimination of continuously formed impurities from the catalyst, with the result that the latter is continuously reactivated. The subject of the inquiry is thus much too specific to be sought under the concept "propylene" alone. This concept is "coordinated" with a number of others, and the requester is interested in only those publications in which these other concepts also occur and in which the relation between the concepts is the desired one.

To provide keywords suitable for inquiries as specific as that in the above example, in order to be able to narrow the literature selected, these keywords would have to be in the form of complete sentences. This would require many billions of highly "compounded" keywords of this type. No documentalist could memorize a keyword vocabulary of this size to ensure the assignment of the most appropriate keyword(s) to each publication in his literature analysis, since he would be unable to visualize all the relationships between these keywords. This, however, is a necessary condition for the selection of the most appropriate of a group of keywords. Moreover, the cost of compiling such an index would be prohibitive, as would the insuperable difficulties in its technical handling. Even with a much smaller vocabulary of such "precoordinated" keywords, as used *e.g.* in conventional subject indexes, the completeness of the references under each keyword leaves much to be desired. This is a necessary consequence of the size of the vocabulary from which a choice must be made during literature analysis and of the limited possibilities in the conventional, strictly one-dimensional index. There is thus no advantage to be gained from a further expansion of such keyword vocabularies in order to allow more specific inquiries.

A highly precoordinated vocabulary of keywords would also be unsuccessful for another reason. It is quite common for an author's statements to be so general and to embrace so many cases that it would take much too long to file each case individually with its own keyword. For example, the starting material for an oligomerization process may be given as ethylene, propylene, 1-butene, 2-butene, isobutylene, 1,3-butadiene, or a certain pentene. A separate keyword would have to be used for each of these processes to prevent the mistaken idea that several of these substances take part in the reaction simultaneously. If the monomers in a copolymerization process are given as A and (B or C or (D and E)) and F and/or G, one cannot expect to be able to represent such a complex logic by a single precoordinated keyword.

It has occasionally been suggested that these difficulties could be overcome by feeding the entire original text of a publication into a computer memory and providing the possibility of retrieving any word or any sequence of characters, *e.g.* "propylene" or "oligomerization", from such a text. It may appear from a superficial examination that this satisfies all the requirements for a reliable search, since all the information supplied has apparently entered the memory in a retrievable form. Before the machine can carry out the search, however, it needs a precise order indicating which particular sequences of characters and words are to be retrieved from the stored texts. It is however a fundamental error to believe that it is easy to formulate such an order, or even that it is a task with which the scientist is familiar from his own literature searches. Recognizing the intended meaning of a given text, which is an operation that is always carried out by the expert reader, is quite different from guessing the words in which an author might have described the subject in question. But just that is required in phrasing an inquiry for a mechanized search in the original texts. The first case involves *a posteriori* judgment, while the second requires *a priori* judgment.

Reliable predictions of this nature are possible only if some law governing the event in question is known. No such law is known at present for the words chosen by an author to describe a given subject. One is therefore reduced to guesswork when one wishes to carry out a mechanical search for propylene in the original text ("C_3H_6"?, "propene"?, "C_2 to C_4 olefins"?, "olefinic cracking gases, with a boiling range of 50–60 °C at 20–22 atm?, "... the gaseous reaction products from the dehydration of isopropanol"?, *etc.*). Moreover, how can one allow for the possibility that only the structural formula is given? Lucky finds can undoubtedly be made by these methods, but the procedure could never be described as reliable.

A first step toward the solution of this problem is to bring all the concepts named or implied by the author into a form that is *foreseeable* for future searches. To do this one must either keep a continuous record of all the words that have already been used for a given concept in the stored documents or else translate all the important concepts into a controlled, standardized vocabulary. Morever, in case of an inquiry, instead of using a highly compounded, precoordinated keyword for the concept or for a combination of concepts (*e.g.* "continuous oligomerization of propylene to give hexene and nonene with continuous regeneration of the trialkylaluminum catalyst", *etc.*), one uses a number of "elementary" keywords, which serve merely as conceptual building units. Thus the keywords assigned to a patent might be "catalyst", "continuous process", "cracking", "dimerization", "fractional distillation", "hexene", "isoprene", "nonene", "propylene", "recovery", "regeneration", "trialkylaluminum", and "trimerization". For an inquiry of this kind, the highly compounded keyword under which the relevant literature is to be listed is formed only at the time of the inquiry, *i.e.* by "postcoordination". A special multidimensional search technique must then ensure that only publications in which all the keywords of the inquiry occur in coordination are retrieved from the literature store. A vocabularly of these elementary keywords can be kept much smaller and is easier to memorize than a corresponding vocabulary for all anticipated precoordinated keywords that can be built up from them. This is a principle common to all present-day mechanized documentation methods, such as manual and mechanical punched card systems, magnetic tape files, *etc.*

Mechanized literature searches based on this principle can still be disappointing. Though all the elementary concepts of the inquiry will be contained in the references retrieved, they will often occur in a context quite different from the one desired. For example, a publication may describe the oligomerization of hexene, the cracking reaction may lead to propylene, and

the recovery may apply to excess hexene instead of to propylene. The number of irrelevant publications retrieved in this way will increase with the volume of literature in the subject field in question. If *e.g.* only ten to twenty relevant references are present among one thousand references retrieved in a mechanical search, the subsequent intellectual separation of the relevant from the irrelevant will be tedious in view of the large proportion of the latter, and the usefulness of the documentation system will accordingly be doubtful.

In the long term, therefore, we cannot be content with breaking down highly compounded concepts into their elementary concepts and posting the respective documents under these concepts. In addition, it is necessary to show how these elementary concepts fit together to give the meaning of the original publication. Only then are the author's statements satisfactorily represented, and only then can relations among concepts be used as a condition for the mechanical search.

The documentation literature contains many suggestions and reports on the representation of relations between concepts in storage and in inquiries. A survey of the present position in this field was provided by a symposium devoted to this topic[1]. In one method that is relatively widely used, for example, a syntactic indicator (role indicator, functor, relator) is attached to each concept. This shows more or less clearly the function of a concept in relation to the accompanying concepts in a publication. Examples for these indicators are "starting material", "reaction product", "isolated substance freed from impurities", and "auxiliary material in syntheses". The failure however to specify the particular synthesis in which the substance is a starting or auxiliary material, which impurities in particular have been eliminated from a substance, *etc.*, inevitably leads to irrelevant documents among the ones selected.

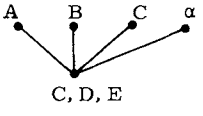
In another method, concepts that occur in the same sentence of a text or in the same paragraph are regarded as being particularly closely related. All the concepts in such a formal section of the document are denoted by a common character ("link"), by means of which they can be distinguished from the concepts in a different section. However, since the boundaries of the conceptual relations frequently do not coincide with these formal sections of the document, inaccuracies and distortions again occur.

Methods based on graph theory have also been used for the mechanical handling of relations between concepts[2]. However, the graphs have always been built up entirely automatically, and not constructed intellectually by an expert after analysis of the publication to be stored.

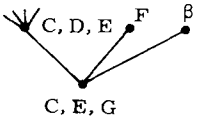
In this article we shall describe a new graphical model for the representation of these relations between concepts, for which we chose the acronym "TOSAR"[*]. In this model a graph is drawn by the documentalist, displaying the relations of the concepts of the documents to be stored or of the inquiry. Since certain principles must be followed in the construction of such a graph, the relations between the concepts assume a form that is forseeable in later searches. All the concepts in this graph and the relations between them are coded and introduced into the memory of a computer. These graphs can then be retrieved by any relevant inquiry with the aid of suitable machine programs.

2. Principles of the Graphical Model

A graph is an abstract system of lines and points, the mathematical rules of which are described by graph theory, a subsidiary field of topology. Concepts whose relations with other concepts are to be represented are assigned to the points. The relations between the concepts are represented in the usual manner by lines joining the points. Each process that is carried out experimentally (or that is thought of as being carried out) is represented by a series of levels. The principal concepts *before* the process in question (α, β, γ, δ, *etc.*) are arranged in a level of their own, and the resulting concepts *after* the process are united in one point on a lower level. All the initial concept points are connected to the result point by lines.

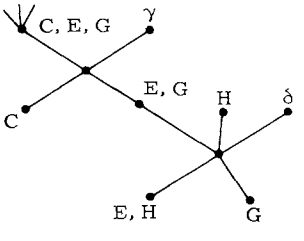


"The substances A, B, and C undergo the reaction α, which leads to the new substances D and E, while the substance C (*e.g.* a solvent) is still present" The fact that A, B, and C are substance concepts whereas α is a reaction concept is also expressed but the details will not be discussed here.



The mixture of substances C, D, and E can undergo a further reaction β on addition of the substance F, as a result of which the substance G is formed from D and F. C and E are still present unchanged in the mixture.

The solvent C is then removed from the mixture of C, E, and G by distillation γ, and E and G in the resi-



[1] *J. M. Perreault*, Proceedings of the International Symposium on Relational Factors in Classification. Information Storage and Retrieval *3*, 177 (1967).

[2] *G. Salton*, Commun. Amer. Assoc. Computing Machinery *1962*, 103.

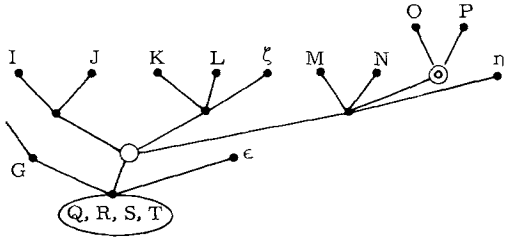
[*] *T*opological Representation of *S*ynthetic and *A*nalytical *R*elations of Concepts.

due are separated (δ) with a solvent H in which only E is soluble.

Just as the figure  is characteristic of the combination of substances, so its inversion denotes any separation of the components of a mixture. If the separation yields several fractions, the topological figure assumes a form such as



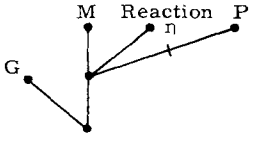
The substance G is now allowed to undergo the reaction ε either with a mixture of I and J or with the product obtained from K and L by the reaction ζ. However, the reaction ε with G may also be carried out using a product obtained from M and N by the reaction η, which is carried out in the presence of O and/or P.



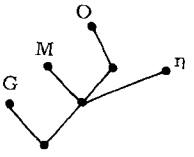
The reaction leads to the class of substances Q, *e.g.* to the individual compound R, S, or T, depending on the reactant used with G.

If two concepts are mutually exclusive, such as the mixture I and J on the one hand and the reaction product of K and L on the other, they are connected to a point indicated by an unshaded circle. If this exclusion occurs at a result point, the alternatives are written inside a circular figure, like the concepts Q, R, S, and T. The mutual exclusiveness of the concepts Q, R, S, T exists insofar as only one concept at a time must be mechanically detectable at that point but never a combination of these concepts. If on the other hand the exclusion is merely potential, a double circle is used, as for the concepts O and P. This logic can be extended over any number of levels, and the relationships can always be clearly recognized by the reader.

For our documentation purposes, it was necessary to be able to store this representation of the relations between concepts and to compare them by computer with the respective representation of an inquiry. An inquiry containing any combination of the concepts α to T should yield a stored graph as an answer if and only if its concepts are connected in exactly the desired manner. For example, the above figure is clearly relevant to an inquiry expressed as follows:

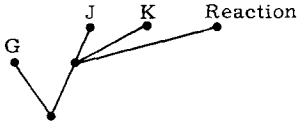


"G is to have reacted with a reaction product of M. Any other substance except P may be present during the reaction of M". (The cancelled line leading to P in the inquiry graph means that P is negated in the connection indicated.) Obviously, the graph in the file contains the partial statement: "G is allowed to react with the reaction product of M, which is formed in the presence of O (and not necessarily of P)":



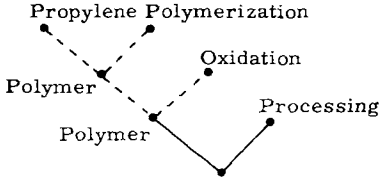
Apparently, a certain concept can be negated in an inquiry only if this exclusion can be precisely restricted to the context intended. No conclusion can be drawn from the mere occurrence of a negated concept in a publication, since the negated concept may be mentioned in a purely incidental, "innocuous" context, *e.g.* as a substance for comparison of properties, as an auxiliary substance for the synthesis of secondary products that are of no interest to the requester, *etc.* However, negations in the inquiry inevitably result in the loss of relevant information if the context of the concepts in the stored documents is not preserved, as frequently occurs in modern mechanized documentation.

The stored figure is not relevant to an inquiry: "Reaction of G with a reaction product of J and K":



It is of no importance in this model whether or not the structure of a substance is known, and indeed whether there is any valid designation for the substance. Its identity *e.g.* as the reaction product obtained from certain starting materials, as an extract from certain organs or plant parts, *etc.*, is unequivocally fixed by the topologically defined position in the graph. The substance concept can thus be reliably retrieved.

Processes for which the experimental procedure was not expressly described, but was merely implied, in the publication or patent to be stored are represented by broken lines. For example, if the processing of a partly oxidized polypropylene is described without a detailed description of the preparation of the polymer itself, the corresponding figure is:



In an inquiry for a particular process, one can choose whether the answer will include only publications in which the process is *expressly described*, or whether *implied* processes are also of interest.

A surprisingly large number of property and process concepts prove on closer examination to be highly compounded. Conceptual analysis to determine the elementary concepts from which they are built up would make them easier to handle in documentation. The elementary concepts, together with the relations between them, would be the ideal replacements for compounded concepts of this nature. Examples of such compounded concepts are "fungistatic thiocarbamic esters", "insecticides that are harmless to bees", "zone melting methods", and "halogenated hydrocarbons having only limited miscibility with glycerin above 60 °C". The analytical approach has been seriously hindered in the past by the fact that while the constituent elementary concepts can be represented with sufficient accuracy, their characteristic mutual relations cannot. Consequently, an essential part of the information contained in the compounded concept would be lost in the analytical treatment of these concepts. This would inevitably lead to the inaccuracies that have already been mentioned. A method of representing relations between concepts precisely and clearly smooths the road to a consistent analytical treatment even of concepts that are not concerned with structural chemistry.

2.1. Example of the Use of the Graphical Model

Let us now take an example from chemical processing (abstract of French Patent 1356225) and consider some of the many types of inquiries that can already be answered by this model using our existing programs:

In the oligomerization of olefins, such as propylene, to obtain unsaturated oligomers, *e.g.* hexenes and nonenes, the activity of the catalyst steadily decreases as a result of the catalyst being loaded with the oligomers formed. A reusable catalyst is regenerated from the oligomerization mixture as follows.

Propylene and the oligomerization products are distilled off from the catalyst in a fractionation column A under pressure. In a second column B in series with the first, propylene is separated from the oligomer mixture, which consists mainly of hexene and nonene, by fractional distillation. The propylene is partly returned to the oligomerization reactor, while the remainder is introduced into the lower part of the column A to free the catalyst collecting there from the last traces of oligomer. This operation is carried out at a temperature below the decomposition range of the catalyst and below the boiling point of the contaminating oligomers.

The purified trialkylaluminum catalyst is continuously removed from the base of the column A and returned to the oligomerization reactor. The hexene fraction formed can be used for the production of isoprene by cracking.

These processes can be represented graphically *e.g.* as shown in Figure 1.

It should be mentioned that it is often impossible to write an abstract of a patent until the relations have been represented graphically in some way.

The partition or separation of a system of substances and the subsequent recombination of the substance flows is evident from the presence of a cycle in a graph of this process.

If a substance or a mixture of substances is recycled, this is also shown in the graph in a characteristic manner. If one follows the purely chronological flow of such a substance, the substance will be found in the same apparatus twice, having left it once in between, and on both occasions it will be associated in this apparatus with exactly the same other substance and reaction concepts. The points at which the same set of concepts is found at different times are joined in the above graph by nonlinear arrows.

It is also possible to see whether a substance is introduced into a reaction as fresh material, or whether it is recovered from the reaction products and returned to the reaction. For example, only part of the propylene used in the oligomerization is fresh feed, while the remainder has been recovered from the process. The point representing freshly introduced

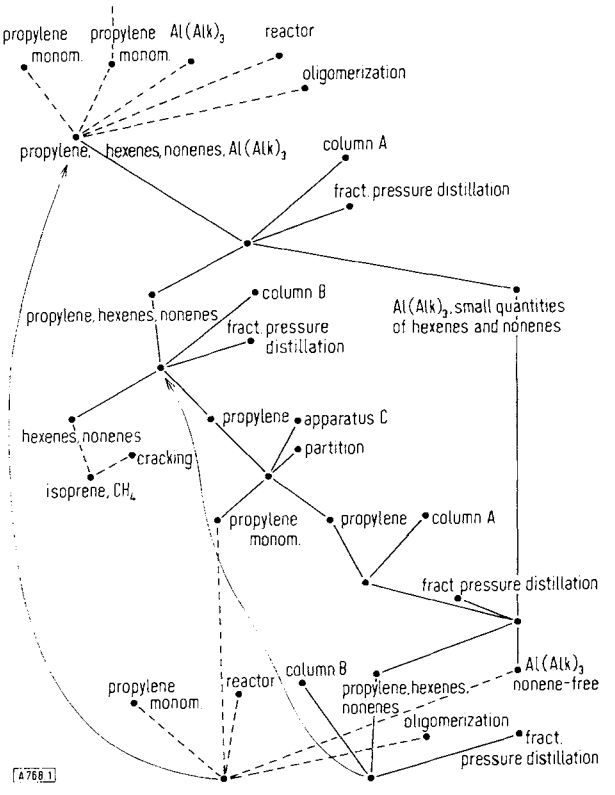


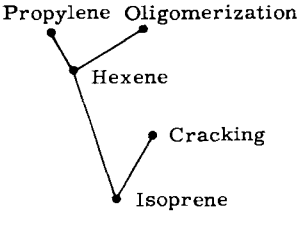
Fig. 1. Relations between the concepts in French Patent 1356225.

propylene has no connecting line from above. However, this is not covered by our coding method at present, and therefore cannot be specified in an inquiry.

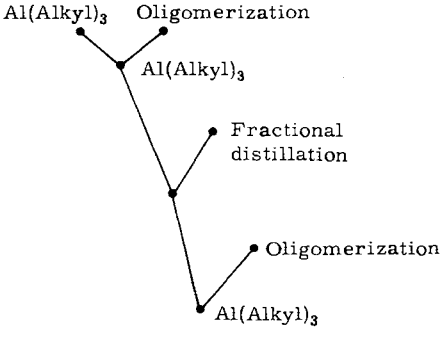
We now consider a series of relevant inquiries from this field, and describe their formulation in accordance with our model, as well as the result of the mechanized comparison of the inquiries with the stored graph.

1. "Production of isoprene by cracking of hexene obtained by oligomerization of propylene".

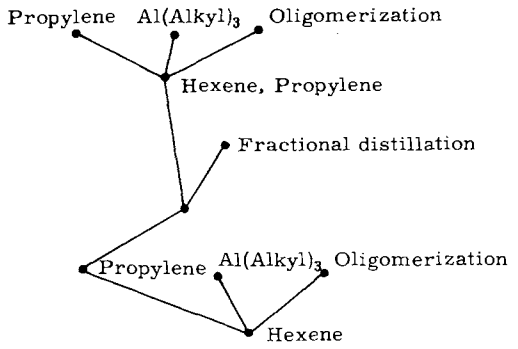
The inquiry can be formulated graphically as follows:



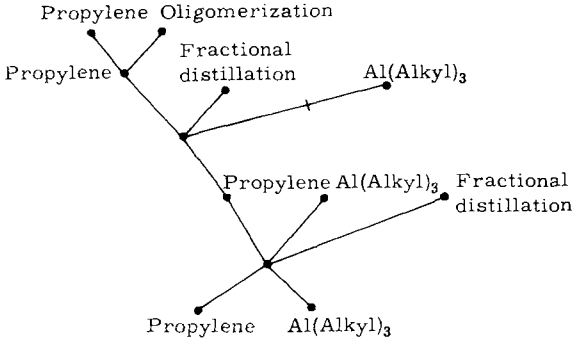
2. "Use of an Al(alkyl)$_3$ catalyst for an oligomerization and its reuse for the same process after purification by fractional distillation".



3. "Oligomerization of propylene with the aid of Al(alkyl)$_3$ to obtain hexene, and separation and purification of the excess propylene by fractional distillation and recycling of the propylene".

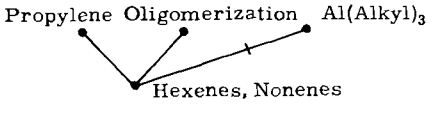


4. "Fractional distillation of $Al(alkyl)_3$ with the aid of added $Al(alkyl)_3$-free propylene that has previously been fractionally distilled and recovered from an oligomerization process".



Topological comparison of the inquiry graph with the stored graph shows that agreement exists in all these cases, *i.e.* the bibliographical data for the stored graph are retrieved in response to these inquiries.

On the other hand, this patent would rightly not be selected as an answer to an inquiry of the type: "Oligomerization of propylene with catalysts other than $Al(alkyl)_3$ with formation of hexenes and nonenes".



3. Principles of the Comparison of the Inquiry Graph and the Stored Graph

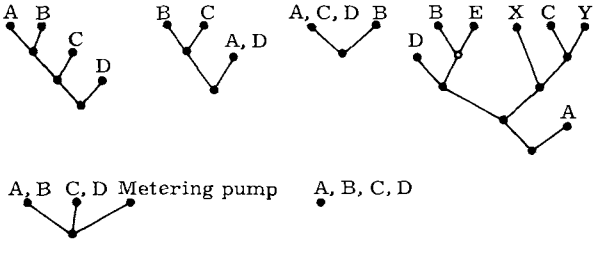
As can be seen from the examples, the mechanized check to establish whether a stored graph is relevant to an inquiry graph cannot be a simple process. For example, a process can never be satisfactory which merely aims at finding those stored graphs of which the inquiry graph is a congruent part. More exactly, one cannot simply try to recognize the inquiry graph homeomorphically and simplicially in the stored graph and regard stored graphs for which this is possible as being relevant to the inquiry.

Such a simple process would fail even for the first of our examples, since the stored graph showing the treatment of the oligomerization products of propylene contains no direct connection between the hexene formed and the isoprene produced from it, whereas such a connection is present in the inquiry graph. On the contrary, the hexene passes through a series of separation and purification steps in the stored graph before being subjected to cracking. However, these are processes whose occurrence or non-occurrence may be purely incidental to the requester and in respect of which he consciously does not wish to commit himself. Moreover, the publication could be of interest to the requester even if the hexene were combined with other substances before reacting further. The hexene may have formed inclusion compounds, been distributed in two-phase systems, *etc.* to allow the separation of impurities. If the requester was always forced to commit himself with regard to details of this nature, which are of no interest or of no importance to him, and whose occurrence in the interesting publications is unforeseeable, the documentation system would be of no help to him. By making a decision about restrictive details of this type, he would be cutting himself off from valuable sources of information. His position would be similar to that of someone looking for a *group* of substances in a molecular formula index; in looking for a basic structure he is compelled to specify the nature and number of the substituents, which are of no importance to him.

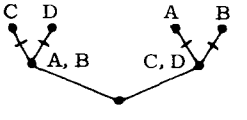
For the same reason, it must not be necessary, *e.g.* in an inquiry for a certain multicomponent system, to specify the order in which the components are brought together, whether *e.g.* two of them are premixed before being combined with another component (or with a mixture of other components), *etc.* If these requirements are satisfied, an inquiry graph having the structure

A, B, C, D

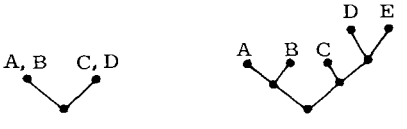
will yield as responses graphs of the following types:



If on the other hand a condition of the inquiry is that a mixture of A and B be combined with a preformed mixture of C and D, the inquiry graph



should produce as a response only the stored graphs of the types:



The mathematical theories now in existence offer no help for the comparison of two graphs in the system described above. Thus graph theory, *i.e.* one-dimen-

sional combinatorial topology, describes in detail the general properties of graphs, and the inquiry and stored graphs described here are no exceptions in this respect. However, graph theory provides no solution for the special procedure according to which the comparison of an inquiry graph with a stored graph must be performed in order to satisfy the requirements of chemical documentation.

Symbolic logic, on the other hand, shows how logical expressions can be transformed in various ways, but does not deal with the logic described above on the basis of which the relevance of a stored graph to an inquiry graph must be judged.

These mathematical disciplines merely suggest certain machine-processable forms for the representation of the publication and of the inquiry in the memory. The principles in accordance with which the two graphs must be compared in a practical literature search, on the other hand, had to be constructed by us specially for this purpose, on the basis of numerous individual pragmatic considerations. The outcome of these considerations has been a very comprehensive computer program. This program is still being improved to increase convenience of storage, as well as precision of retrieval and flexibility in the inquiry.

To enable such a machine program to be advantageously used in chemical documentation, it must be combined with another program whose purpose is to find the *desired concepts themselves*, irrespective of their mutual relations. For, until it has been established that the concepts of the inquiry do indeed occur in a stored document, it is pointless to instruct the machine to search for the desired relation between these concepts. We are currently engaged in bringing about the successive execution of two such machine programs. The preselection on the basis of the concepts themselves is being carried out by the method already being used by the IDC in searches for chemical concepts [3].

4. Outlook

If one considers the familiar structural formula from this angle, it may also be regarded as a graph, though one with special properties. Here, each point is occupied by an atom. The bonds between the atoms form the lines of the graph. The structural formula may in fact be regarded as a highly compounded concept built up from many elementary concepts, *i.e.* the atoms themselves. Experience spanning more than a hundred years has shown that this analytical consideration and representation of the structural formula is incomparably clearer than the complex nomenclature or any arbitrarily fixed trivial name for a substance. This approach is also much more fruitful heuristically, since it clearly displays the relations between substance concepts.

In this light, the graphs described are nothing but the application of the idea of the structural formula to the whole context of a publication. The gain in clarity becomes obvious if one compares the graph drawn above with the original patent. We are therefore watching very carefully the reactions of our colleagues engaged in research and production to graphs of this nature which serve them purely as a rapid information medium, possibly in conjunction with an abstract or with the original text.

This work was supported by the Bundesministerium für Bildung und Wissenschaft. We are grateful to the member companies of the macromolecular chemistry documentation study group for stimulating discussions.

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Translated by Express Translation Service, London

[3] *S. Rössler* and *A. Kolb*, J. Chem. Doc. 10, No. 2, p. 128 (1970); *E. Meyer*, Angew. Chem. *82*, 605 (1970); Angew. Chem. internat. Edit. *9*, 583 (1970).

The "Dokumentationsring der chemisch-pharmazeutischen Industrie"; Aims and Methods

By Wolfgang Nübling and Walter Steidle [*]

The members of the Documentation Ring have chosen the "punched picture" method for coding of chemical and pharmaceutical literature. Chemical, biochemical, and medical facts gleaned from a publication are broken down into basic concepts, each of which is allocated a certain position on the punched card. This system has proved to be reliable over a period of twelve years.

1. Introduction

The "Dokumentationsring der chemisch-pharmazeutischen Industrie" was founded in 1958 [1] to provide, by improving present methods and developing new ones, a more thorough collecting of chemical and related literature, thereby allowing better use to be made of this material. The Documentation Ring enables the individual member to make use of the Society's large total store of material at reasonable cost. Each member processes an essentially equal part of the whole of the sources (journals, patents, or other literature), this division of labor permitting even small and medium sized institutions to operate an extensive documentation system with punched card machines nowadays accessible almost everywhere.

In particular, the pharmaceutical, biochemical, and medical range covered by the Documentation Ring allows the members to supply universities and clinics with literature which is normally not available to them in such diversity. A desirable by-product of this development was the possibility of processing, on the same principles, the results of research carried out by the members themselves, and thus of collating published and unpublished material.

2. Organization of the Documentation Ring

Fifteen members [2] have now come together to find economical and quickly realizable solutions to the problems of documentation. The development of suitable codes for data processing plays a very important part in this work.

Collecting and processing literature from the field of pharmaceutical chemistry involves special difficulties. The subjects concerned cover a particularly wide field, including medicine, chemistry, and pharmacy. Data relating to all of these fields must be collected from the publications and stored in suitable filing systems, since only then is it possible to retrieve the required data later at reasonable cost. At all times it must be possible to establish the relationship between a chemical substance and its application or effect.

The numerous users [3] employ widely different computer systems; punched cards, however, constitute a suitable input medium for almost all of them. In addition there are no problems involved in exchanging punched cards at short intervals, *i.e.* when their numbers are small. This ensures that all members can quickly be supplied with up-to-date material. Our aim originally was to make sure that the system could be used with simple punched card machines. In spite of the fact that the majority of users in the meantime are making use of magnetic tapes and disk units for retrieval even today some members are still coping with the material assembled up to now [4] with the aid of simple sorters *etc.*

Furthermore, punched cards allow special card indexes to be set up which cover separate fields only or which are presorted on specific principles. If decentralized, these special card indexes can considerably facilitate the work of individual centers, or in conjunction with very simple sorting machines, they can solve certain problems with a minimum of time and expense. Finally, other interested people can acquire and use such subindexes, thus solving their special problems with a reasonable expenditure of effort.

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[1] Founding members: Farbenfabriken Bayer AG, Leverkusen (Germany); CIBA AG, Basel (Switzerland); Knoll AG, Ludwigshafen (Germany); E. Merck, Darmstadt (Germany); Dr. Karl Thomae GmbH, Biberach (Germany).

[2] Founding members together with the following companies: Boehringer Mannheim GmbH, Mannheim (Germany); Laboratoires Diamant S.A., La Plaine-Saint-Denis (France); L'Equilibre Biologique, Boulogne-sur-Seine (France); J. R. Geigy AG, Basel (Switzerland); Chemie Grünenthal GmbH, Stolberg (Germany); N. V. Philips-Duphar, Weesp (Netherlands); Rhône-Poulenc, Vitry-sur-Seine (France); Roussel-Uclaf, Romainville (France); Schering AG, Berlin (Germany); Troponwerke Dinklage & Co., Köln-Mülheim (Germany).

[3] Since 1964 Derwent Publications Ltd., London, have been evaluating the literature on the basis of the system developed by the Documentation Ring for processing "pharmaceutical" literature in the widest sense. Since then this literature service has been available in an extended form to more than 100 subscribers under the names Ringdoc (literature on pharmaceutical chemistry), Pestdoc (pest control literature), and Vetdoc (veterinarian literature).

[4] Since the Documentation Ring was founded, about 500000 articles *etc.* have been abstracted. Their content is recorded on more than 1.5 million punched cards.

We prefer a decentralized retrieval system to a centralized one. It takes less time to process data within one's own organization. The best result is assured only by a permanent dialogue between the inquirer and the file. This implies good collaboration between the inquirer and the documentation center, since only the documentation specialist is able to put the inquirer's question into the form which suits the storage method best.

The ever-increasing costs for the machinery of a modern documentation center, however, will sooner or later necessitate a central storage unit which is at the disposal of all members by means of suitable terminals. Moreover, only such a solution will allow optimal use to be made of the material stored by provision of suitable computer programs. This optimal use naturally involves not only the usual information concerning sources but also answers to unusual inquiries which, for example, give an early indication of development trends or automatically draw attention to advantageous combinations of methods in such fields as analytical or preparative chemistry.

3. The Documentation Ring's Coding Methods

In our choice of coding system we were governed by the desire to find a simple code that would as far as possible accord with the habits and thought processes of the specialists concerned with coding. It should be possible to encode quickly and without errors. The more complicated and unusual the coding system is, however, the more numerous become the errors. The filing of the material, *i.e.* the coding, should not take too long, since any system is acceptable only if the given volume of work can be dealt with in the time available. The coding time determines when the material stored is available for searches. Furthermore, the system should be easy to learn so that it can be used by the largest possible number of members. Only then can the costs be kept within acceptable limits.

These considerations led us to choose simpler and cheaper methods than the topological system for chemistry. These, however, do not always supply clear-cut results; in addition to the correct answers there is often a proportion of false drops, the number of which varies according to the inquiry. The documentation specialist, therefore, sometimes has to sift through the material supplied by the machine before he hands it over to the inquirer. In fact, since according to experience only a fraction of the total material stored is ever required again, the cost of input plays a very important role. Moreover, excessively narrow coding frequently leads to incomplete retrieval and loss of data that might be relevant or even necessary for a particular topic. To avoid this disadvantage all necessary concepts must initially be thought out at length. In the majority of cases, however, the specialist whose job is the correct formulation of such precise inquiries for the computer comes up against considerable difficulties.

A carefully constructed fragmentation system eliminates these difficulties at source; the very act of selecting the fragments that have to be taken into account for a special question makes it possible to increase or reduce the number of relevant answers as desired. By separating the interconnecting characteristics from the fragments, the search often reveals combinations which neither the inquirer nor the documentation specialist has thought of, but which may be of great value for the inquirer's work.

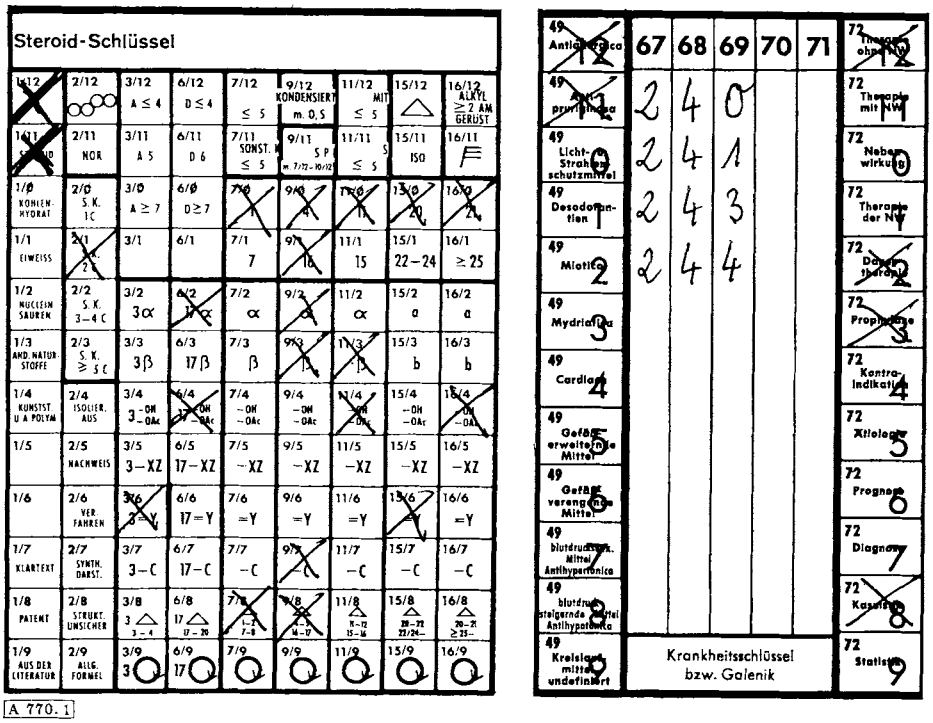
The punched picture system has proved to be a particularly good way of recording the chemical, biochemical, and medical facts of a publication on a single punched card. Each fact to be included is broken down into basic concepts, and every basic concept is allocated a certain position on the punched card. In this way it is possible to request each basic concept alone or in any combination with other basic concepts. Each of the 960 punching positions, *i.e.* every bit, thus has a definite meaning. This holds good not only for chemistry, where the fragment code is nowadays already in general use but also for medicine, biochemistry, and biology, where organisms, organs, pharmaceutical activities, metabolism, and physiology are covered on the same principle.

The coding of a publication usually involves the preparation of several punched cards. Superposition rules show which compounds and facts can be overcoded on the same card. These rules prevent the store from becoming too large but on the other hand may lead to false drops being obtained during searches.

In this way the use of keywords is avoided even for non-chemical facts. We believe that, because of the linguistic nonuniformity, because of the possibility that different keywords will be used by different workers, and because of their one-dimensional nature, keywords are not an ideal medium for the documentation of facts. Furthermore, they take up a relatively large amount of space on the magnetic tape or in the store, which, in view of the large and ever-increasing volume of literature, should be used sparingly, despite the enormous capacity of modern machines. It is naturally possible to avoid these difficulties to some extent by standardizing the terms and compiling thesauri in which the permitted terms are collected and the unacceptable expressions are referred back to the acceptable ones. This activity, however, entails a lot of work, must necessarily be spread out over a number of years, and is practically never-ending.

Bitwise classification, however, which means that there is a fixed address for every basic concept, allows unequivocal storage with very few aids. At the same time very rapid access is possible. By combining building blocks and by using numerical and alphanumerical codes in partial fields one can satisfactorily reproduce all required data. Figure 1 shows an example for coding the treatment of diseases.

A further major advantage of our method lies in the fact that, because they are attached to punched cards, forms can be used as coding sheets on which the positions provided for chemical and biochemical data and



Casuistics, prophylaxis, and therapy
72/8 72/3 72/12,2

of hay fever, of bronchial asthma,
WHO code 240 WHO code 241

of urticaria, and of
WHO code 243

allergic eczema as well as suppression of
49/12
WHO code 244

itching by the steroid
49/11 01/12,11

Decortilen®

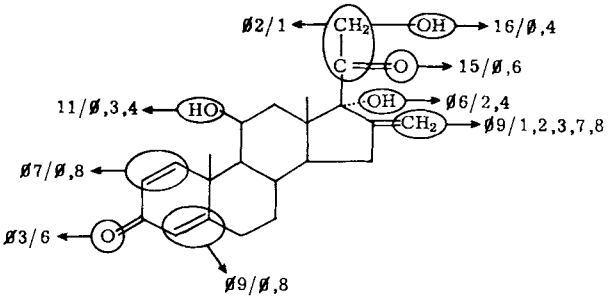


Fig. 1. Above: Section from the coding sheet with medical and partial chemical coding for the treatment of hay fever, bronchial asthma, urticaria, and allergic eczema with Decortilen ®. Below: Coded notes on and coded formula of Decortilen ®.

reaction steps are printed so that it is easy for the coder to do the work correctly. The necessity for coding on preprinted coding sheet ensures that the encoder is always aware of the possibilities that exist and also causes him to use these. Coding errors and the omission of codable concepts are thus reduced to a minimum. The use of document readers nowadays saves manual input with its scope for error.

We know no other system with such an ideal relationship between input and output costs, especially since the percentage of punched cards retrieved in one search averaged out over a fairly long period, is only 0.02% of those consulted. Because the indexes are presorted, only a fraction of the store is generally searched through. Furthermore, since normally several punched cards lead to the same abstract, the number of literature sources obtained as a result is extremely small, despite the false drops described above. We therefore came to the conclusion that more expensive systems would be uneconomical.

After laying the foundations for documentation in pharmaceutical chemistry [5], the Documentation Ring now turns its attention to other problems. We wish to mention here only the documentation of chemical reactions [6], and the coding of carbohydrates, pharmaceutical specialities, and Markush formulas. All these projects rely on the same basic principles, thus building up one integrated system of documentation.

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[5] Cf. *M. Scheublein, W. Steidle, W. Germann, W. Nübling,* and *R. Wilhelmi,* Naturwissenschaften *55,* 362 (1968).

[6] *O. Schier, W. Nübling, W. Steidle,* and *J. Valls,* Angew. Chem. *82,* 622 (1970); Angew. Chem. internat. Edit. *9,* 599 (1970).

A System for the Documentation of Chemical Reactions

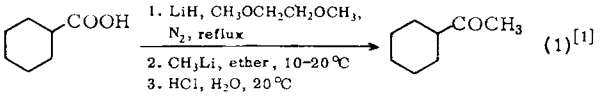
By Oswald Schier, Wolfgang Nübling, Walter Steidle, and Jacques Valls[*]

The Documentation Ring of the chemical and pharmaceutical industries uses a punched card system to record chemical reactions. The starting materials and the end products are encoded with a fragmentation code, and the bonds that change during the reaction are recorded in the same way. Reaction modifiers and physical data can also be stored. In the case of multistage reactions, both the individual stages and various groups of stages are recorded.

1. Introduction

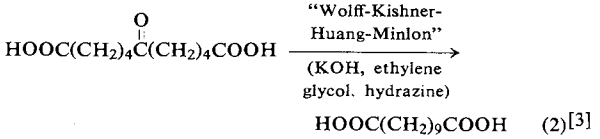
It is basically more difficult to record chemical reactions than it is to record chemical substances. A substance is an independent concept, generally defined by formula or name, if not by both. On the other hand, in a reaction we usually have several substances reacting with one another under defined conditions to form new substances.

A chemical reaction involves a large number of data: The starting materials; the end products; the bonds that react; the reagents used; and the reaction conditions. Even the simple reaction shown in eq. (1) comprises a considerable number of concepts which must be taken into consideration when it is recorded.



(1)[1]

Such reactions are not only difficult to record, they are often even difficult to name. In many cases this problem is solved by naming the reaction after its discoverers[2] rather than after the structural change that it brings about [eq. (2)].



(2)[3]

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Dr. J. Valls
Roussel-Uclaf S.A.
Romainville (France)

[1] *T. M. Bare* and *H. O. House*, Org. Syntheses *49*, 81 (1969).

[2] *K. G. Wagner*: Autoren-Namen als chemische Begriffe. Verlag Chemie, Weinheim 1951; *A. R. Surrey*: Name Reactions in Organic Chemistry. Academic Press, New York 1954; *J. E. Gowan* and *T. S. Wheeler*: Name Index of Organic Reactions. Longmans, London 1960; *H. Krauch* and *W. Kunz*: Reaktionen der organischen Chemie. Hüthig-Verlag, Heidelberg 1966.

[3] *L. J. Durham, D. J. McLeod*, and *J. Cason*, Org. Syntheses, Coll. Vol. IV, 510 (1963).

These difficulties in the documentation of reactions are one of the reasons why it is not merely the chemist's experience and intuition that are put to the test when he is trying to devise a new synthetic route. The decisive factor may often be his ability to find the appropriate individual reactions in the literature.

Conventional methods of recording facts fail when it comes to the complex network of data represented by a chemical reaction. Only modern documentation techniques can achieve this. Some years ago *Ziegler*[4], among others, described a method for recording chemical reactions on field-punched cards.

Having solved problems in medicinal chemistry documentation[5], the Documentation Ring of the chemical and pharmaceutical industries turned to the task of developing a card system for chemical reactions. The present article reports the results of this work. After extensive tests, the system is to be made generally available with a data base of 25000 abstracts.

2. Method of Documentation with the Reaction Card File

The choice of a documentation system is determined by the amount of material to be recorded and the number of concepts occurring together or in conjunction with one another. In the case of a card system for reactions, the minimum number of individual reactions to be recorded is of the order of 20000; for example, the 24 volumes of *Theilheimer*'s "Synthetic Methods of Organic Chemistry"[6] which have appeared up to now contain in themselves more than 22000 examples of reactions, with many additional literature references. We must also reckon that our card file is going to grow at the rate of at least 2000 references per year.

A file of this size would be difficult to operate as an ordinary card index and would not work well with peephole cards or with edge- or field-punched cards. It would be unable to cope with the multiplicity of

[4] *H. J. Ziegler*, J. chem. Documentation *6*, 81 (1966).

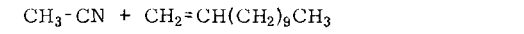
[5] a) Cf., *e.g.*, *M. Scheublein, W. Steidle, W. Germann, W. Nübling*, and *R. Wilhelmi*, Naturwissenschaften *55*, 362 (1968); b) *W. Nübling* and *W. Steidle*, Angew. Chem. *82*, 618 (1970); Angew. Chem. internat. Edit. *9*, 596 (1970).

[6] *W. Theilheimer*: Synthetic Methods of Organic Chemistry – Synthetische Methoden der Organischen Chemie. S. Karger, Basel, New York, Volumes 1–24 (1946–1970).

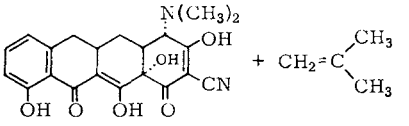
concepts to be considered for each reaction. Peephole cards can only represent one concept per card, and are limited in the number of items that can be handled. In the case of edge- and field-punched cards there are mechanical limitations, since the sorters have a maximum capacity of 250–500 cards and would thus need to be reloaded an impracticable number of times for an extensive collection.

We therefore asked ourselves whether the code for our reaction file should also be suitable for machine-sortable punched cards, or only for a computer. The normal punched card contains 960 punch positions, which is sufficient for a reaction card file. Modern punched card sorters are well able to cope with the number of cards expected; for example, an IBM 108 sorter can sort about 60000 cards per hour for up to 12 questions.

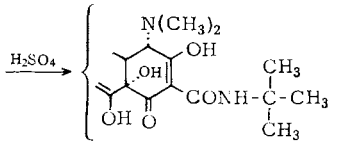
For the Documentation Ring's reaction card file a code suitable both for machine sorters and for computers was developed. We knew that this would deny us certain advantages that a system intended purely for computer can frequently offer. However, the deciding factor was the thought that a reaction card file should benefit the widest possible circle of potential users. Users with access to a computer can of course transfer the contents of the cards to tape, disk, or drum.

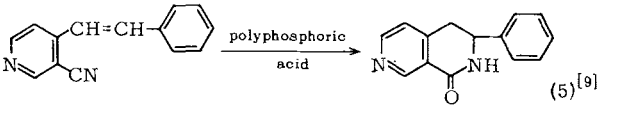


(3)[7]



(4)[8]





(5)[9]

3. Data Recorded in the Reaction Card File

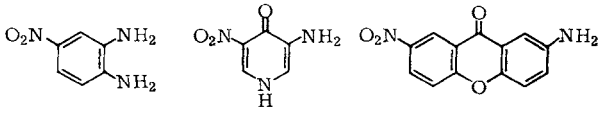
At the start of any documentation system it is necessary to decide which data are to be recorded. It goes without saying that all the important data should be retained and all the unimportant data eliminated. These general considerations determine the code to be used.

3.1. Starting Materials and End Products

3.1.1. General Considerations

How important is the detailed recording of the starting materials and end products in a reaction card file? On this point we may note that when a chemist wants to make use of a reaction he is often looking for substances that have structural characteristics in common with the materials treated by him. For example, a synthesis described in the literature for a substituted amide from a nitrile can also be valuable in the preparation of an amide or a lactam of a completely different class of substances [eq. (3)–(5)].

In reactions (3) to (5) the sole search requirement was the reacting and the final functional groups. Often, however, it is necessary to search for parts of the molecule that do not take part in the reaction. For example, in the search for a selective reduction of dinitro compounds to nitroamines a second, nonreacting nitro group is assumed to be present. The nitroamines which are obtained from dinitro compounds by the same method (action of ammonium sulfide) can belong to completely different groups of substances [examples (6) to (8)].



(6)[10] (7)[11] (8)[12]

The previously mentioned search for "Amides from nitriles" could also be narrowed down by specifying that they should be aliphatic or heterocyclic nitriles, as in (3) and (5), or a nitrile of the tetracycline series, as in (4).

These requirements relate to parts of the molecule that react and also those that do not. The reaction card file should therefore contain the fullest possible record of the structures of the substances. However, the essential features are not the overall structures but rather those general formulas and partial structures which permit questions of the kind described.

3.1.2. Encoding the Data

The starting materials and the end products are encoded by means of the code developed by the Documentation Ring in 1958–1960 (see[5b]). In this code the substance concerned is broken down into partial structures, giving just the type of fundamental units

[7] *T. Clarke, J. Devine,* and *D. W. Dicker,* J. Amer. Oil Chemists' Soc. *41,* 78 (1964).

[8] *C. R. Stephens, J. J. Beereboom, H. H. Rennhard, P. N. Gordon, K. Murai, R. K. Blackwood,* and *M. Schach von Wittenau,* J. Amer. chem. Soc. *85,* 2643 (1963).

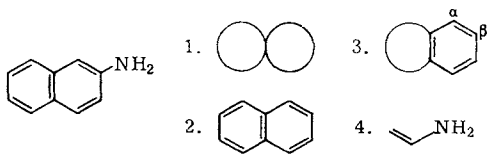
[9] *J. M. Bobbitt* and *R. E. Doolittle,* J. org. Chemistry *29,* 2298 (1964).

[10] *K. P. Griffin* and *W. D. Peterson,* Org. Syntheses, Coll. Vol. III, 242 (1955).

[11] *W. H. Crowe,* J. chem. Soc. (London) *127,* 2028 (1925).

[12] *S. Dhar,* J. chem. Soc. (London) *109,* 744 (1916).

that are important in a reaction card file. For example, β-naphthylamine is encoded to give the fragments 1–4:



where

1. is a system of two condensed rings
2. is two condensed benzene rings
3. is a β-substitution in a condensed benzene ring
4. is a primary amine group at a double bond.

These data correspond to six holes in a punched card. Other naphthylamines with different substitutions would give the same punching (with the exception of the hole for the β-substitution) together with other holes for the appropriate additional concepts.

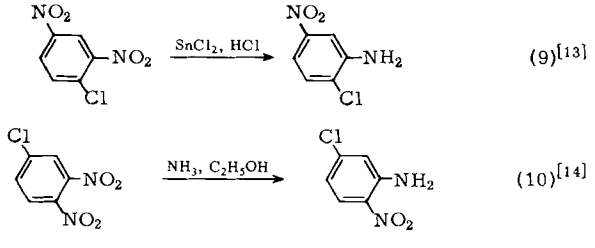
The coding and searching operations are simple. In breaking the substance down into its structural fragments, the code uses the same basic units to which the chemist himself is accustomed, and requires neither code numbers nor letter combinations.

The starting materials and the reaction products each require 27 columns of a machine-sortable punched card (324 hole positions each).

3.2. Modified Bonds

3.2.1. General

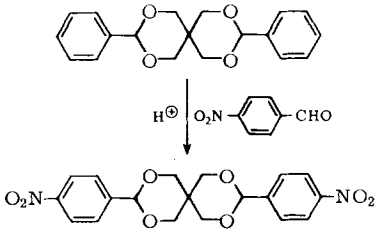
In general, the encoding of the starting materials and end products is not a sufficient record of a reaction. Even in simple cases it is often hardly possible to recognize the type of reaction if only the structures and no data on the reagents are given. Thus, in eq. (9) the nitro group is being reduced to an amino group, whereas in (10) it is being replaced by the amino group, which is a completely different reaction.



(9)[13]

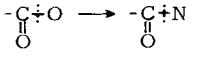
(10)[14]

In the transacetalization in eq. (11), a comparison based on structures alone could lead to the assumption that it was a nitration[*].



(11)[16]

In any case, data on bond changes are also required for other reasons; for example, they permit a classification of reactions. Conversions of the type ester → amide, ester → lactam, ester → hydrazide, ester → acylurea, *etc.* can be summarized as



Bond change data are here independent of whether the reaction occurs in an acyclic structure or in a ring.

3.2.2. Encoding the Data

The bonds which are broken down in the starting material and formed in the end product are easily recorded. Thus, the reaction H–N → C–N (*e.g.* the alkylation of an amine) is recorded by the code as the two punch positions "H–N broken" and "C–N formed".

In many cases the environment of the modified bond is also of interest. For this reason it is possible to distinguish in the code whether, in the case of a C–H cleavage, the C–H is present in the structure $>C=\overset{|}{C}-H$ (*e.g.* in benzene), $>C=\overset{|}{C}-\overset{|}{C}-H$ (*e.g.* allyl), $-C(=Y)-\overset{|}{C}-H$ (*e.g.* the α-position in ketones, acids, *etc.*), or in some other structure.

The code enables the bond data to be amplified by providing further positions for the formation, cleavage, decrease or increase in the size of rings, and further reactions such as rearrangements, the conversion of a racemate into optically active compounds, stereospecific and asymmetric syntheses, and many more.

Eight columns (96 punch positions) are allowed for these data in the punched card used in our system.

3.3. Reaction Modifiers

3.3.1. General

Any organic chemical reaction usually involves a number of substances that are described as "starting materials", "reagents", "solvents", and other terms. In many cases the distinction between "starting material" and "reagent" is merely a reflection of the availability and frequent use of one substance as opposed to the other. For example, in eq. (12) to (16) the reagent is the substance above the arrow.

In the last two examples, the same substance is the "starting material" in one case and "reagent" in the other.

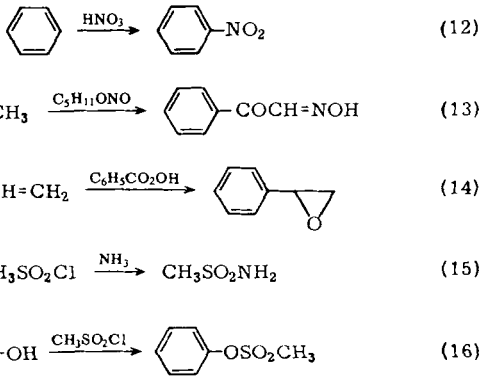
[13] *A. Claus* and *A. Stiebel*, Ber. dtsch. chem. Ges. *20*, 1379 (1887).

[14] *A. Laubenheimer*, Ber. dtsch. chem. Ges. *9*, 1826 (1876).

[*] Attempts have been described [15] to record chemical reactions by a computer analysis of the structural changes. Our own studies show that the computer requires considerably more data for such an analysis if it is not to yield false results; cf. eqs. (10) and (11).

[15] *J. E. Armitage, J. E. Crowe, P. N. Evans, M. F. Lynch*, and *J. A. McGuirk*, J. chem. Documentation *7*, 209 (1967).

[16] *E. Bograchov*, J. Amer. chem. Soc. *72*, 2268 (1950).



(12)

(13)

(14)

(15)

(16)

In order to avoid errors, a documentation system should define its concepts in the way normally used by chemists. The best way to achieve this is to describe the following substances as "reaction modifiers" (reagents, solvents, *etc.*):

inorganic substances (cf. eqs. (12), (15));

organic substances that do not provide any of the carbon atoms in the end product (cf. eqs. (13), (14));

some 30 other organic substances such as methyl iodide, methanol, acetic anhydride, or mesyl chloride, which count as reaction modifiers if they react with an organic substance [cf. eq. (16)].

The separation into starting materials and reagents is justified from the point of view of the reaction. In a reaction card file for organic chemistry it would be pointless to record reagents like hydrochloric acid, nitric acid, *etc.* time after time as starting materials whose bonds were broken in the reaction.

3.3.2. Encoding the Data

The reaction modifiers are recorded in our system in ten columns of the punched card (120 hole positions). In order to permit general questions, broad concepts such as oxidizing, reducing, and condensing agents, catalysts, inhibitors, biological agents, and others are included. The code also permits the recording of whether the reaction occurs in an acid, basic, or buffered medium.

The encoding of the reaction modifiers is simple. Frequently occurring substances like alcohol, acetone, pyridine, $LiAlH_4$, HCl, and iron are coded directly, and the others are coded by combinations of partial structures, *e.g.* lead acetate as metal acetate + lead.

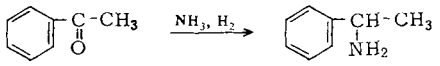
3.4. Physical Data and Other Information

In addition to the substances reacting and present in the reaction medium, the physical data of the reaction are also of interest since they can have a decisive influence on the course of the reaction. These data include temperature, pressure, effect of light, *etc.*, and are given explicitly in one column of the punched card.

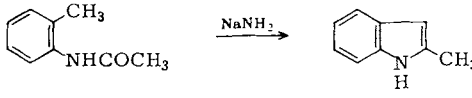
In addition, the code can indicate whether the article is a review and also whether it deals in some detail with the reaction mechanism.

3.5.1. General

When we talk of a synthesis we are generally considering a single starting material which is to give a single end product.

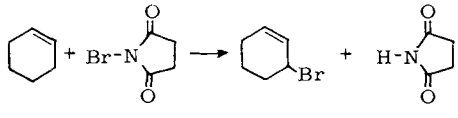


(17)[17]



(18)[18]

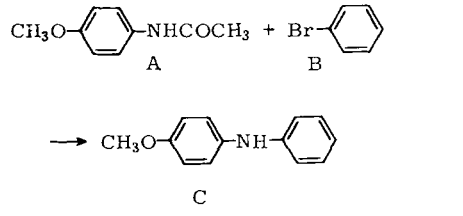
This corresponds to the previously mentioned division into starting material, reaction modifier, and end product. Even where two organic substances are reacting to give two end products, it is often only one of the four possible combinations that is of interest. Thus, in eq. (19) we are only interested in recording the conversion of cyclohexene into the 3-bromocyclohexene which can be isolated from the preparation (A → C). It is certainly necessary to record the reagent bromosuccinimide, but its reactions to give succinimide (B → D) or even to give 3-bromocyclohexene (B → C) are of little interest. The conversion of cyclohexene into succinimide (A → D), which is the fourth possible combination, is of no interest.



A B C D

(19)[19]

This is not the case with reactions of the type shown in eq. (20). Here both the conversions A → C and B → C are of interest and must be recorded.



(20)[20]

A is the starting material in (19) and A and B are the starting materials in (20); the bromosuccinimide in (19) is, however, a reaction modifier in the sense of the definition given previously. In both reactions it is only the substance C, isolated from the preparation, that is of

[17] *J. C. Robinson jr.* and *H. R. Snyder*, Org. Syntheses, Coll. Vol. III, 717 (1955).

[18] *C. F. H. Allen* and *J. VanAllan*, Org. Syntheses, Coll. Vol. III, 597 (1955).

[19] *K. Ziegler, A. Späth, E. Schaaf, W. Schumann*, and *E. Winkelmann*, Liebigs Ann. Chem. *551*, 80 (1942).

[20] *F. E. King, T. J. King*, and *J. H. M. Muir*, J. chem. Soc. (London) *1946*, 5.

interest as the reaction product. This defines the range of reactions to be recorded: any conversion of a starting material into a reaction product which is isolated from the preparation is to be recorded.

3.5.2. Encoding the Data

Each punched card is used to record the reaction of *one* starting material (punched in columns 1–27) to form *one* end product (columns 28–54). If several such combinations are possible, as for example in (20), then two or more punched cards are used, related to one another by the use of the same abstract number which also enables them to be searched in common.

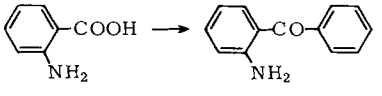
The bonds that are modified and certain other data are punched in columns 55–62. After column 63, which is left blank for the purposes of the individual user, the reagents and solvents (reaction modifiers) are punched in columns 64–73. The operating conditions are given in column 74.

Columns 75–80 contain the abstract number, which relates the card to the abstract.

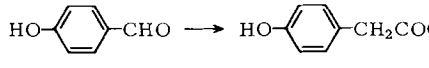
3.6. Multistage Reactions

3.6.1. General

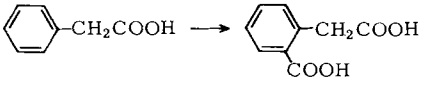
The reactions shown in eqs. (21) to (23) are syntheses requiring two or more steps and giving good yields and, as such, of considerable interest.



(21)[21]



(22)[22]



(23)[23]

Despite this fact, if they are recorded in the usual way they will usually not be found in the form given, since generally it is not the overall reaction but rather the individual stages as such that are recorded. A reaction card file should not fall into this error.

3.6.2. Encoding the Data

In our reaction card file, multistage reactions are recorded not only as the individual stages but also as combinations of two or more stages. The reaction sequence A → B → C → D, is encoded as a number of punched cards, which contain the individual reactions A → B, B → C, C → D, but also A → C, A → D, and B → D. In this way it is possible to encode and search for reactions that would have been lost by the single-stage approach. The amount of trouble that our system can save the chemist involved in synthesis work can easily be estimated.

4. Practical Applications of the Reaction Card File

4.1. Methods of Searching

Figure 1 shows the way in which the concepts for reaction (24) (chosen at random from Vol. 23 of *Theilheimer*'s "Synthetic Methods of Organic Chemistry") are encoded. The 24 concepts given appear on the punched card as 24 holes. For example, the nitro group shown in box 7 is punched in column 17, line 4 of the card; the same is true of any nitro group in any starting material.

Questions may be formulated using any desired combination of punch positions ("multidimensional searching"). The searches may range from specific to quite general inquiries. For example, the specific search for reactions of 2-nitrocyclohexane would match on positions 1 to 9. A specific search for the synthesis of 6-nitrocaproic acid would match on positions 17 to 22.

The code does contain a certain degree of ambiguity. The same positions 17 to 22 are also used to encode the closely related compounds 5-nitro-*n*-valeric acid and 7-nitroheptanoic acid.

Apart from these specific questions, a large variety of general questions can also be put. The combination of structure and reagent, *e.g.* the effect of bases on oxo compounds (positions 8 + 9 + 12 for reaction (24)), provides information on the reactions that a structure can undergo when treated with a given reagent. Among other things, this is important in the prediction of side reactions.

More general questions on the stability of compounds are, of course, possible. Reaction (24) as encoded will match the following search requests: cleavage of alicyclic rings (positions 3 + 11); stability of nitro groups at an active methylene group (6 + 7); reactions of cyclohexanones (2 + 3 + 8 + 9); and the influence of α-substituents on the stability of oxo compounds (6 + 8 + 9).

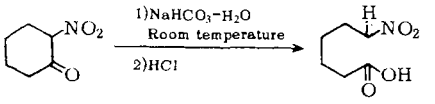
Again, if one is carrying out a synthesis with sensitive materials which will not permit the use of high temperatures, one can use the concept "Room temperature", and, for example, search for reactions of α-nitro ketones at room temperature (positions 6–9, and 16 for reaction (24)).

General questions on the end products can also be put in a number of ways. On the punched card for reaction (24), the positions given will answer the following questions: synthesis of ω-nitro carboxylic acids from other nitro compounds (positions 19–22 and 7); synthesis of nitro carboxylic acids (positions 20–22); synthesis of carboxylic acids (positions 21 and 22).

[21] *H. J. Scheifele jr.* and *D. F. DeTar*, Org. Syntheses, Coll. Vol. IV, 34 (1963).

[22] *G. Billek*, Org. Syntheses *43*, 49 (1963).

[23] *P. A. S. Smith* and *R. O. Kan*, Org. Syntheses *44*, 62, 91 (1964).



(24)[24]

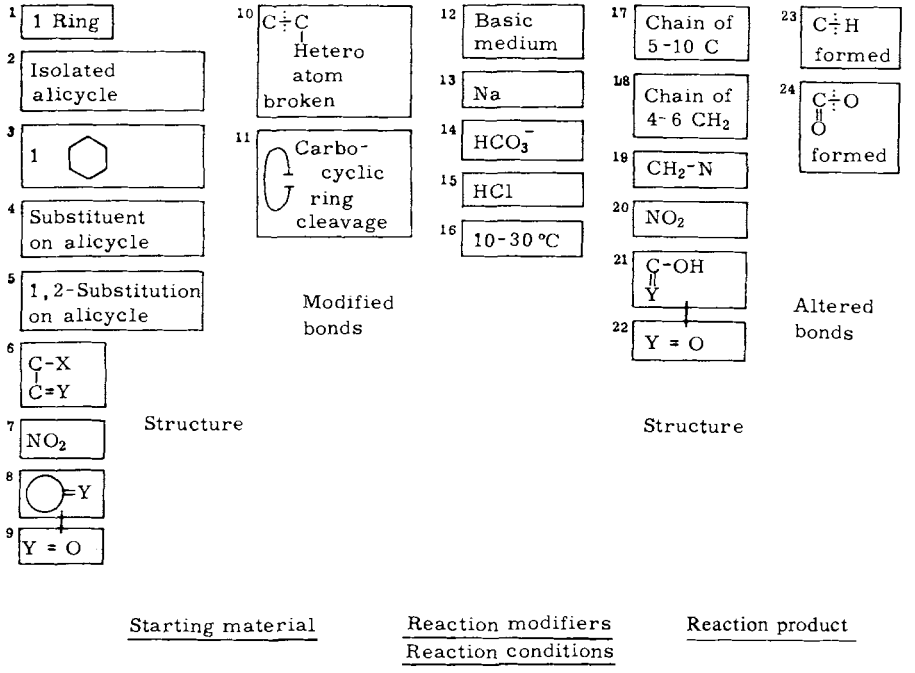


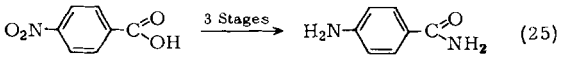
Figure 1.

4.2. Quality of the Answers

The described code uses the simplest possible concepts familiar to any chemist. This makes the cost of coding relatively low (about 8 DM per abstract). The searching is also quite a simple process. Does this also mean that we must expect a high number of false drops?

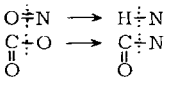
A structural fragmentation code does not normally give a unique and unambiguous coding for every single substance. In the case of reaction (24) it was mentioned that the coding of the end product could also apply to two closely related nitro carboxylic acids. This, however, is no drawback, since a highly detailed structural coding is generally not required in a reaction card file.

Substances and bonding are encoded together, and they supplement one another to give a high degree of selectivity. Even in cases like (25), where there are parallel reactions of several groups in the same molecule, so that false combinations of punch positions could give rise to wrong answers, a simultaneous search for structures and bonds generally excludes the irrelevant answers. For this reason, the punched card for reaction (25) would not match the incorrect combinations shown.

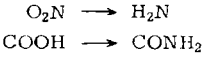


(25)

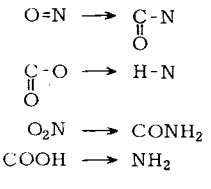
Modified bonds:



Modified structures:



Combinations giving false drops



A fundamental refinement of the code could enable the very small proportion of irrelevant material to be reduced still further. However, this would complicate the code and make the encoding process more tedious; hardly any user would then be in the position to supplement the card file by encoding his own material. In addition to this, in the case of parallel reactions like (25) the independent reactions would be encoded separately, which would make it impossible to search for such reactions [*e.g.* amino carboxylic acid amides from nitro carboxylic acids as in (25)].

The reaction card file described represents the joint efforts of 14 firms in the Documentation Ring of the chemical and pharmaceutical industries. We should like to express our particular thanks to the following: O. Dold (Boehringer Mannheim, Mannheim/Germany), G. Hallermann (CIBA A.G., Basel/Switzerland), R. Payer (Chemie Grünenthal, Stolberg/Germany), H. Lebrecht and M. Scheublein (Knoll A.G., Ludwigshafen/Germany), K.-H. Bork (Merck, Darmstadt/Germany), U. de la Vaissiere (Roussel-Uclaf S.A., Romainville/France), H. Seidel (Schering A.G., Berlin/Germany), I. Schuler (Thomae GmbH, Biberach/Germany), and H. Lehwald (Troponwerke, Köln-Mülheim/Germany).

Received: May 13, 1970 [A 772 IE]
German version: Angew. Chem. *82*, 622 (1970)
Translated by Express Translation Service. London

[24] *A. S. Matlack* and *D. S. Breslow*, J. org. Chemistry *32*, 1995 (1967).

CCBF – A System for the Computer Processing of Chemical and Biological Facts[**]

By Gerhard Ohnacker and Werner Kalbfleisch[*]

A computer-based system for the documentation of company research results in drug research is described. The system stores the numerous results of standardized biological tests and processes chemical formulas by topological techniques. The stored material is processed to provide computer-printed card indexes and lists on chemical and/or biological topics. The programs enable searches to be made for any desired substructure and for pharmacophoric groups, thus providing highly effective assistance in the search for structure-activity relationships.

1. Introduction

The development of a new, biologically active substance to the point where it can be introduced as a drug takes at present an average of six to eight years. As a rule it requires the synthesis of a few thousand new chemical substances, which must be tested by a wide variety of biological test methods. The requirements for proof of biological activity, medical usefulness, and the relative degree of safety are continually refined and made more stringent, and we must give serious consideration to the predictions[1] that in future the time required to develop a new drug resulting from a large research project might increase to as much as 15 to 20 years.

During this long period scientists in many disciplines will be working simultaneously or successively on a large number of promising groups of substances, and as the project progresses the number of data that must be evaluated will increase. In such a case individual results are only meaningful when confirmed by other similar results. Thus for a given substance large numbers of results, obtained either simultaneously or at different times, have to be compared with other individual values or with the activity profiles of other substances.

Such comparisons can assist the scientists efforts in optimizing biological activity by variation of both substance groups and substituents. The usefulness of these comparisons increases with:

– the size of the cooperating team, *i.e.* with the number and range of the tests from which the given individual results are derived;

– the degree of certainty of the biological results, *i.e.* with the number of standardized tests that can be used, the results of which remain comparable over long periods and are largely unaffected by external influences;

– the extent and accuracy of the physicochemical data that can be used for regression and correlation analyses.

Today the ever-increasing mass of data can be stored and processed efficiently by large computers. The usefulness of computers depends on the speed and certainty with which access is offered to the collection of formulas and results, and on the clearness and readability of the answer. In an effort to meet these requirements as closely as possible, a system for the documentation of company research results can use different approaches and more specific techniques than those used by a documentation system for published material in the same field which is of interest to numerous people.

Every documentation system of published material has to strive for completeness. It aims to cover every publication in a given field and all publications in the marginal fields. In addition, it must try to ensure that each document is indexed to the same depth. Often this is only partly achieved, because it is determined not only by the actual content of the publication but also by a more or less detailed thesaurus which lists the terms considered worth indexing, and also by the subjective on-the-spot decisions of the abstractor. Contrariwise, company research results can be deliberately indexed at different levels and depths, because the subsequent use of the system can be planned very exactly to match the needs of a team of limited size.

If the documentation system is to give effective support to the research effort, the best system for a given case will depend not only on the nature and extent of the data to be stored and processed but also on the specific scientific requirements. For this reason we need the collaboration of the scientists themselves in the design of the means for data recording, in the establishment of SDI (Selective Dissemination of Information) profiles, and in the continuous enlargement of the system.

This is the basis upon which the CCBF system for the computer processing of chemical and biological research results was developed. As in all documentation

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[**] CCBF = Computer processing of Chemical and Biological Facts.

[1] Medicine in 1990 – a technical forecast by the Office of Health Economics, London, Med. Pharm. Studienges. e.V., Frankfurt, 1969.

systems, data recording is the bottleneck. Therefore, particular care was taken that the various possibilities of the system can be offered with a minimum expenditure of data recording.

2. Functions of the CCBF System

The system is required to:

- store chemical structures and biological results;
- provide information in the search for structure-activity relationships;
- supply the scientist, either in a current awareness or at special request, with computer-produced card indexes and lists of results;
- prepare statistical data for management.

To meet these requirements the programs enable the chemical file to be searched for individual compounds, substructures, and general formulas. The biological file can be searched for individual results or activity profiles. The computer prints out the appropriate formulas and data. To a large extent the printouts can be arranged to suit the inquirer's wishes. Table 1 shows examples of some of the types of questions that can be put, together with the types of printouts. In addition to these specifically requested searches, the CCBF system also offers a continuing service in the form of chemical (Fig. 1) and biological (Fig. 2) card index systems. These subsystems are continually updated and distributed to the scientific workers.

Table 1. Summary of types of questions and answers in the CCBF system.

Type of question	Format of search result
Chemical questions:	
Search for a definite structure	Printout of structural formula
Search for a definite class of compounds Search for a general formula Search for any given substructure	Printout of the structural formulas of all the compounds found. The list can be arranged by code names or by substituents
Combined questions:	
Search for the biological action of a definite substance	Printout of all biological data stored for this substance
Search for compounds which are effective in one or more tests; dosage limits can be set	Printout of the code names and/or formulas of the substances found together with the pharmacological data. The substances can also be arranged in order of effectiveness
Search for compounds with one or more given side effects	Printout of code names and/or formulas of the compounds found, arranged by dose, animal, and mode of application
Statistical questions:	
Summary of all new compounds synthesized in a given period	List of code names and/or formulas, arranged by classes of substances
Summary of all biological results reported in a given period	List arranged by test number and/or customer

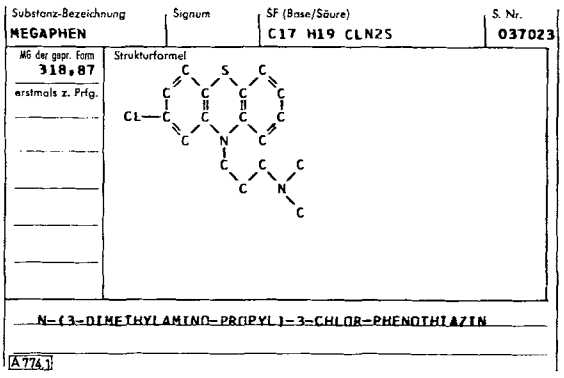


Fig. 1. CCBF chemical index card. (Original format 6" × 4".)

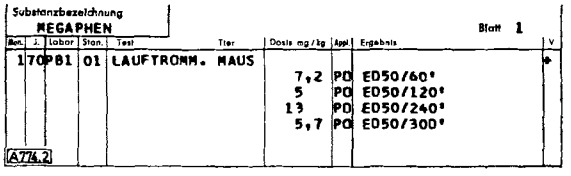


Fig. 2. CCBF biological index card. (Original format 6" × 4".)

3. Scope of the CCBF Store

3.1. Biological Facts

All results obtained on screening with standardized biological test methods in pharmacology, biochemistry, and microbiology are stored numerically. Results from special studies of individual substances are also stored, but they are not indexed in such depth since they have no significance in the search for structure-activity relationships. These can only be detected with standardized tests on a series of structurally related compounds. However, the individual results are important in searching for activity profiles of individual substances. But in these cases it is usually sufficient to find indications of the dates, authorships, and locations of the reports on the results of special biological tests.

3.2. Chemical Facts

The file contains the structures of all new compounds synthesized within the company for biological testing. It also includes the formulas of published compounds that have been used for biological testing within the company.

4. Documentation Techniques

4.1. Biological Results

The indirect coding of biological information with numerical codes or thesauri [2] is certainly of universal application, but it also involves considerable ex-

[2] For example the Biology Code of the Chemical Biological Coordination Center, ed. by *P. G. Seitner, G. A. Livingston,* and *A. S. Williams,* National Academy of Sciences, National Research Council, Washington D.C., 1960.

penditure. Conversion of the information into combinations of numbers or keywords, and also the continual amplification of the codes and thesauri, can only be performed with the necessary degree of accuracy by well trained experts. The same applies to direct codings with coding forms on which the relevant information must be marked.

The great majority of the biological results stored in the CCBF system is derived from tests performed by standardized methods. For this reason the format of all the results from a given test is always the same; therefore, a data sheet suitable for direct data recording has been developed for each test method. All the data sheets can be filled in while experiments are going on. The data on these forms are transferred to the biological file either in text form or as numerical values. For example, Fig. 3 shows the data sheet for the motility test with the revolving drum. The entry of data becomes still simpler in the case of tests whose results are calculated using biometrical methods by computer. In these cases the results form (Fig. 4) is also produced by computer; it is first sent to the scientist so that he can eliminate any useless results. Only the data worth recording are transferred from the results tape to the CCBF store. All the data are first checked by the computer for formal errors and plausibility. Formal errors are indicated, for example, if the substance tested has not yet been entered in the chemical file, or if the sequence of results (card sequence) is incorrect. Testing for plausibility shows whether the data supplied make good sense; the program will give a warning if, for example, the results are illogical or the doses are nonsensical.

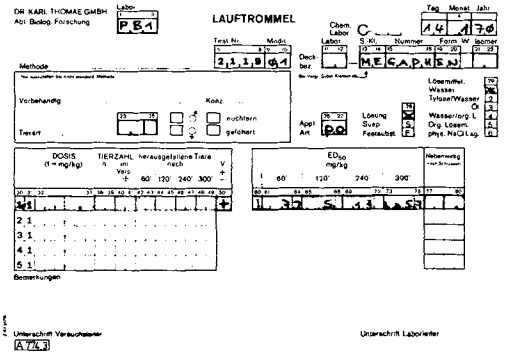


Fig. 3. Data sheet for the input of biological data into the CCBF system. Code symbols are only used in the "Test No." and "Modif." fields for the method of test, in the "Type of animal" field, and in the "Side effects" field. Anything that the scientist has entered in the "Remarks" section will be stored as text. Such remarks cannot be searched for but they can be printed out together with biological search results. (Original format 8'' × 6''.)

BA4 GLUCOSE COLOR. 192001 24.03.70

B -DF 0001 NA

DOSIS 12,500 MG/KG PO RAB

W 180 0 S 7,5 PK

TIERE	ZEIT	MITTELW.	SXQ	AEND.	
21	0	82,5	1,53		
21	60	68,4	2,37	- 17%	SIGN.
20	120	72,5	2,96	- 12%	SIGN.
20	180	73,3	3,34	- 11%	SIGN.
20	240	75,4	3,30	- 9%	N. SIGN.

A774.4

Fig. 4. Computer-produced results form for biometrically calculated biological data.

The data record of all the results relating to an individual substance in the biological file begins with the key data of the compound, which also provide the link to the chemical file. The test results follow in the order of their entry. For each test there are the characteristic data (test number, type of animal, mode of application, *etc.*), the dosages, the numerical results, and finally any remarks made by the investigator, in clear text.

4.2. Chemical Structures

Only substances of clearly defined structure are entered into the chemical file of the CCBF system; Markush formulas do not occur [*]. Thus it is possible to process the chemical formulas topologically. In this method, the fundamentals of which were first described by *Mooers* [3], the structures are stored unambiguously and searches may be carried out for any desired substructure. In developing our coding system for formulas we took advantage of the experience of *Horowitz* and *Crane* [4], *Waldo* [5], and *Meyer* [6]. The formulas are entered manually onto a grid sheet (Fig. 5). Certain rules have to be observed mainly with regard to the data recording equipment.

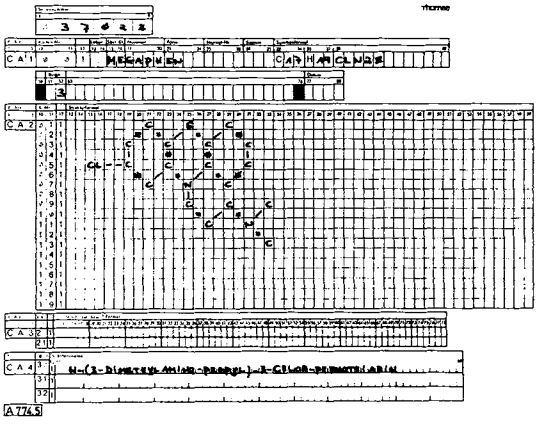


Fig. 5. Coding sheet for recording chemical formulas in the CCBF system. (Original format 12'' × 8''.)

For printing formulas by computer we use a high-speed IBM 1403/N 1 line-printer with additional characters to print some chemical symbols not included in the normal character-set. These are: ⟍, for this one single bond, ⫴, ⫽, and ⟍, for the double bonds, ≡ and ⫼ for the triple bonds, and the symbol □ to characterize an aromatic ring. In order to get a

[*] A Markush formula is a general formula such as $R'NH_2$, in which R' might for example stand for any alkyl group from C_1 to C_{10}.

[3] *C. N. Mooers*, Zator Techn. Bull. *59*, 1 (1951).

[4] *P. Horowitz* and *E. M. Crane*: Hecsagon: A System for Computer Storage and Retrieval of Chemical Structure. Eastman Kodak Company, Rochester, N.Y., 1961.

[5] *W. H. Waldo*, J. chem. Documentation *2*, 1 (1962).

[6] *E. Meyer*, Angew. Chem. *77*, 240 (1965); Angew. Chem. internat. Edit. *4*, 347 (1965).

suitable printed formula, the line density is altered to eight lines per inch. Since these symbols do not appear on a normal key punch, the aromatic ring is coded as @, the single bond \ as ×, the double bond in any direction as #, and the triple bond as ∏. The coding program ensures that the correct symbols are filed. For the bonds of six-membered aromatic systems the program generates the "aromatic" bond type. With regard to a suitable printed formula it is also possible to draw dotted bonds to indicate ionic bondings or steric positions; furthermore, signs of charges can be drawn. A special code relates these and other data (*e.g.* radioactive labeling) to the corresponding atoms. This code gives the grid coordinates (row and column number of the atom in the grid-sheet) together with a keyword for the special fact.

Topological coding is concerned solely with atoms other than hydrogen. Hydrogen atoms are therefore not drawn on the grid-sheet, unless they are required for the improvement of the formula printout. Not only the descriptive data, such as key-data of the compound, month of its synthesis, and the chemical name or bibliographical data, but also for test purposes the empirical formula and the number of rings present in the molecule are given.

One technician is able to fill in the grid-sheets for an average of 40 formulas per hour. The coding is easy to check visually and does not involve any worries about future eventualities; for instance, later on they might be processed by optical scanners [7]. Moreover, this kind of input provides the information for computer printing of the formulas without any additional manual operation. The input data are checked by the computer for formal validity. Error messages are produced for invalid atom or bonding symbols, missing lines of the formula matrix, and similar formal errors.

In order to produce the topological connectivity table, the computer numbers the atoms of each formula. The program also ascertains the quantity and type of the bonds from each atom. No attention is paid to hydrogens, unless they are specially coded. The computer then produces a compact list [8] by removing the redundant information from the connectivity table. In order to achieve higher speed in searching by higher selectivity we have deviated from the topological methods described by *Gluck* [8] and *Morgan* [9], insofar as the CCBF encoding program calculates further information about the individual atoms and includes it in the compact list. This information records whether or not the atom is a ring member, and also the number of hydrogen atoms attached to it (this can shorten the search time if it is required that hydrogen atoms should be present at definite places in the structure or substructure that is searched for).

In the computer file, each atom of a structure is described by:

– the code for the type of atom;

– the information "Ring member or not ring member";

– the information "Bond from atom No. ...";

– the code for the type of bond;

– the code for the number of hydrogens connected with the atom;

– the codes for any special data.

Some of these codes are bit chains, thus Boolean logic operators (AND, OR, NOT) can be used in searches.

The computer calculates the empirical formula and the number of rings and compares them with the values given. Erroneous codings are rejected.

Since even third generation computers still require too much time for the iterative atom by atom comparison described by *Ray* and *Kirsch* [10], the CCBF system also employs some preliminary checks. These screens are produced by the computer. At present the system uses:

– an empirical formula screen;

– a two-atom fragment screen, which indicates how often multiple bonds occur between two carbon atoms or single and multiple bonds between carbon and hetero atoms or between two hetero atoms; single, double, aromatic, and triple bonds are counted separately;

– a ring screen, in which every basic ring in the molecule is described. This ring screen corresponds approximately to the ring fragments of the Ring Code [11].

These preliminary checks eliminate at least 90 %, and in many cases over 99 %, of the stored compounds very quickly as "not relevant". Only those remaining need to be subjected to a topological comparison.

The entire data record for a structural formula thus comprises:

– the key data (for company-produced substances the company code, for compounds known in the literature the name in clear text);

– the computer-generated screens:

– the computer-generated compact list;

– the information for the printing of the formula (a computer condensed form of the input data);

– the chemical name and/or bibliographic details.

On average such a data record occupies 330 bytes, so that one magnetic tape can hold about 120000 formulas. The CCBF encoding program processes an average of 150 formulas per minute.

5. Search Program

Not only does the CCBF system perform the continuing service of producing card index subsystems (Figs. 1 and 2) but it also enables searches to be made on chemical or biological topics or on structure-activity relationships (Table 1).

5.1. Coding of Biological Questions

In biological searches every field of the biological data record can be searched. Logical connections are possible within similar parts of different records. All

[7] *W. E. Cossum, M. E. Hardenbrook*, and *R. N. Wolfe*, Proc. Amer. Documentation Inst. *1964*, 269.

[8] *D. J. Gluck*, J. chem. Documentation *5*, 43 (1965).

[9] *H. L. Morgan*, J. chem. Documentation *5*, 107 (1965).

[10] *L. C. Ray* and *R. A. Kirsch*, Science (Washington) *126*, 814 (1957).

[11] *W. Steidle*, Pharm. Ind. *19*, 88 (1957).

questions about dosages and results must be connected with the appropriate test code. It is also possible to put an overall request for certain data, *e.g.* toxicity data (percentage of animals that died during the test) and side effects. Biological questions are generally coded in free form in the order keyword – operator – search requirements. The keywords name the data fields in the biological record that are to be checked in the search. The operators and search requirements define all the conditions that must be fulfilled or items that must be excluded in order to answer the question. The permitted operators are "equal to", "not equal to", "greater than", "lower than". The search requirements can also include ranges of values, *e.g.* ED-50 "between 10 and 50 mg/kg".

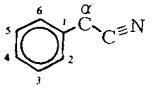
5.2. Coding of Chemical Questions

The formula file can be searched for definite structures, for general formulas, and for substructures of any desired type and size. Substructures are sets of connected atoms within complete structures, and may contain straight chain, branched, and ring elements or ring fragments in any desired combination.

A chemical search starts with manual coding of the connectivity table of the required structure or substructure. The search time can be shortened by choosing numbers as low as possible for those elements of the structure that are "rare" in relation to all the stored formulas [12]. In addition, all the screens relevant for the required structure or substructure are coded. In topological searches for definite compounds the number of H atoms with which every non-H atom in the formula is to be connected is given. This means that in fact only the formula explicitly requested would be retrieved.

In topological searches for substructures and general formulas it is possible to replace one or more atoms by dummy symbols, *e.g.* "Any halogen", "Any hetero atom", "N or O or P or S", and "C or O or N or S". In this way it is possible to search for groups of isosteric compounds in a single question. In coding of the bond type it is possible to choose for each bond OR or NOT combinations, *e.g.* "Single or double bond", "Single or aromatic or double bond (=NOT triple bond)" and "Any bond".

By specifying the number of hydrogen atoms that are to be attached to a non-H atom of a given substructure or general formula it is possible to request that, for example, in substructure *(1)* the α-carbon shall have two hydrogens, and each of the carbon atoms 3, 4, 5, and 6 of the phenyl group shall carry one hydrogen.

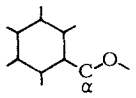


(1)

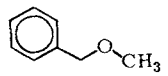
[12] *W. E. Cossum, M. L. Krakiwsky,* and *M. F. Lynch,* J. chem. Documentation *5,* 33 (1965).

Thus, in this example only phenylacetonitrile and those mono-*ortho* derivatives which are not substituted in the α-position are retrieved.

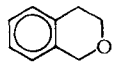
By specifying that an atom should or should not be a ring member, we can, for example, request for substructure *(2)* that the α-carbon be a ring member; then only formula *(4)* will give a match. Without this restriction, the question would also retrieve structure *(3)*.



(2)



(3)



(4)

5.3. Searching

The search program first converts the coding of the biological and/or chemical questions from punched cards to an internal format. It is checked for formal and logical errors analogous to the input checking. In combined searches it is possible to select whether the chemical or the biological file shall be searched first. If, for example, the question refers to a rare biological test, then the biological file is searched first. If, on the other hand, the structures required do not occur frequently, then the chemical file is searched first.

The search program transfers the data records of all the substances retrieved to an intermediate file. From this file the editing program selects all the parts for the desired printout (Table 1). Printout instructions are given at the same time as the initial question. Provision is also made for printout instructions to be given even after the search has been completed, so that the whole of the information for all the substances retrieved can be used repeatedly and for different purposes.

6. Experience Gained

In 1968, after two years of development, the CCBF system was installed to modernize a research documentation system which for the previous eight years had been recording chemical formulas with the Ring Code [11] and biological information by direct coding. Our experience with these documentation systems enables us to make the following statements:

– a research documentation system which is to be an effective aid both now and in the future must continually be adjusting its techniques to keep up with developments in the field of data processing and with progress in the documentation methods for the particular subject concerned;

– in a documentation system concerned with chemical formulas in drug research, the selectivity of pure fragmentation codes is insufficient and, particularly for substructure searching, only topological methods meet all the requirements;

– the only expedient way to run a biological documentation system is to keep the data recording so simple that no specialists are required for encoding;

– a research documentation system will only be attractive to the scientist if it provides both the opportunity to carry out individual searches and also a continuing service in the form of SDI;

– a research documentation will only remain up-to-date if the system is controlled by the research department, and if the scientist whose research results are documented continually collaborates in its extension and maintenance.

In cooperation with the department Zentrale Datenverarbeitung der Firma C. H. Boehringer Sohn, Ingelheim, the programs for the CCBF system were written partly in Assembler and partly in PL/I for an IBM 360/40. Dr. B. Braun, Ingelheim, coordinated the programs for the various sections of the system and made many valuable suggestions for the system analysis, the system maintenance, and the continual extensions to the system. Fräulein U. Zech helped considerably in the extensive planning for the computer processing of biological information and supplied numerous practical ideas. Herr J. Becker in his writing of the encoding program for chemical formulas contributed very useful details. Herr J. Gruber programmed the biological section; his shrewd suggestions helped considerably in the development of the system. The updating and editing programs were written by Herr P. Oppitz with many fruitful ideas.

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Gas-Liquid Chromatography and Mass Spectrometry in Methylation Analysis of Polysaccharides

By Håkan Björndal, Carl Gustaf Hellerqvist, Bengt Lindberg, and Sigfrid Svensson[*]

New methylation procedures and the combined application of gas-liquid chromatography and mass spectrometry for the qualitative and quantitative analysis of mixtures of methylated sugars permit methylation analysis of polysaccharides to be performed more accurately, faster, and with less material than previously.

1. Introduction

Methylation analysis is an important method in structural polysaccharide chemistry. It involves exhaustive methylation of the polysaccharide and hydrolysis to a mixture of monomeric methylated sugars, which are then separated, identified, and quantitatively estimated. The positions of glycosidic linkages in the polysaccharide correspond to the positions of unsubstituted hydroxyl groups in these methylated monosaccharides. The method gives no information on the relative order of the sugar residues or on their anomeric nature.

Determination of the complete structure of a polysaccharide also requires complementary analyses, the most important of which are graded hydrolysis, by acids or enzymes, followed by isolation and identification of the oligosaccharides formed, and various modifications of periodate oxidation. Unlike most other methods used in structural polysaccharide chemistry, methylation analysis provides quantitative information [1].

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2. Methylation of Polysaccharides

2.1. Haworth and Purdie Methylation

The aim of methylation is to achieve etherification of all the free hydroxyl groups in the polysaccharide. In the original procedure, used by *Denham* and *Woodhouse* [2] and by *Haworth* [3], this was achieved by repeated reaction with dimethyl sulfate and sodium hydroxide. Often, only a partially methylated product was obtained which was then fully methylated by repeated treatment with silver oxide in boiling methyl iodide, according to *Purdie* and *Irvine* [4].

Purdie's technique was considerably improved by *Kuhn* and co-workers [5], who carried out the reaction in the polar solvent *N,N*-dimethylformamide. Polysaccharides which dissolve or swell in this solvent may be

[1] *H. O. Bouveng* and *B. Lindberg*, Advances Carbohydrate Chem. *15*, 53 (1960).

[2] *W. S. Denham* and *H. Woodhouse*, J. chem. Soc. (London) *103*, 1735 (1913).

[3] *W. N. Haworth*, J. chem. Soc. (London) *107*, 8 (1915).

[4] *T. Purdie* and *J. C. Irvine*, J. chem. Soc. (London) *83*, 1021 (1903).

[5] *R. Kuhn*, *H. Trischmann*, and *I. Löw*, Angew. Chem. *67*, 32 (1955).

methylated directly. Silver oxide, however, causes oxidative degradation of free or partially methylated polysaccharides; more recent modifications using barium hydroxide[6] or sodium hydroxide[7] are therefore preferred. With these bases, reaction can be performed in dimethyl sulfoxide, which is a better solvent for polysaccharides.

2.2. Hakomori Methylation

The simplest and most convenient method for methylation of polysaccharides and other carbohydrates is probably that recently developed by *Hakomori*[8]. The polysaccharide is treated with the strong base methylsulfinylmethylsodium in dimethyl sulfoxide; the hydroxyl functions are thus ionized to give the corresponding polyalkoxide ions which then react readily with methyl iodide. Complete methylation may be accomplished in one step; isolation of the methylated polysaccharide is simple and the procedure is suitable for work both on a macro and on a micro scale.

The base is prepared by adding sodium hydride to dimethyl sulfoxide[9]. Solutions of methylsulfinylmethylsodium may be prepared in advance (they are stable for several weeks in the frozen state), or sodium hydride may be added directly to a solution of the polysaccharide in dimethyl sulfoxide[10]. In either procedure, ultrasonic treatment facilitates reaction between sodium hydride and dimethyl sulfoxide[11]. Ultrasonic treatment also assists dissolution of the polysaccharide and seems to facilitate the final reaction with methyl iodide. It is essential that the solution of methylsulfinylmethylsodium is protected from contact with air. When methylation is complete, the reaction mixture is poured into water and the fully methylated polysaccharide isolated by dialysis or by extraction. Polysaccharides that do not dissolve or swell in dimethyl sulfoxide cannot be methylated by this technique; they may *e.g.* first be partially methylated by the Haworth[3] method and the process then completed by the Hakomori procedure.

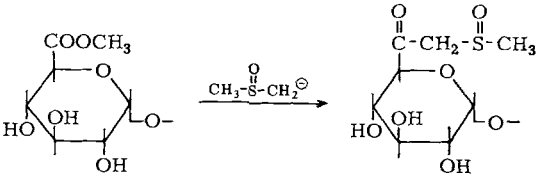
The ionization of the hydroxyl groups in the polysaccharide is a comparatively slow reaction[8] and the polysaccharide is therefore left in contact with the base for several hours before the methyl iodide is added. Reaction of alkoxide ions with methyl iodide is presumably much faster. Methyl iodide is also consumed by the base.

Price and *Whiting*[12] studied the reaction of glycerol with methylsulfinylmethylsodium and found that only 1.5 equivalents of the base were consumed. Since it is well established that carbohydrates containing several adjacent hydroxyl groups are completely methylated by the Hakomori procedure, ionization of hydroxyl groups probably occurs also during the methylation stage, *i.e.* after methyl iodide has been added to the system.

Estimation of the completeness of the methylation is difficult. Methylated polysaccharides are hygroscopic and the last traces of dimethyl sulfoxide or other solvents are difficult to remove. Methoxyl analyses therefore often give erroneously low values, and are impractical when only a few mg of polysaccharide are available. The absence of OH absorption in the 3400 to 3600 cm^{-1} region of the infrared spectrum is a better criterion, but the presence of traces of water will obscure the result.

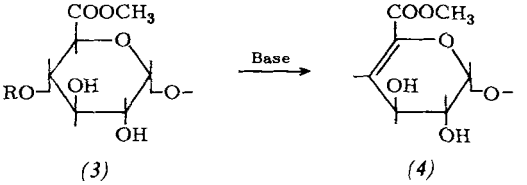
In practice, estimation of the degree of methylation is unnecessary since undermethylation reveals itself when the relative proportions of methylated sugars are determined. A reasonably good agreement between terminal residues and branching points should be obtained. The presence of sugars bearing more than two unmethylated hydroxyl groups, even in traces, indicates severe undermethylation. A perfect agreement and quantitative recovery of methylated sugars is seldom attained since some demethylation during the hydrolysis and some losses of the more volatile methylated sugars during concentration are unavoidable.

The presence of uronic acid residues in the polysaccharide may cause complications during the methylation. An esterified uronic acid residue *(1)* may react with the methylsulfinylmethyl anion, yielding a methylsulfinylmethyl ketone *(2)*, a reaction of preparative interest[13].



(1) *(2)*

An esterified uronic acid residue *(3)* may also undergo β-elimination in the strongly basic medium, yielding an unsaturated residue *(4)*, and this reaction will become particularly important when C-4 of the original uronic acid residue *(3)* is substituted.



(3) *(4)*

When methyl iodide is added to the alkoxide ion of a polysaccharide containing uronic acid residues its etherification and esterification and also the reaction of the excess base with methyl iodide are probably fast reactions; the ester formed is therefore exposed to the strong base only for a short time. If, however, the carboxyl groups are esterified (either naturally or as a result of a previous methylation) the uronic esters will be in contact with the base for several hours, and the side

[6] *R. Kuhn, H. H. Baer,* and *A. Seeliger,* Liebigs Ann. Chem. *611,* 236 (1958).

[7] *H. C. Srivastava, P. P. Singh, S. N. Harshe,* and *K. Virk,* Tetrahedron Letters *1964,* 493.

[8] *S. Hakomori,* J. Biochemistry (Tokyo) *55,* 205 (1964).

[9] *E. J. Corey* and *M. Chaykovsky,* J. Amer. chem. Soc. *84,* 866 (1962).

[10] *D. M. W. Anderson* and *G. M. Cree,* Carbohydrate Res. *2,* 162 (1966).

[11] *K. Sjöberg,* Tetrahedron Letters *1966,* 6383.

[12] *G. G. Price* and *M. C. Whiting,* Chem. and Ind. *1963,* 775.

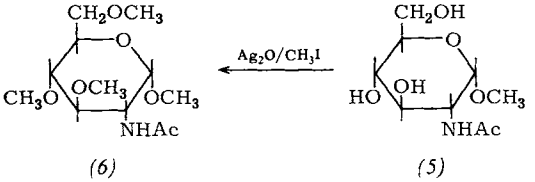
[13] *E. J. Corey* and *M. Chaykovsky,* J. Amer. chem. Soc. *87,* 1345 (1965).

reactions mentioned above may become important. Studies by *Andersson et al.*[14], on acidic polysaccharides, which were subjected to repeated methylations, show that these expected side reactions (β-eliminations) are severe only if the uronic acid residues are substituted on C-4. The reason why the ester groups did not react more extensively with the methylsulfinylmethyl anion, *e.g.* to give ketones such as *(2)*, is obscure; possibly the solution contained enough sodium hydroxide to hydrolyze the ester groups before *(2)* could be formed.

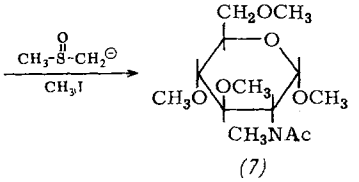
Despite the fact that successful results have been reported in methylation of acidic polysaccharides by the Hakomori procedure, it would seem advisable not to remethylate an undermethylated sample but to start anew and attempt to attain a complete methylation in one step. If this cannot be achieved, it would seem safer to perform any remethylations by other procedures, *e.g.* with methyl iodide-silver oxide, according to *Kuhn et al.*[5].

Most of the *O*-acetyl groups present in an acetylated polysaccharide survive during a Kuhn methylation[15], but acetyl migration is promoted under these reaction conditions. On Hakomori methylation, *O*-acetyl groups are completely replaced by *O*-methyl groups; other *O*-acyl groups may be expected to react in the same manner. The Hakomori methylation of polysaccharides containing sulfonate or phosphate ester groups, or of simple model substances in which these groups are present, has not been investigated.

Aminodeoxy sugars, generally *N*-acetylated, are common components of polysaccharides. When polysaccharides or other carbohydrates containing such residues, *e.g.* methyl 2-acetamido-2-deoxy-α-D-glucopyranoside *(5)*, are methylated by the Haworth or Kuhn procedures, the acetamido group remains intact *(6)*[16]. When *(5)* was methylated by the Hakomori procedure, the fully *O*-methylated *N*-methylacetamido derivative



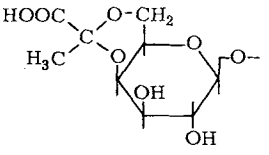
(6) *(5)*



(7)

(7) was obtained[17]. This important difference between the methylation procedures, which is probably of general validity, reflects the much stronger basic conditions under which the Hakomori methylation is performed.

Some polysaccharides contain pyruvic acid residues, linked as ketals to sugar residues [*e.g. (8)*][18]. Acetalization of polysaccharides has been applied for the



(8)

localization of ester groups[19]. As expected, the ketal and acetal groups are stable during the Hakomori methylation.

3. Hydrolysis of Fully Methylated Polysaccharides

Fully methylated polysaccharides are often not soluble in hot aqueous solutions. For this reason methanolysis (with methanolic hydrogen chloride at the boiling point or higher), formolysis (with 90 % formic acid at 100 °C), or treatment with 72 % sulfuric acid (at room temperature) is usually performed before the hydrolysis with hot dilute acid. In this manner degradation and demethylation are kept as low as possible. Treatment with hydrochloric acid in water or in methanol causes more demethylation than either formolysis or treatment with 72 % sulfuric acid followed by hydrolysis in dilute sulfuric acid[20].

Some methylated sugars, *e.g.* a tri-*O*-methylpentose, are rather volatile and are partially lost on concentration of the hydrolyzate. Such losses are avoided if the polysaccharide is subjected to methanolysis, and the mixture of methyl glycosides obtained is analyzed by GLC without preceding neutralization or concentration of the methanolyzate[21].

Certain glycosidic linkages are fairly resistant to acid hydrolysis; complete hydrolysis may then be accompanied by sugar degradation. One example is the uronosyl linkage. To facilitate hydrolysis, uronic acid residues may be first reduced to neutral sugar residues. 2-Acetamido-2-deoxyglycosides are not particularly resistant to acid hydrolysis but concurrent hydrolysis of the amidic linkage gives rise to 2-amino-2-deoxyglycosides, which are extremely resistant to acid hydrolysis. No systematic studies on the hydrolysis of methylated polysaccharides containing 2-acetamido-2-deoxy sugar residues seems to have been carried out. Presumably complete fragmentation into monomers could be achieved by acetolysis.

[14] *D. M. W. Anderson, I. C. M. Dea, P. A. Maggs*, and *A. C. Munro*, Carbohydrate Res. *5*, 489 (1967).

[15] *H. O. Bouveng, P. J. Garegg*, and *B. Lindberg*, Chem. and Ind. *1958*, 1727.

[16] *R. W. Jeanloz*, Advances Carbohydrate Chem. *13*, 189 (1958).

[17] *C. G. Hellerqvist, O. Larm*, and *B. Lindberg*, unpublished.

[18] *P. A. J. Gorin, T. Ishikawa, J. F. T. Spencer*, and *J. H. Sloneker*, Canad. J. Chem. *45*, 2005 (1967).

[19] *A. N. de Belder* and *B. Norrman*, Carbohydrate Res. *8*, 1 (1968).

[20] *P. J. Garegg* and *B. Lindberg*, Acta chem. scand. *14*, 871 (1960).

[21] *G. O. Aspinall*, J. chem. Soc. (London) *1963*, 1676.

4. Separation of Mixtures of Methylated Sugars

4.1. Methyl Glycosides of Methylated Sugars

The separation of the different methylated sugars obtained on hydrolysis of a methylated polysaccharide was accomplished originally by fractional distillation and later by paper, cellulose column, or carbon column chromatography. These chromatographic methods are still in use for the isolation of sufficient material for an unambiguous identification. For analytical separation GLC is presently the preferred method. The methylated sugars cannot be separated directly by GLC but have to be transformed into more stable derivatives, usually the methyl glycosides.

Each methylated sugar gives one or two anomeric pairs of glycosides, depending upon whether one or both of C-4 and C-5 are unsubstituted. This fact may facilitate the identification of components in simple mixtures. In more complex mixtures the multiplicity of peaks becomes a disadvantage, as the quantitative evaluation becomes more difficult. The best GLC separations are obtained on polar columns such as butanediol succinate and polyphenyl ether. Retention times relative to methyl 2,3,4,6-tetra-*O*-methyl-β-D-glucoside (*T*-values) for methyl glycosides of a number of methylated sugars have been determined by *Aspinall*[21].

4.2. Alditol Acetates of Methylated Sugars

By reduction of the methylated sugars to alditols a single derivative is obtained from each sugar. The separation of isomeric alditol derivatives (*e.g.* acetates) was, however, inferior to that obtained for isomeric methyl glycoside derivatives. It was only after the introduction of a new phase for GLC, ECNSS–M (a nitrile silicone-polyester copolymer[*]), that good separation of partially methylated alditol acetates became feasible. This procedure has been used in the authors' laboratory for some years[22]; some representative results are shown in Table 1. The few components that are not well separated on ECNSS–M may be separated on other columns (Table 2). Recently ECNSS–M SCOT-columns have become available which provide much better separation than the packed columns.

Table 1. Retention times (*T*-values) of partially methylated sugars, in the form of their alditol acetates, relative to 1,5-di-*O*-acetyl-2,3,4,6-tetra-*O*-methyl-D-glucitol. Generally, 2-m glass columns of 4-mm internal diameter containing 3 % ECNSS–M on chromosorb Q, 100–120 mesh were used.

Position of CH_3	Parent sugar [a]										
	Ara	Rib	Xyl	Gal	Glc	Man	Fuc	Rha	Abe	Par	Tyv
2				8.1	7.9		1.67	1.52			
3			2.92	11.1	9.6		2.05	1.94			
4								1.72			
2,3			1.54	5.68	5.39		1.18	0.98			
2,4	1.40			6.35	5.10	5.44	1.12		0.32	0.34	0.29
2,5	1.10			3.70							
2,6				3.65	3.83	3.35					
3,4	1.38		1.54	6.93		5.37		0.92			
3,5		0.77	1.08	6.35							
3,6				4.35	4.40						
4,6				3.64	4.02	3.29					
2,3,4	0.73		0.68	3.41	2.49	2.48	0.65	0.46			
2,3,5	0.48	0.40		3.28			0.62				
2,3,6				2.42	2.50	2.20					
2,4,6				2.28	1.95	2.09					
2,5,6				2.25							
3,4,6				2.50	1.98	1.95					
2,3,4,6				1.25	1.00	1.00					
2,3,5,6				1.15							

[a] Ara = arabinose, Rib = ribose, Xyl = xylose, Gal = galactose, Glc = glucose, Man = mannose, Fuc = fucose, Rha = rhamnose, Abe = abequose (3,6-dideoxy-D-*xylo*-hexose), Par = paratose (3,6-dideoxy-D-*ribo*-hexose), Tyv = tyvelose (3,6-dideoxy-D-*arabino*-hexose).

Table 2. Retention times (*T*-values) of partially methylated sugars in the form of their alditol acetates on OS 138 [a] columns of the same dimensions as in Table 1.

Alditol acetate of	*T*
3,4-Di-*O*-methyl-L-rhamnose	0.80
2,3-Di-*O*-methyl-L-rhamnose	0.86
2,3,4-Tri-*O*-methyl-D-mannose	1.93
2,3,6-Tri-*O*-methyl-D-galactose	1.74
2,3,4,6-Tetra-*O*-methyl-D-glucose	1.00
2,3,4,6-Tetra-*O*-methyl-D-mannose	1.06

[a] OS 138 consists of polyphenyl ether.

Manufacturer: Applied Science Laboratories Inc., P.O. Box 140, State College, Pa. (USA).

The reproducibility of a *T*-value is good, generally 1 % or better, provided that *two* internal standards with considerably different retention times are used and that the values are determined by interpolation. This is also true for different columns and at different temperatures. Partially methylated alditol acetates are preferably separated at 160–200 °C, fully acetylated

[*] Manufacturer: Applied Science Laboratories Inc., P.O. Box 140, State College, Pa. (USA).

[22] *H. Björndal, B. Lindberg,* and *S. Svensson,* Acta chem. scand. *21*, 1801 (1967).

alditols at 200–220 °C. The optimum temperature range depends on the percentage of ECNSS–M phase on the support. Since this phase leaks out on usage the temperature range should be decreased accordingly. SCOT columns are used at somewhat lower temperatures.

Alditol acetates containing any number of *O*-methyl groups, or none at all, can be separated on the same column. Undermethylation (see above) is therefore easily detected.

The partially methylated alditol acetates deriving from aminodeoxyhexoses have high retention times on ECNSS–M columns but no systematic study of these substances has been made.

Although it is usually necessary to determine response factors for the different components in quantitative GLC, this does not seem to be essential for the partially methylated alditol acetates when glass columns and flame ionization detector are used. The assumption that the molar response is the same for all components is probably true within ± 5 % or better, as demonstrated by the results of several methylation analyses of oligosaccharides and polysaccharides. Errors introduced by this assumption are probably less severe than those due to degradation during hydrolysis and to losses during concentration of solutions of methylated sugars.

5. Characterization of Methylated Sugars

5.1. Crystalline Derivatives

An enormous amount of ingenious and time-consuming work has been devoted to the synthesis of different methyl ethers of natural sugars required for identification purposes in methylation analysis. (For tables listing crystalline derivatives of methyl ethers of the natural sugars see ref. [23].) In classical methylation analyses, each methylated sugar is isolated in pure state, transformed into one or more crystalline derivatives, and compared whenever possible with authentic samples.

5.2. Characterization by GLC

For simple polysaccharides it may suffice to identify the methylated sugars obtained on methylation analysis by GLC. This identification, which may be confirmed by GLC on other columns, by other chromatographic procedures, or by electrophoresis, is of course only tentative. For complex polysaccharides, it may be impossible, or too risky, to identify the components from the methylation analysis by chromatographic methods only.

[23] *R. L. Whistler*, Methods Carbohydrate Chem. *5*, 298 (1965).

[24] *N. K. Kochetkov* and *O. S. Chizhov*, Advances Carbohydrate Chem. *21*, 39 (1966).

[25] *W. Heyns* and *H. Scharmann*, Liebigs Ann. Chem. *667*, 183 (1963).

[26] *O. S. Chizhov*, *N. V. Moldotsov*, and *N. K. Kochetkov*, Carbohydrate Res. *4*, 273 (1967).

[27] *G. Pettersson*, *O. Samuelson*, *K. Anjou*, and *E. von Sydow*, Acta chem. scand. *21*, 1251 (1967).

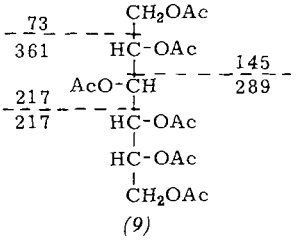
5.3. Characterization by Mass Spectrometry

5.3.1. Glycosides

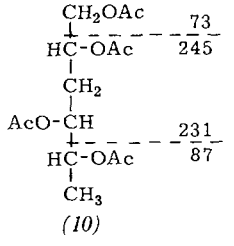
Recently, mass spectrometry has become an important tool in organic chemistry and several groups have studied the mass spectra of various carbohydrates [24]. *Heyns et al.* investigated the mass spectra of fully methylated glycosides [25], and *Kochetkov et al.* [26] and *Samuelson et al.* [27] examined the mass spectra of the trimethylsilyl derivatives of partially methylated glycosides. These studies, and the use of combined GLC-mass spectrometry, in which the components from the chromatographic column are introduced directly into the ionization chamber of the mass spectrometer, have led to new methods for the qualitative and quantitative analysis of the mixtures of methylated sugars.

5.3.2. Alditol Acetates of Methylated Sugars

Mass spectrometry of partially methylated alditol acetates has been studied in the authors' laboratory [28]. The fragmentation of alditol acetates, *e.g.* D-glucitol hexaacetate *(9)*, is easily interpreted, as demonstrated by *Chizhov et al.* [29]. The main peaks of the mass spectrum correspond to ions formed by primary fission between two adjacent carbon atoms in the chain and to those arising by elimination of acetic acid (*m/e* 60) or ketene (*m/e* 42) from these primary fragments. The intensities of the fragments decrease with increasing molecular weight. A deoxy group inhibits the cleavage of the neighboring bonds, as exemplified by abequitol tetraacetate *(10)*, derived from the natural sugar abequose (3,6-dideoxy-D-*xylo*-hexose). Mass spectra of isomeric alditol acetates having the same structure but different configurations are practically indistinguishable. The same has been found for various glycosides [24] and other stereoisomeric substances.



(9)



(10)

A systematic investigation of mass spectra of partially methylated alditol acetates has led to the following generalizations:

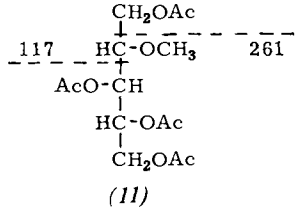
1. Derivatives with the same substitution pattern (*e.g.* 2,3,4,6-*O*-methyl derivatives of hexitols) give very similar mass spectra, typical of that substitution pattern. The small differences that may be observed in the relative intensities of peaks for stereoisomers are insufficient for unambiguous identification.

[28] *H. Björndal*, *B. Lindberg*, and *S. Svensson*, Carbohydrate Res. *5*, 43 (1967).

[29] *O. S. Chizhov*, *L. S. Golovkina*, and *N. S. Wulfson*, Izvest. Akad. Nauk SSSR, Otd. chim. Nauk *1966*, 1915.

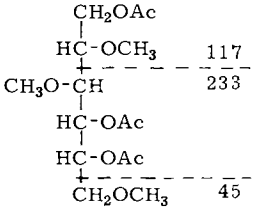
2. The base peak of the spectrum is generally *m/e* 43 ($CH_3C\overset{\oplus}{\equiv}O$).

3. Primary fragments are formed by fission between carbon atoms in the chain. Fission between a methoxylated and an acetoxylated carbon is preferred over fission between two acetoxylated carbons. The fragment with the methoxyl group carries the positive charge. The alditol acetate derived from 2-*O*-methyl-D-xylose *(11)* therefore only gives two main primary fragments.

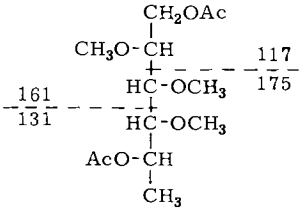


(11)

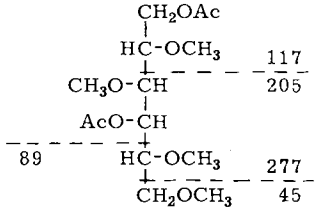
4. When the molecule contains two adjacent methoxylated carbons, *e.g.* the alditol acetates derived from 2,3,6-tri-*O*-methyl-D-glucose *(12)* and 2,3,4-tri-*O*-methyl-L-fucose *(13)*, fission between them is preferred over fission between one of these and a neighboring acetoxylated carbon. Both fragments from this fission



(12)



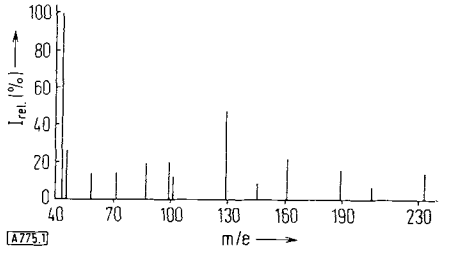
(13)

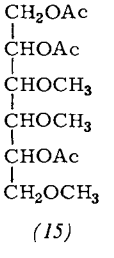


(14)

are found as positive ions. An important exception to this rule are the 1,2-di-*O*-methylalditol derivatives which, like the alditol acetate derived from 2,3,5,6-tetra-*O*-methyl-D-galactose *(14)*, always give the primary fragment *m/e* 89 as a strong peak.

5. Secondary fragments are formed from the primary fragments by single or consecutive loss of acetic acid





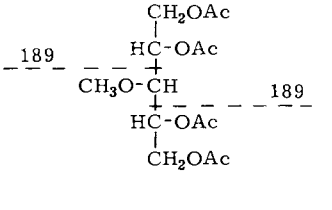
(15)

Fig. 1. Mass spectrum of a 1,2,5-tri-*O*-acetyl-3,4,6-tri-*O*-methylhexitol.

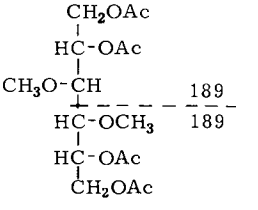
(*m/e* 60), ketene (*m/e* 42), methanol (*m/e* 32), or formaldehyde (*m/e* 30). A typical mass spectrum of a 1,2,5-tri-*O*-acetyl-3,4,6-tri-*O*-methylhexitol *(15)*, is given in Fig. 1.

The mass spectra of a number of partially methylated alditol acetates are listed in Table 3. It is thus possible, by mass spectrometry, to determine the substitution pattern in a partially methylated alditol acetate, either by comparing the spectrum with previously determined spectra or by analyzing it according to the principles outlined above.

There are two alditol acetates which, in spite of their different structures, give similar mass spectra, namely those derived from 3-*O*-methyl-pentoses [*e.g. (16)*] and 3,4-di-*O*-methyl-hexoses [*e.g. (17)*]. This is to be expected since both give one and the same main primary fragment (*m/e* 189). The acetates of mono-*O*-methylpentitols and di-*O*-methylhexitols have very different *T*-values and therefore this similarity in mass spectra need not cause any confusion.

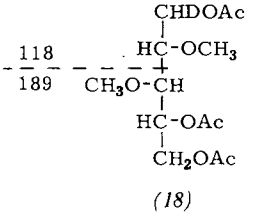


(16)

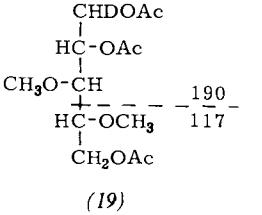


(17)

On reduction some pairs of methylated sugars, *e.g.* a 2-*O*-methyl- and a 4-*O*-methyl-pentose or a 3-*O*-methyl- and a 4-*O*-methyl-hexose, give alditols with the same substitution pattern, as indicated in Table 3. These may even be identical, as in mannose derivatives, or enantiomorphs, as in galactose derivatives, and thus inseparable by GLC. The information lost when the sugars are reduced to alditols can be readily compensated if the reduction is performed with sodium deuterioborate. This is exemplified by the alditol acetates derived from 2,3- and 3,4-di-*O*-methyl-D-xylose *(18)* and *(19)* respectively, which, although not separable by GLC, give different mass spectra.

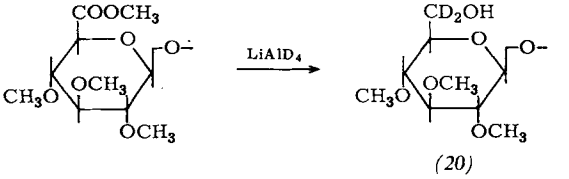


(18)



(19)

The uronic acid residues of polysaccharides are reduced to neutral sugar residues, either before or after methylation. If this reduction is performed with a deuterium compound the neutral sugar residue obtained [*e.g. (20)*] is readily distinguished by mass spectrometry



(20)

Table 3. Primary fragments [a] in the mass spectra of partially methylated sugars in the form of their alditol acetates.

Position of CH_3	*m/e*														
	45	59	89	117	131	161	175	189	203	205	217	233	261	305	333
Pentoses															
2 (4)				×									×		
3								×							
2,3 (3,4)				×				×							
2,4				×								×			
2,5	×			×								×			
3,5	×					×		×							
2,3,4				×		×									
2,3,5	×			×		×									
Hexoses															
2 (5)				×											
3 (4)								×					×		
6	×														
2,3				×									×		
2,4 (3,5)				×				×							
2,5				×											
2,6	×			×											
3,4								×							
3,6	×							×				×			
4,6	×					×							×		
5,6	×		×												×
2,3,4				×		×		×				×			
2,3,5				×								×			
2,3,6	×			×								×			
2,4,6	×			×		×						×			
2,5,6	×		×	×										×	
3,4,6	×					×		×							
2,3,4,6	×			×		×				×					
2,3,5,6	×		×	×						×					
6-Deoxyhexoses															
2				×											
3								×	×						
4					×								×		
2,3				×					×						
2,4				×	×							×			
3,4					×			×							
2,3,4		×		×	×	×	×								
2,3,5				×			×								
3,6-Dideoxyhexoses															
2				×							×				
2,4				×	×		×	×							

[a] Primary fragments having mass numbers higher than *m/e* 261, which are formed by fission between a methoxyl and an acetoxyl group, are of low intensity and are not included in the Table.

from other sugar residues present in the same polysaccharide.

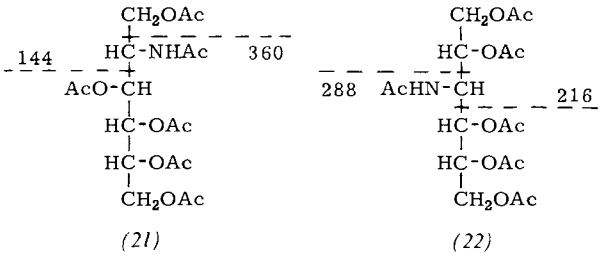
This labeling technique was used during methylation analysis on a fungal glucuronoglucan [30]. Mass spectrometry revealed that one of the sugars obtained, 2,3,4-tri-*O*-methyl-D-glucose, was derived from both the glucose and the glucuronic acid residues. From the intensities of pertinent peaks in the mass spectrum it was also possible to estimate their approximate proportions.

When a heteropolysaccharide contains only one sugar of each class (*e.g.* one pentose and one hexose), the methylated sugars obtained can be unambiguously identified by mass spectrometry. If, however, the polysaccharide contains different sugars of the same class (*e.g.* two or more different hexoses) an unambiguous identification of the different methylated sugars can be accomplished only if the *T*-values of the relevant alditol acetates are sufficiently different. It is generally possible to find chromatographic columns that fulfil such requirements. When the *T*-value for a presumed component of the mixture is not available, it can be readily determined by subjecting a suitable sugar derivative to partial methylation, converting the reaction product into alditol acetates, and characterizing the various methyl ethers by GLC-mass spectrometry. Components with different substitution patterns which are not resolved on the chromatographic column would necessarily give a mixed mass spectrum. If separation of these components cannot be achieved on other columns, or at different temperatures, it is still possible to make a semiquantitative estimate of the relative proportion of these components from the mass spectrum.

5.3.3. Alditol Acetates of Amino Sugars

No systematic study on GLC-mass spectrometry of alditol acetates derived from acetamidodeoxy sugars has been made. Preliminary studies show that they have much higher retention times than the corresponding neutral sugars. In the unmethylated compounds, *e.g. (21)* and *(22)*, fragmentation is governed by the acetamido group. Secondary fragments are formed from

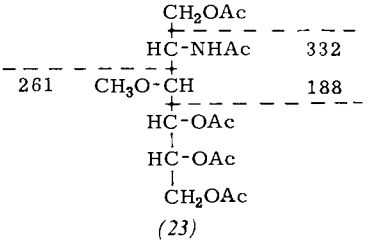
[30] *H. Björndal* and *B. Lindberg*, Carbohydrate Res. *12*, 29 (1970).



(21) (22)

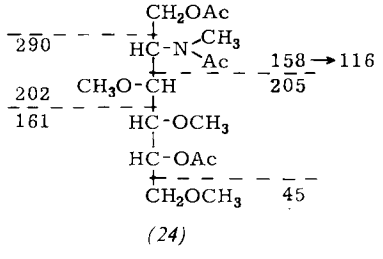
the primary ones by elimination of acetic acid (*m/e* 60), acetamide (*m/e* 59), and ketene (*m/e* 42).

When a methoxyl and an acetamido group are adjacent, as in *(23)*, fission between these groups is preferred and the positive charge is carried almost exclusively by the fragment containing the methoxyl group. Fission between C-1 and C-2 and between C-3 and C-4 is however also observed.

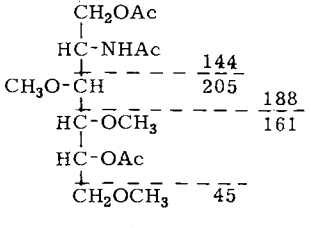


(23)

As mentioned in Section 2, acetamido groups are methylated by the Hakomori procedure [*e.g.* to *(24)*] but not by other methylation procedures [see *(25)*]. The resulting alditol acetates have similar mass spectra.



(24)



(25)

One important difference is that for *(25)* the primary fragment (*m/e* 144) containing C-1 and C-2 is insignificant but for *(24)* it becomes the strongest primary fragment (*m/e* 158). The secondary fragment of *m/e* 116, derived from *m/e* 158 by loss of ketene, is the base peak of the spectrum, and is even stronger than $CH_3C\overset{\oplus}{\equiv}O$ (*m/e* 43).

These preliminary studies indicate that GLC-mass spectrometry may also become a valuable tool in methylation analysis of polysaccharides containing aminodeoxy sugar residues.

6. Examples

6.1. Methylation Analysis of a Fungal Fucoxylomannan[31]

Acid hydrolysis of a fungal fucoxylomannan from *Polyporus pinicola* (Fr.) yielded L-fucose, D-xylose, and D-mannose in the relative proportions 0.8:0.7:1. The polysaccharide was methylated, hydrolyzed, and the mixture of methylated sugars converted into their alditol acetates and analyzed by GLC-mass spectrometry (Table 4, I). Part of the polysaccharide was also subjected to a mild acid hydrolysis, with 0.05 M sulfuric acid at 100 °C for 1.5 h. Nearly all the L-fucosidic linkages were cleaved by this treatment. The residual, polymeric material was subjected to methylation analysis (Table 4, II).

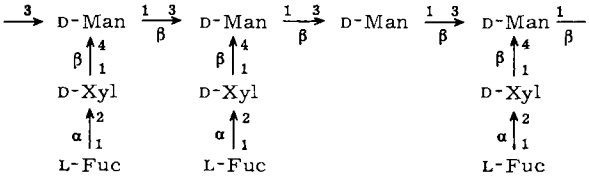
Table 4. Retention times (*T*-values) of partially methylated sugars in the form of their alditol acetates from the hydrolyzate of the methylated fucoxylomannan (I) and of the previously partially degraded and subsequently methylated fucoxylomannan (II). The *T*-values were measured at 175 °C; standard and column as in Table 1.

Alditol acetate of	*T*	I (mole-%)	II (mole-%)
2,3,4-Tri-*O*-methyl-L-fucose	0.65	30.2	–
2,3,4-Tri-*O*-methyl-D-xylose	0.68	–	38.8 [a]
3,4-Di-*O*-methyl-D-xylose	1.54	29.5	3.4
2,4,6-Tri-*O*-methyl-D-mannose	2.10	9.7	19.4
2,6-Di-*O*-methyl-D-mannose	3.35	30.6	38.4

[a] Including traces of 2,3,4-tri-*O*-methyl-L-fucose.

The almost complete disappearance of 3,4-di-*O*-methylxylose and the concomitant appearance of 2,3,4-tri-*O*-methylxylose show that the L-fucose residues are linked to C-2 of the D-xylose residues.

As a result of these and other studies structure *(26)* was proposed for the polysaccharide.



(26)

6.2. Methylation Analysis of the Lipopolysaccharide from *Salmonella typhi*[32]

Lipopolysaccharides from gram-negative bacteria consist of a lipid part, of the "O-specific" side chains, composed of repeating oligosaccharide units, and of a "basal core" linking the lipid to the "O-specific" side chains.

The lipopolysaccharide from *Salmonella typhi* contains D-glucose, D-galactose, D-mannose, L-rhamnose, and tyvelose (3,6-dideoxy-D-*arabino*-hexose) in the side chains and D-glucose, D-galactose, 2-acetamido-2-deoxy-D-glucose, and a heptose in the core. Some sugar residues also contain *O*-acetyl groups.

GLC of the alditol acetates of methylated sugars obtained from the fully methylated lipopolysaccharide gave a complicated picture. Mass spectra were determined at the beginning, maximum, and end of each major peak, and at the maxima of minor peaks. Peaks B and D were found to contain two components. Those in peak B were later separated on a polyphenyl ether column (OS-138), those in peak D on an ECNSS—M column at a lower temperature. From mass spectra and *T*-values it was possible to identify and determine

[31] *K. Axelsson, H. Björndal,* and *B. Lindberg,* Acta chem. scand. *23,* 1597 (1969).

[32] *C. G. Hellerqvist, B. Lindberg, S. Svensson, T. Holme,* and *A. A. Lindberg,* Acta chem. scand. *23,* 1588 (1969).

the relative proportions of 12 methylated sugars in the mixture (Table 5, I). Small amounts of methylated heptoses, which should have been present, escaped detection. Methylated derivatives of 2-acetamido-2-deoxyglucose, which have high *T*-values, were not looked for.

Table 5. Retention times (*T*-values) of partially methylated sugars in the form of their alditol acetates from the hydrolyzate of the methylated lipopolysaccharide (I) and the previously partially degraded and subsequently methylated lipopolysaccharide from *Salmonella typhi* (II). Standard and column as in Table 1.

Aldol acetate of	Peak	*T*	I (mole-%) [a]	II (mole-%) [a]
2,4-Di-*O*-methyltyvelose	A	0.29	8.0	
2,3-Di-*O*-methyl-L-rhamnose	B	0.98	20.0	20.0
2,3,4,6-Tetra-*O*-methyl-D-glucose	B[1]	1.00	13.5	10.4
2,3,4,6-Tetra-*O*-methyl-D-galactose	C	1.25	0.8	2.0
3,4,6-Tri-*O*-methyl-D-mannose		1.95		22.6
2,4,6-Tri-*O*-methyl-D-mannose	D	2.08	0.8	
3,4,6-Tri-*O*-methyl-D-glucose	D	2.11	2.1	
2,4,6-Tri-*O*-methyl-D-galactose	E	2.28	8.2	7.0
2,3,6-Tri-*O*-methyl-D-galactose		2.42		
3,4,6-Tri-*O*-methyl-D-galactose	F	2.50	0.5	
4,6-Di-*O*-methyl-D-mannose	G	3.29	24.5	
2,6-Di-*O*-methyl-D-galactose	H	3.62	16.5	10.5
3,6-Di-*O*-methyl-D-galactose	I	4.30	0.8	
2,4-Di-*O*-methyl-D-glucose	K	5.10	1.0	
2,4-Di-*O*-methyl-D-galactose	L	6.35	–	

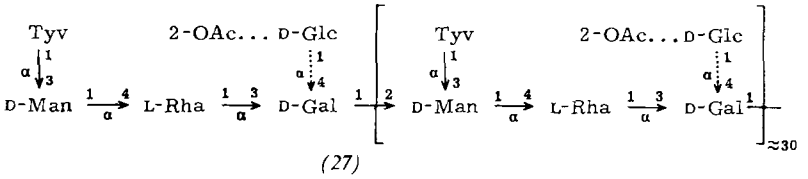
[a] Since a considerable amount of 2,4-di-*O*-methyltyvelose was lost during the methylation analysis the amounts of the methylated sugars are given relative to that of 2,3-di-*O*-methyl-L-rhamnose which is assumed to represent the amount of L-rhamnose in the original lipopolysaccharide.

There is a good agreement between the sugar analysis and the methylation analysis, except for tyvelose. It is reasonable to assume that a considerable amount of 2,4-di-*O*-methyltyvelose and derivatives was lost during concentration of solutions.

Part of the lipopolysaccharide was subjected to a mild acid hydrolysis, which cleaved all tyvelosidic and part of the L-rhamnosidic linkages, and a methylation analysis was performed on the polymeric and oligomeric material recovered (Table 5, II). The finding that 4,6-di-*O*-methyl-D-mannose was completely replaced by 3,4,6-tri-*O*-methyl-D-mannose shows that the tyvelose residues are linked to the 3-position of D-mannose. Likewise, it became evident that the L-rhamnose residues are linked to the C-3 of D-galactose.

All the minor components obtained in the methylation analysis of the original lipopolysaccharide, except 2,4,6-trimethyl-D-mannose, derive from the core polysaccharide. The presence of this sugar and of a considerably higher percentage of 4,6-di-*O*-methyl-D-mannose demonstrates that the non-reducing terminal of the "O-specific" side-chains is a 3-*O*-tyvelosyl-D-mannose residue and also allows an approximate estimation of the average number of repeating units in the chain.

From these and other studies, structure *(27)* was proposed for the O-specific side-chains of the lipopolysaccharide (a dotted line indicates that only part of the residues are substituted).

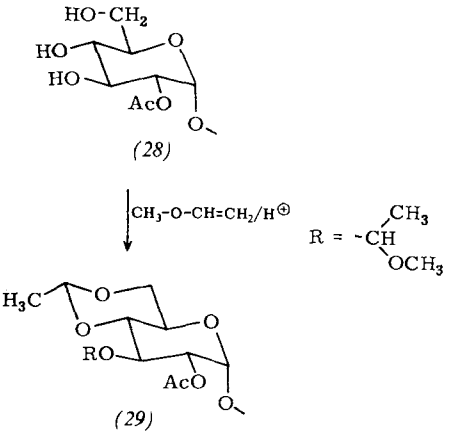


(27)

6.3. Localization of *O*-Acetyl Groups in Polysaccharides

Several polysaccharides contain *O*-acetyl groups, and the localization of such groups previously proved difficult. The problem can be solved by a modified methylation analysis, according to *de Belder* and *Norrman*[19]. All free hydroxyls are converted into acetals by reaction with methyl vinyl ether and an acidic catalyst in dimethyl sulfoxide. The polymer is best recovered by gel filtration on Sephadex LH 20 in acetone. It could then be methylated either directly by the Hakomori procedure, with automatic loss of the *O*-acetyl groups, or first deacetylated and subsequently methylated. Acid hydrolysis gives a mixture of sugars and partially methylated sugars. The original points of acetylation correspond to the positions of methoxyl groups.

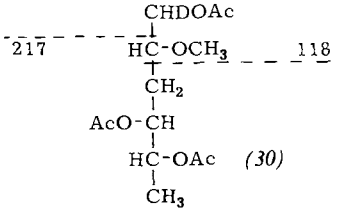
The reaction between carbohydrates and methyl vinyl ether gives acyclic acetals and, when the stereochemistry is favorable, cyclic acetals[33] as well, *e.g. (28)* → *(29)*.



(28) *(29)*

(28) is the terminal *O*-acetylated α-D-glucopyranose residue found in the lipopolysaccharide from *S. typhi (27)*.

The lipopolysaccharide from *S. typhimurium* 395 MS contains abequose (3,6-dideoxy-D-*xylo*-hexose) instead of tyvelose, but otherwise the same sugar components as the lipopolysaccharide from *S. typhi*. It also contains immunologically significant *O*-acetyl groups. After acetalization, methylation, and hydrolysis the sugars were reduced with sodium tetradeuterioborate and acetylated[34]. GLC of this mixture showed that abequose was virtually absent; the only new component not present in the mixture of alditol acetates from



(30)

the original lipopolysaccharide had a lower retention time than abequitol acetate. Although *T*-values of methylated derivatives of abequose were not available, the unknown was readily identified as the alditol acetate of 2-*O*-methylabequose *(30)* from its mass spectrum. These results demonstrate that only C-2 of abequose residues, and no other position in the side chain sugars was acetylated.

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7. Conclusions

Methylation analyses of polysaccharides from wood [35,36], fungi [30,31,37–40], lichens [41], and bacteria [32,34,42] have recently been performed in the authors' laboratory using the Hakomori procedure for methylation and GLC-mass spectrometry for the qualitative and quantitative analysis of the methylated sugars. This technique has the following advantages:

1. It is more accurate and sensitive than previous procedures. It is thus possible to identify and determine the relative proportions of minor components, which may be structurally significant.

2. Only small amounts of material are required. Two to ten mg of polysaccharide can be handled conveniently, but a complete methylation analysis has been done with as little as 0.5 mg. This may be a decisive factor for biologically active materials.

3. It is faster than previous methods. A complete methylation analysis can be accomplished in one week.

4. Access to a great number of methylated sugars as reference standards is not essential. When a new methylated sugar is obtained, its identification is far simpler than previously.

5. The ease and accuracy of the method should prompt research workers to perform additional methylation analyses of chemically modified polysaccharides, and thus obtain complementary structural information.

These advantages are considerable and the methods described above, or related methods based upon GLC-mass spectrometry, will probably largely replace classical methods used for methylation analysis of polysaccharides and other carbohydrates.

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Solvated and Stabilized Electrons in Radiation-Chemical Processes

By Klaus Eiben[*]

The electrons solvated in metal-ammonia solutions are relatively stable; by contrast, hydrated electrons are very unstable and have been discovered only recently during radiolysis of water. They can be regarded as the simplest radicals. Radiation chemical production of solvated electrons has proved to be a particularly elegant method for the qualitative and quantitative investigation of the reactions between these electrons and numerous compounds, whose rates are partly controlled by diffusion. It has been possible in some cases to identify optically and ESR-spectroscopically the resulting short-lived products (radical-anions). The similarity between the physical and chemical properties of electrons solvated in solutions and those of electrons stabilized in the solid phase suggests that the two species are identical.

1. Introduction

It was first suggested in 1952 that hydrated electrons are formed as short-lived intermediates in the radiolysis of water [1]. Shortly afterward, *Platzman* [2] outlined the expected properties of such electrons on the basis of data for the deep blue metal-ammonia solutions [3], known for the past hundred years or so. Several indirect proofs for the existence of hydrated electrons were published in the following years [4–7]. The first direct proof was obtained in 1962 when an intense blue color was observed after the irradiation of glasses formed by NaOH solutions [8,9], and when – shortly

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afterward – the same color was observed in liquid water [10]. It was found in the subsequent rapid development of this field that *solvated* electrons and electrons *stabilized* in the solid phase are formed quite generally in the radiolysis of polar and nonpolar compounds [11]. These electrons, which can be regarded as the simplest radicals, are currently under detailed investigation, and in fact few free radical reactions have been investigated more than theirs [11–21].

2. Radiation Induced Formation of Solvated and Stabilized Electrons

2.1. Absorption of Energy and Thermalization [15, 16]

When corpuscular or electromagnetic radiation is absorbed in gaseous, liquid, and solid matter, high-energy electrons, called primary and secondary electrons, are liberated by the Compton effect and the photoelectric effect (Table 1). These electrons enter into Coulombic interactions with molecules, thereby ionizing or exciting the latter.

Table 1. Time scale for radiation-chemical formation of solvated and stabilized electrons.

Primary ionization	10^{-18}s	
Secondary ionization	10^{-18}s e_c^-	High-energy electrons (10^4–10^6 eV)
	e_{sec}^-	Secondary electrons (10–10^4 eV)
	10^{-16}s e_n^-	Low-energy electrons (< 10 eV)
	10^{-13}s e_m^-	Thermalized but not yet solvated electrons ($E = 3/2\,kT$)
Chemical reactions	10^{-11}s e_t^- e_{solv}^-	Stable electrons in solid phase: e_s^- Solvated electrons in liquid phase: e_{solv}^-, e_{aq}^-
	$\approx 10^{-11}$s	Shortest resolution time so far achieved in pulse radiolysis studies [29]
	$\approx 10^{-8}$s	Homogeneous distribution of primary radicals produced by radiation-chemical techniques in solution [17]

The resulting, mainly low-energy electrons (< 10 eV) give up most of their energy in exciting electronic transitions and vibrational states. When their energy reaches or drops below 0.5 eV, the electrons, now called subexcitation electrons, are thermalized which means that they are slowed down to about 10^7 cm/s (at room temperature), and their energy is reduced to about 0.03 eV.

During this stepwise loss of energy by the electrons (Fig. 1), the distance between the cations and the electrons (ion pairs) increases, and the thermalized electrons (e_m^-) may leave the track and possibly also the Coulombic field of the cations. However, they can recombine, with charge neutralization, this process being known as geminate combination.

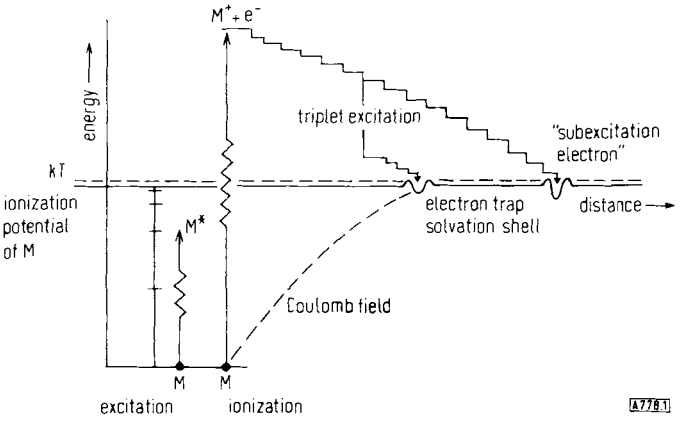


Fig. 1. Thermalization of electrons. Schematic representation after *Dainton* [16].

The probability that thermalized electrons will escape from the Coulombic field depends on the system's polarity, degree of order (crystalline or glassy amorphous state), and temperature (viscosity). For example, the charge neutralization is about five times as intense in nonpolar media, in which the Coulombic field is strong because of the low dielectric constant. In water, by contrast, more than half of the thermalized electrons recombine [16].

The thermal equilibrium of the irradiated system, which is perturbed by the rapid absorption of energy, is reorganized in various simultaneous processes, which will not be discussed here in detail. It should be noted, however, that unlike the energy of light quanta in the first step of photochemical processes, the energy of the ionizing radiation is not absorbed selectively. Therefore the solvent molecules are decomposed in the radiolysis first, while the solutes are attacked only in the subsequent reactions of the primary radicals. The initial distribution of the latter is inhomogeneous (in tracks and spurs), and calls for a distinction between *spur reactions* (recombination and molecular rearrangement) and *radical reactions* (initiated by diffusion).

2.2. Solvation and Stabilization

A previous article [22] dealt with the theory of the formation and the structure of the solvation shells of electrons in polar solvents, this theory having been

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developed mainly for the metal-ammonia solutions. In this connection, the electrons solvated in liquids and the electrons stabilized in glasses are described mostly on the basis of *Jortner*'s continuum model [23].

According to this, the thermalized electrons e_m^- induce electronic polarization in the medium, which is followed by a much slower orientation polarization of the solvent molecules in polar liquids, leading to the solvation of the electrons. The solvents under consideration (*e.g.* water and alcohols) have a negative electron affinity, which means that they have no accessible orbitals for the incorporation of additional electrons. *Onsager* [24] assumes that the excess electrons are accommodated in cavities formed by the positive ends of a number of polar molecules.

Several authors have examined whether the thermalized electrons can bring about a solvation shell by self-induced dipole orientation [23] (*i.e.* whether they "dig themselves a hole"), or whether they are captured on anionic defect sites [25] (positive holes), produced by irradiation, or in cavities formed accidentally [26]. As regards solvation in liquids, no clear answer has yet emerged in this connection. *Schiller* [27] estimates that the rate of solvation of electrons *e.g.* in water is thirty times as high (10^{-13} s) as the dipole relaxation time of water. On this basis, the electrons must accelerate the dipole orientation of the solvated molecules, or they must be captured by pre-oriented water molecules. It is not possible to decide experimentally which of these two mechanisms of formation is valid, because not even the fastest method of detection (pulse radiolysis in the picosecond range; cf. Section 3) can resolve the electron solvation period [28].

In the case of frozen solutions, on the other hand, the electrons are assumed to be captured and stabilized in partially or wholly preformed traps [26, 29–31]. Glassy or amorphous systems, which lack short-range order, are characterized by a much higher concentration of preformed electron traps compared to crystals, where short-range order dominates. Thus, no electrons are detected in irradiated $NaOH \cdot 7\,H_2O$ and $NaOH \cdot 3.5\,H_2O$ [32], but electrons are stabilized in high yields [*] in frozen glassy solutions of the same compositions (6.5 N and 13.5 N NaOH) [8, 26, 33, 34] (Tables 2 and 4). The same difference has been found in the case of crystalline aliphatic alcohols and their corresponding glassy forms, obtained by rapid freezing [32].

Electrons solvated in liquids reach a homogeneous distribution through diffusion about 10^{-8} s after formation (Table 1), while electrons in glasses are stabilized in the immediate vicinity of the spur produced by the irradiation. As found from ESR relaxation data [36], the mean distance from the spur center increases with decreasing polarity of the medium, being 40, 59, and 72 Å in 7 N NaOH [35], methanol, and methyltetrahydrofuran [36], respectively. Accordingly, the density of preformed electron traps is greater, and the range of thermalized electrons is smaller, in polar glasses than in nonpolar ones.

2.3. Properties

Solvation reduces the mobility of electrons in polarized dielectrics. Paramagnetism and intense absorption in the red-infrared region are the most conspicuous and – as far as detection is concerned – the most valuable properties of electrons (Table 2).

The light absorption is attributed to a 1s → 2p transition of the electron localized in the cavity [23]. The absorption maximum shifts toward shorter wavelengths in any solvent as the temperature is lowered, which means that the depth of the potential well of the solvation shell increases. In *Jortner*'s semi-empirical

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[*] By definition, the yield (*G*) is the number of molecules formed or reacted per 100 eV of absorbed energy.

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Table 2. Optical and ESR spectroscopic data for solvated and stabilized electrons.

Solvent	T (°K)	Method [a]	Static dielectric constant (DK)	Ref.	λ_{max} (nm) λ_{max} (eV)	Ref.	ε (l mole^{-1} cm^{-1}) yield: G_{e^-}	Ref.	$\lambda_{max}/2$ (eV)	Ref.	$\Delta\lambda_{max}/dT$ (eV/deg) $\times 10^3$	Ref.	ESR singlet: g factor and line width (gauss)	Ref.
Water	293	PR	78.2	[38]	720 1.72	[37]	17000 2.76	[37] [39]	0.92	[40]	−2.9	[40]	2.0002 < 0.5	[41]
Ice	138	PR			630 ± 8 1.98	[29]	17000 ≈ 3×10^{-3}	[29]	0.70	[29]	−1.2	[29]		
	77	γ-R			640 ± 10 1.93	[42]	17000 ≈ 3×10^{-4}	[42]	0.47	[42]			2.0009 10.6	[43]
Heavy water	293	PR	78.5	[38]	700 1.77	[44]	20200 3.06	[44] [46]	0.88	[45]				
Heavy ice	77	γ-R			630 ± 10 1.97	[47]	20200 ≈ 6×10^{-4}	[47]	0.62	[47]			2.0007 2.7	[43]
7 N Sodium hydroxide solution	293	PR			660 1.88	[48]	19000	[48]			−1.6	[48]		
7 N Sodium hydroxide glass	77	γ-R			580 ± 5 2.16	[26]	19000 2.0 ± 0.1	[26]	1.05	[26]			2.0006 15	[34]
Ethylene glycol	293	PR	38.7	[38]	580 2.16	[38]	14000 1.2	[50]	1.35	[50]				
Methanol	293	PR	32.6	[38]	630 1.97	[38]	17000 1.1	[50]	1.29	[50]	−2.2	[38]		
Methanol glass	77	γ-R			526 ± 5 2.35	[53]	11000 2.7 ± 0.3	[53]	1.1	[53]			14	[51]
Ethanol	293	PR	24.5	[38]	700 1.77	[38]	15000 1.0	[50]	1.55	[50]	−3.4	[38]		
Ethanol glass	77	γ-R			540 2.30	[34]	2.4	[52]	1.05	[51]			2.0010 12	[34] [51]
n-Propanol	293	PR	20.1	[38]	790 1.67	[38]	15000	[50]						
n-Propanol glass	77	γ-R			555 2.22	[51]	8400 1.7	[54]					12	[51]
Isopropanol	293	PR	18.6	[38]	820 1.51	[38]	13000 1.0	[50]	1.22	[50]	−3.5	[50]		
Isopropanol glass	77	γ-R			615 2.02	[55]	15300 1.9	[55]					2.0018 10	[34] [51]
n-Butanol	293	PR	17.8	[38]	680 1.82	[38]			1.47	[38]	−4.5	[38]		
n-Butanol glass	77	γ-R			561 2.21	[51]							8	[51]
Methyltetrahydrofuran (MTHF-) glass	77	γ-R	4.6	[38]	1250 1.00	[56]	16800 2.6	[56]	0.55	[56]			2.0011 4.5	[34] [53]
Ammonia	228	PR	22	[58a]	1350 0.92	[57]	40000 ≈ 3.00	[57] [58]	1.1	[59]				

[a] PR: Pulse radiolysis; γ-R: ^{60}Co-gamma radiolysis.

continuum model[59] this is explained by the temperature-dependence of the cavity radius (R_0)[*] and of the dielectric constant of the solvent. In the case of alcohols the absorption maximum shows a red shift and the band-width of the ESR singlet decreases as the dielectric constant decreases[51]. As the polarity decreases, R_0 increases and the interaction between the electrons and the protons of the solvate molecules become weaker. The absorption maximum in heavy water lies at shorter wavelengths than that in ordinary water[44]. An increase in the pressure by 1000 atm similarly causes λ_{max} of the hydrated electrons to shift toward shorter wavelengths by 200 ± 50 Å[49]. This indicates that the volume of hydrated electrons is less than 20 ml/mole, the corresponding value in the case of ammonia being 60–90 ml/mole[49].

The band-width of the ESR singlet is smaller in D_2O than in H_2O[43] which is explained by the smaller nuclear magnetic moment of deuterium. The isotope effect, which is observed also with deuterated alco-

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[58] *B. Ward* [12], p. 601.

[58a] *R. C. Weast:* Handbook of Chemistry and Physics. The Chemical Rubber Co., Cleveland, Ohio.

[59] *J. Jortner* in *G. Stein*: Radiation Chemistry of Aqueous Systems. Interscience, New York 1968, p. 91.

[*] Not to be confused with the effective ionic radius of the electron (r_0) (Table 3).

hols[43] and heavy ammonia[60], indicates that the protons of the solvent participate in the formation of the solvation shell.

Table 3. Physical and thermodynamic constants of hydrated electrons at 25 °C

		Ref.
Charge	-1	
Diffusion constant	$D_{e^-_{aq}} = 4.5 \times 10^5$ cm^{2}s^{-1}	[61]
Equivalent conductivity	$\Lambda_c = 170\ \Omega^{-1}$ cm^2 equiv.$^{-1}$	[61]
Redox Potential	$E_0 = -2.7$ V	[19]
pK ($e^-_{aq} \overset{H^+}{\rightleftharpoons}$ H)	p$K = 9.6$	[62]
Heat of solution	$\Delta H = -40$ kcal	[19]
Cavity radius	$R_0 = 1.45$ Å	[59]
Effective ionic radius	$r_0 = 2.5$–3 Å	[25]

The absorption maxima of electrons stabilized in some glassy hydrocarbons (Table 4) lie in the infrared region. The yield and the thermal stability of the electrons are clearly lower here than in polar glasses, but they can be raised by adding unreactive but polar substances such as triethylamine (TEA)[65, 66]. Mixtures of polar and nonpolar solvents show a similar behavior, but they give two absorption maxima in the visible and the infrared region[51, 67]. This is explained by an association of the polar molecules in the nonpolar solvent, and by preferential stabilization of the electrons near the polar molecules.

Table 4. Absorption and ESR spectra of stabilized electrons in nonpolar glasses [63].

	λ_{max} (nm)	λ_{max} (eV)	ESR singlet ΔH (gauss)	G_{e^-} in pure glass	G_{Anion} biphenyl	$G_{e^-(TEA)}$ [65]
3-Methylpentane	1600	0.78	3.9 ± 0.2	0.65	1.57	1.08
3-Methylhexane	1650	0.75	3.8 ± 0.2	0.89	1.60	0.96
3-Methylheptane [64]	1700	0.73	4.0 ± 0.2	0.58	1.23	
Methylcyclohexane	1650	0.75	4.4 ± 0.2	0.30		0.96
4-Methylheptane	1700	0.73	4.1 ± 0.1	0.55		
Methyltetrahydrofuran (MTHF) [56]	1250	1.0	4.5 ± 0.3 [53]	2.6	2.6	

2.4. Structure of the Hydration Shell

The Natori-Watanabe model[68] of hydrated electrons is based on the concept that the molecules of liquid water have an ice-like tetrahedral arrangement. According to this model, the electrons occupy the position of an accidentally missing H_2O molecule at the center of the tetrahedron. The tetrahedral structure is slightly widened, and in addition, it is assumed that polarization of the surrounding H_2O molecules leads to the binding of the electron.

Like *Jortner*'s empirical cavity radius[59] ($R_0 = 1.45$ Å for water), however, this model gives only a mean value for the size of the hydration shell of the electrons. However, to account for the large half-widths observed in the absorption spectrum, it must be assumed that electrons populate traps of different depths (Table 2)[15]. One of the experimental proofs of this is seen in the blue shift of the absorption maximum, observed when the blue color of stabilized electrons of irradiated glasses is photobleached with light whose wavelength exceeds λ_{max}[30] [this process remobilizes only those electrons that are stabilized in the shallow traps (cf. Section 4.3)]. The other experimental proof is that glasses formed from a mixture of polar sol vents give only a broadened absorption band whose maximum is shifted according to the proportion of the components of the mixture[30]. The distribution of the electron traps is obviously influenced by the size of the substituents acting as functional groups for the solvation (OH and NH_2).

By contrast, the half-width of the absorption bands is smaller in crystalline systems [hexagonal ice (Table 2) and F-centers in ionic crystals[69]], where the dimensions of the electron traps differ only slightly.

The participation of a certain number of water molecules (*e.g.* four in the Natori-Watanabe model[68]) in the formation of the hydration shell of electrons should also be manifested in the hyperfine structure of the ESR spectra, but this has not yet been detected either in the liquid or in the solid phase[25, 26, 33, 34]. The ESR singlet of irradiated glasses can be described by a Gauss function, and therefore it points to an unresolved hyperfine structure. An observation[70] frequently quoted is that the ESR singlet obtained for condensates of alkali metals and water and assigned to electrons stabilized at −196 °C shows binomial hyperfine splitting into five to seven lines when the sample is warmed to −140 °C. However, this is probably due to a phase transition of ice from the amorphous to the cubic state, occurring under special conditions, and thus leads to a preferred orientation of the solvation shell. Furthermore, one cannot exclude the possibility that the alkali metal cations are involved in this phenomenon, since the annealing of condensates prepared without any alkali metals is not accompanied by hyperfine splitting. In these condensates the electrons are formed by irradiation in the vapor phase and stabilization in the ice matrix occurs 15 μs later[43]. The lack of hyperfine splitting of the ESR singlet in liquid water[41] is probably due to the fast exchange interaction with protons of the hydration shell.

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3. Experimental Methods

The detection of electrons formed during radiolytic processes is hampered by their short lifetime. Two main methods are employed. The technique of *matrix stabilization* is used to accumulate radicals and electrons in the frozen matrix during irradiation *e.g.* with ^{60}Co γ-rays [26,71]. Their properties can be studied by optical and ESR-spectroscopic methods using instruments specially equipped for low temperatures. Kinetic investigations can be carried out while the frozen solutions are warmed until the stabilized electrons become diffusive. Photochemical remobilization of the stabilized electrons can initiate reactions in the irradiated glasses. The matrix isolation method first proposed by *Lewis et al.* [72] is used to stabilize radicals and electrons produced during irradiation in the vapor phase. The reactive radicals are frozen on to a cold-finger at −196 °C about 15 μs after their formation [43,73].

In the second method, the light absorption [10], the paramagnetic properties [41], or the changes in the conductivity [61] of a system are investigated by rapid techniques directly after the formation of the solvated electrons. In pulse radiolysis [20,28,74], the most favored technique to date, the sample is irradiated with 1–10-MeV electron pulses of 10^{-5} to 10^{-11} s duration, the decrease in the optical absorption of the solvated electrons is measured, and the formation of new absorbing species is observed. Only recently has it become possible to use ESR spectroscopy for direct investigation of solvated electrons and their short-lived products in irradiated solutions [41,75]. In this technique the polar solution flows through a flat cell in the resonator of the ESR spectroscope, and a focused beam of highly accelerated electrons (2.8 MeV) is used to maintain a stationary concentration of radicals in the solution while the ESR spectrum is being recorded (Fig. 2).

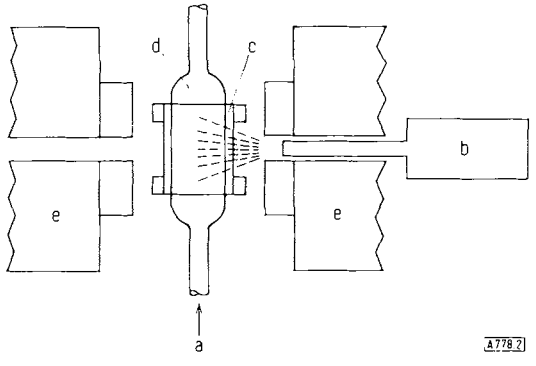


Fig. 2. Schematic representation of the ESR-spectroscopic investigation of short-lived radicals in polar solutions. a, solution; b, electron accelerator; c, ESR resonator; d, flat cell; e, magnet.

4. Reactions of Solvated and Stabilized Electrons

Owing to their high reduction potential, solvated electrons can react with numerous compounds, these reactions involving either *electron addition* or *dissociative electron attachment*.

Electron addition to an acceptor molecule produces either a radical-anion

$$e^-_{solv} + A \rightarrow A^- \qquad (1)$$

or reduces a metal cation (M^{n+}) by one valence stage.

$$e^-_{solv} + M^{n+} \rightarrow M^{(n-1)+} \qquad (2)$$

Dissociative electron attachment by an acceptor molecule leads to stable anions and radicals.

$$e^-_{solv} + RX \rightarrow R^{\bullet} + X^- \qquad (3)$$

We now know from pulse-radiolytic measurements the bimolecular rate constants for the reactions between solvated electrons and well over 500 organic and inorganic compounds in aqueous and other polar solutions [76], but do not yet have a clear picture of the structure and the properties of all these short-lived intermediates. *Habersbergerova et al.* [77] have published a survey on the optical absorption spectra of unstable radicals generated by photochemical and radiolytic reactions.

4.1. Reactions of Solvated Electrons in Solutions

Hydrated electrons and their reactions in aqueous solutions have been investigated most extensively. Essentially the same behavior is exhibited by solvated electrons in irradiated alcohols [78,79]. The following primary radicals and products are formed in the radiolysis of water:

$$H_2O \rightsquigarrow e^-_{aq}\ (2.8);\ OH\ (2.4);\ H\ (0.6);\ H_2\ (0.45);\ H_2O_2\ (0.7);\ H_3O^+\ (2.8) \qquad (4)$$

The figures in brackets give the yields of primary radicals, which have been detected indirectly by the addition of suitable radical scavengers, and in some cases by analysis of the products [80]. Hydrogen atoms [81] and electrons [41] are detected directly by ESR measurements. The molecular prod-

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ucts H_2 and H_2O_2 are formed in the spur by radical reactions, and their yield is affected only slightly by the addition of radical scavengers [82].

The following reactions are responsible for the disappearance of hydrated electrons in irradiated pure water:

a) Reactions with the primary radicals of water:

$$e^-_{aq} + H \rightarrow H_2 + OH^-; \quad k_5 = 2.5 \times 10^{10}\ \text{lmole}^{-1}\text{s}^{-1} \quad (5)$$

$$e^-_{aq} + OH \rightarrow OH^-; \quad k_6 = 3.0 \times 10^{10}\ \text{lmole}^{-1}\text{s}^{-1} \quad (6)$$

$$e^-_{aq} + O^- \rightarrow 2\,OH^-; \quad k_7 = 2.2 \times 10^{10}\ \text{lmole}^{-1}\text{s}^{-1} \quad (7)$$

$$e^-_{aq} + e^-_{aq} \rightarrow H_2 + 2\,OH^-; \quad k_8 = 0.5 \times 10^{10}\ \text{lmole}^{-1}\text{s}^{-1} \quad (8)$$

b) Reactions with the radiolysis products of water:

$$e^-_{aq} + H_2O_2 \rightarrow OH + OH^-; \quad k_9 = 1.2 \times 10^{10}\ \text{lmole}^{-1}\text{s}^{-1} \quad (9)$$

$$e^-_{aq} + H_3O^+ \rightarrow H + H_2O; \quad k_{10} = 2.0 \times 10^{10}\ \text{lmole}^{-1}\text{s}^{-1} \quad (10)$$

c) Reaction with water molecules:

$$e^-_{aq} + H_2O \rightarrow H + OH^-; \quad k_{11} = 8.9 \times 10^2\ \text{s}^{-1} \quad (11)$$

Reactions (5–10) are very fast and in part diffusion-controlled. In the case of reaction (10), *Sworski* [83] has assumed the formation of H_3O or H_9O_4 as an intermediate, since – according to *Debye* [84] – diffusion-controlled charge neutralization should be about twice as fast.

By contrast, the pseudo-first order reaction (11) between the hydrated electrons and the solvent is very slow. This reaction has been investigated very carefully, since it is decisive for the lifetime of hydrated electrons in pure water and for the determination of thermodynamic constants [85]. To investigate reaction (11), the water must be very pure: substances capturing electrons (*e.g.* oxygen [12] and CO_2 [13]) interfere even in very low concentrations ($> 10^{-8}$ mole/l).

$$e^-_{aq} + O_2 \rightarrow O_2^- \quad k_{12} = 2.2 \times 10^{10}\ \text{lmole}^{-1}\text{s}^{-1} \quad (12)$$

$$e^-_{aq} + CO_2 \rightarrow CO_2^- \quad k_{13} = 2.7 \times 10^{10}\ \text{lmole}^{-1}\text{s}^{-1} \quad (13)$$

A lifetime of 780 μs has been found for hydrated electrons at very low e^-_{aq} concentrations, but it may be assumed that even longer lifetimes will become possible when the technique is improved [85].

The corresponding reaction between solvated electrons and aliphatic alcohols [86] is very much faster:

$$e^-_{solv} + ROH \rightarrow RO^- + H \quad (11a)$$

The rate constants k_{11a} are 4.6×10^5, 10^5, 5×10^5, and $3 \times 10^5\ \text{s}^{-1}$ in the case of methanol, ethanol, 1-propanol, and 2-propanol, respectively. Thus the solvated electrons have a shorter lifetime (*ca.* 5 μs) in alcohols than in water; *Freeman* [86] has attributed this to a difference between the activation energy for reorientation of the solvent molecules from the solvation shell of electrons to the OH^- and RO^- anions respectively.

4.1.1. Acid-Base Equilibrium and the Difference between Hydrogen Atoms and Solvated Electrons

Hydrogen atoms and hydrated electrons form acid-base pairs in water, the corresponding equilibrium being dependent on the pH.

$$e^-_{aq} + H_3O^+ \rightleftharpoons H + H_2O; \quad pK = 9.6\ [62] \quad (14)$$

Pulse-radiolysis investigations [87] have shown that the transformation of hydrated electrons into hydrogen atoms (10) is faster than the reverse reaction (15) by three orders of magnitude.

$$H + OH^- \rightarrow e^-_{aq}; \quad k_{15} = 2.2 \times 10^7\ \text{lmole}^{-1}\text{s}^{-1} \quad (15)$$

The transformation of hydrogen atoms into solvated electrons (15) has also been demonstrated [88] in a reaction in which hydrogen atoms formed in a discharge tube were introduced into an alkaline aqueous chloroacetate solution (pH 13.5). Reaction (15) then took place on account of the high basicity, and the resulting solvated electrons reacted with the chloroacetate to yield Cl^- ions.

$$e^-_{aq} + ClCH_2COO^- \rightarrow Cl^- + {\cdot}CH_2COO^-; \quad k_{16} = 1.2 \times 10^9\ \text{lmole}^{-1}\text{s}^{-1} \quad (16)$$

By contrast, hydrogen atoms react with chloroacetic acid in an acidic solution (17) comparatively slowly to yield hydrogen [76]:

$$H + ClCH_2COOH \rightarrow H_2 + {\cdot}CHClCOO^-; \quad k_{17} = 2.6 \times 10^6\ \text{lmole}^{-1}\text{s}^{-1} \quad (17)$$

The historical significance of reactions (16) and (17) is that it was through the pH-dependent formation of Cl^- and H_2 that *Hayon* and *Weiss* [4] first detected in 1958 the acid-base equilibrium of "two reducing species obtained during radiolysis of water", thereby proving indirectly the existence of hydrated electrons (polarons) as intermediates.

The conversion of hydrated electrons into hydroxyl radicals with N_2O is another reaction (18) where hydrated electrons and hydrogen atoms behave differently; this reaction was first investigated by *Dainton* and *Peterson* [89].

$$e^-_{aq} + N_2O \rightarrow [N_2O^-] \xrightarrow{H_2O} N_2 + OH^- + OH; \quad k_{18} = 5.6 \times 10^9\ \text{lmole}^{-1}\text{s}^{-1} \quad (18)$$

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The corresponding reaction in alcohols leads to O^- radical anions [90].

$$e^-_{solv} + N_2O \rightarrow N_2 + O^-; \quad k_{CH_3OH} = 1.4 \times 10^{10}\ l\,mole^{-1}s^{-1} \qquad (18a)$$

The existence of transient electrons during radiolysis of N_2O-saturated hydrocarbons is established by the production of nitrogen [91]. The reaction between hydrogen atoms and N_2O in water is slower by a factor of 10^5 [76].

Reaction (9) between H_2O_2 and hydrated electrons is 145 times as fast as the reaction between H_2O_2 and hydrogen atoms. This difference was noticed by *Barr* and *Allen* [5] in the radiolysis of aqueous solutions of H_2O_2, and was attributed already in 1959 to the coexistence of two different reducing radical species. Similarly, the formation of the trinitromethyl anion from tetranitromethane is 100 times faster in the presence of hydrated electrons [reaction (19)] than in the presence of hydrogen atoms [92]

$$e^-_{aq} + C(NO_2)_4 \rightarrow C(NO_2)_3^- + NO_2; \quad k_{19} = 4.6 \times 10^{10}\ l\,mole^{-1}s^{-1} \qquad (19)$$

Since the formation of trinitromethyl anion can be detected optically, this reaction offers a possibility of determining the molar extinction coefficient of hydrated electrons (ε = 15800 l mole^{-1} cm^{-1} at G_{e^-} = 2.6) [92].

Solvated electrons also differ from hydrogen atoms in their optical absorption spectrum (H atoms absorb below 200 nm [93]), ESR spectrum (H atoms show a characteristic 503-gauss doublet [81]), electric conductivity [61, 94], and the kinetic salt effect [6, 7] (this effect has an influence only on the reactions of electrons and not on the reactions of H atoms, which are electrically neutral).

4.1.2. Reactions between Solvated Electrons and Organic Compounds

The reductions brought about by solvated electrons in irradiated solutions can be compared to those occurring in metal-ammonia solutions [95]. Simple and dissociative electron attachment [reactions (1) and (3)] have been shown to be the first steps in electron transfer.

Table 5. Rate constants of bimolecular reactions of organic compounds with hydrated electrons (after [76]).

k (l mole^{-1} s^{-1})	Amino acids (pH)	Heterocycles (pH)	Aliphatic compounds (pH)
↑		adenosine (5) purine (7) thymine (6)	tetranitromethane carbon tetrachloride chloroform, nitromethane 1-iodoethane
10^{10}	cystine (6)	uracil (7)	1-iodobutane
↑	cysteine (6)	uric acid adenine (7)	butadiene chloroacetic acid (1) acetone
10^9	histidine (6)	[thiourea (6)] pyridine (7)	acetaldehyde chloroacetate (11)
↑	hydroxyproline (7) tryptophan (7) phenylalanine (7)	indole uracil (11) guanine (6)	1-chloropropane 2-chlorobutane 1-chlorobutane maleic acid (6)
10^8	arginine (8)	imidazole (8.7)	formic acid (5)
↑	methionine (8) lysine (7)	thiophene (7) imidazole (9.1)	cyanoacetic acid (11) acetonitrile
10^7	serine (7)		
$< 10^7$	glycine; alanine; valine; leucine; isoleucine; threonine; formaldehyde; fluoroacetic acid; diethyl ether		

Aliphatic Compounds [18, 76]

Solvated electrons react very slowly ($k < 10^7$ l mole^{-1} s^{-1}) with aliphatic compounds having stable C–C, C–O–C, COOH, OH, and NH_2 groups, *i.e.* compounds without low-lying orbitals accessible to electrons. Halogen substituents enhance the reactivity of aliphatic compounds in the order F $\ll$ Cl $<$ Br $<$ I, which can be attributed to dissociative electron attachment (3) at the halogen substituents [96].

Electrophilic groups next to halogen substituents reduce the reactivity toward solvated electrons. *Anbar* and *Hart* [98] found a linear relationship between the

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[98] *M. Anbar* and *E. J. Hart,* J. Phys. Chem. *69,* 271 (1965).

experimental rate constants of halogen-containing aliphatic compounds and *Taft*'s σ* values [97] for these electrophilic substituents. Polychlorinated hydrocarbons, *e.g.* CCl_4 and $CHCl_3$, are among the organic compounds with the highest reactivity toward electrons. Nitromethane and tetranitromethane (19) [100] are also good electron acceptors. The absorption spectra and the kinetic behavior of the nitroalkane radical anion *(3)*, formed as an intermediate, have been investigated [99], and the structure of this radical anion has been confirmed by the *in-situ* ESR-spectroscopic technique [75]. According to the findings, hydrated electrons react both with nitromethane *(1)* and with its *aci*-form *(2)* to give the radical anion *(3)*.

$$\begin{array}{ccc} CH_3NO_2\ (1) & \underset{H_2O}{\overset{OH^-}{\rightleftharpoons}} & CH_2{=}NO_2^-\ (2) \\ \downarrow + e_{aq}^- & & \downarrow + e_{aq}^- \\ CH_3\dot{N}O_2^-\ (3) & \underset{OH^-}{\overset{H_2O}{\rightleftharpoons}} & CH_2{=}\dot{N}O_2^{2-} \end{array} \qquad (20)$$

Carbonyl compounds such as aldehydes and ketones [101,102] give hydroxyalkyl radicals *via* the formation and protonation of an electron adduct.

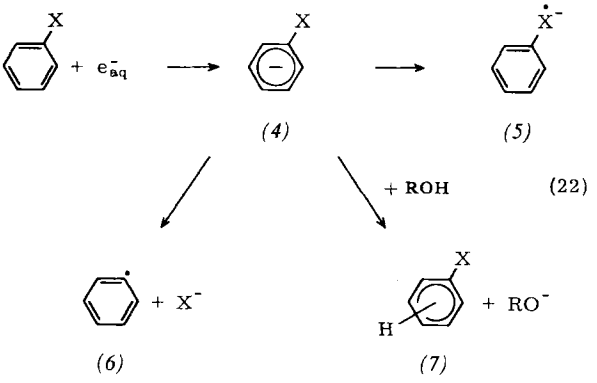
$$R_2CO + e_{aq}^- \rightarrow R_2\dot{C}O^- \underset{}{\overset{H^+}{\rightleftharpoons}} R_2\dot{C}OH \qquad (21)$$

The ketyl radical formed during the irradiation of aqueous acetone has been identified as an intermediate at pH > 12 by use of the *in-situ* ESR technique (at lower pH values the protonated form, *i.e.* the hydroxyisopropyl radical, is observed) [103]. Enols react slowly, and so does also formaldehyde, in the case of which the electron affinity of the carbonyl group is reduced by hydrate formation.

Double bonds in aliphatic compounds enhance the reactivity to electrons only when they are conjugated or are adjacent to CN and CS groups. The addition of an electron is generally followed by rapid protonation, giving hydrogenated products [101]. The case of chloroacetic acid in Table 5 illustrates the observation that aliphatic acid anions react with electrons more slowly than do the undissociated acids.

Aromatic Compounds

As in the nucleophilic substitution of aromatic compounds by the S_N2 mechanism, the reactions of hydrated electrons with monosubstituted benzenes (22) first give a carbanion radical *(4)*, but the existence of this species can be detected only in certain cases (X = NO_2, NO, COOH) in which resonance stabilization involving *(5)* is possible [85, 98, 104].



R = H, CH_3, C_2H_5, $(CH_3)_2CH$

In the case of halogen-substituted aromatic compounds it has not yet been demonstrated that the dissociative electron attachment (3) proceeds *via* the intermediate formation of carbanions. Phenyl radicals *(6)* have been found as transient products.

Protonation of the aromatic carbanion *(4)* gives products of the cyclohexadienyl type *(7)*. The protonation of the carbanions of *e.g.* biphenyl, naphthalene, and anthracene in alcohols [105] is slower by a factor of about 10^5 to 10^6 with the solvent molecules

$$A^- + ROH \rightarrow RO^- + {}^{\cdot}AH \qquad (23)$$

than with alkoxonium ions.

$$A^- + ROH_2^+ \rightarrow ROH + {}^{\cdot}AH \qquad (24)$$

As in the case of nucleophilic substitutions, the effect of substituents on the reactivity of the aromatic ring can be deduced from the rate constants and can be expressed by *Hammett*'s σ function [106] (Fig. 3). The

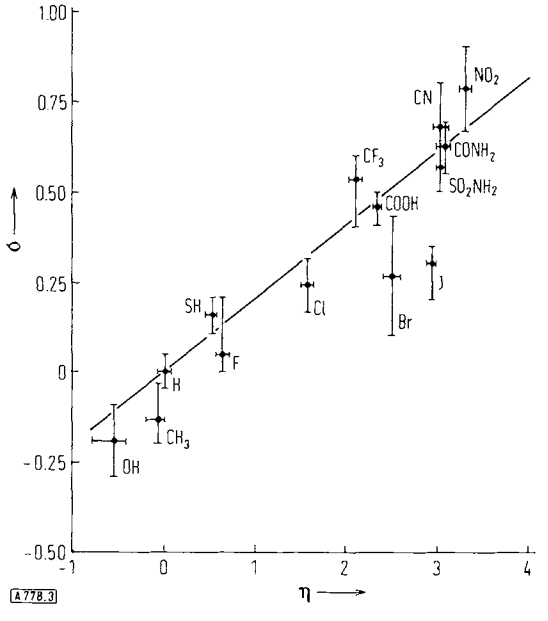


Fig. 3. Variation of *Hammett*'s σ function with $\eta = \log (k_{C_6H_5X} + e_{aq}^-)/(k_{C_6H_6} + e_{aq}^-)$ [106].

[99] *K. D. Asmus, A. Henglein,* and *G. Beck,* Ber. Bunsenges. Phys. Chem. *70,* 459 (1966).

[100] *K. D. Asmus, A. Henglein, M. Ebert,* and *J. P. Keene,* Ber. Bunsenges. Phys. Chem. *68,* 657 (1964).

[101] *E. J. Hart, S. Gordon,* and *J. K. Thomas,* J. Phys. Chem. *68,* 1271 (1964).

[102] *J. Lilie* and *A. Henglein,* Ber. Bunsenges. Phys. Chem. *73,* 170 (1969).

[103] *K. Eiben,* unpublished.

[104] *K. D. Asmus, A. Wigger,* and *A. Henglein,* Ber. Bunsenges. Phys. Chem. *70,* 862 (1966).

[105] *L. M. Dorfman, N. E. Shank,* and *S. Arai* [13], p. 58.

[106] *M. Anbar* and *E. J. Hart,* J. Am. Chem. Soc. *86,* 5633 (1964).

reactivity is greater in the presence of *meta*-directing substituents than in the presence of *ortho*- and *para*-directing ones.

Bromine- and iodine-substituted aromatic compounds are exceptions: they react faster with hydrated electrons than with other nucleophilic species. This is ascribed to the possibility of bromine and iodine "transferring" electrons to the aromatic ring, or to the possibility of direct attachment to halogen (3) occurring besides the ring addition [106]. Transfer by halogen ligands has also been observed in the reduction of transition metal complexes by hydrated electrons (Table 6) [107].

The reactions between disubstituted aromatic compounds (Fig. 4) and hydrated electrons are complex.

Sherman [108] has investigated the rate of the reactions between solvated electrons and substituted aromatic compounds in methanol and isopropanol in comparison with the reaction with N_2O (18a). *Dainton et al.* [90] have obtained by pulse radiolysis the value $k_{18a} = 1.4 \times 10^{10}$ l mole^{-1} s^{-1} for the absolute rate constant of the reaction with N_2O in methanol. If the relative rates are taken into account the reactions are generally found to be about 2–3 times as fast in methanol as in water.

Substances of Biological Importance [109, 110]

Physiological reactions mainly take place in aqueous systems, in which – as we have seen – irradiation produces hydrated electrons. Investigations of the reactions of these electrons in radiobiological processes are therefore of great interest. However, the investigations are complicated by the simultaneous presence of other primary radicals (OH and H), and so they have been mainly confined to simple systems such as the aqueous solutions of amino acids, peptides, compounds of nucleic acid, and sugars. The mechanisms of the electron transfer and the reactive centers in the acceptor molecules are still hardly known. The reactions between electrons and simple amino acids containing only C, H, O, and N atoms proceeding with the loss of NH_3 or CO_2, are relatively slow ($k < 10^7$ l mole^{-1} s^{-1}), whereas the reactions between electrons and amino acids containing aromatic substituents or sulfur are very much faster (Table 5). This is explained by the increase in the electron affinity, caused by the

Table 6. Rate constants of bimolecular reactions of inorganic compounds with hydrated electrons.

k (l mole^{-1} s^{-1})	Nonmetallic compounds	Oxo anions	Metal cations	Lanthanide ions	Metal complexes
↑	I_2		Cd^{2+}; Cr^{3+}	Eu^{3+}	$Co(NH_3)_6^{3+}$
	CS_2; OH	MnO_4^-	Cr^{2+}; Ag^+	Yb^{3+}	$[CoO(NH_3)_5]_2^{5+}$
	H; H_3O^+	$Cr_2O_7^{2-}$	Cu^{2+}; Ni^{2+}		$Cr(H_2O)_6^{3+}$
	O_2; SF_6	BrO^-		Sm^{3+}	$[CoO(CN)_5]_2^{5-}$
	Br_2; H_2S				$Fe(CN)_5NO^{2-}$
10^{10}	H_2O_2	IO_4^-; NO_3^-	Pb^{2+}; Co^{2+}		$Cu(NH_3)_4^{2+}$
					$Cr(CN)_6^{3-}$
↑	CO_2	NO_2^-; BrO_3^-			$PdCl_4^{2-}$
	NO_2	$S_2O_8^{2-}$; IO_3^-			$Zn(NH_3)_4^{2+}$
	e_{aq}^-				$Fe(CN)_6^{3-}$
				Tm^{3+}	$Co(CN)_6^{3-}$
				Ho^{3+}	
			Al^{3+}		FeF_6^{3-}
10^9	CO		Zn^{2+}		$Zn(CN)_4^{2-}$
↑		$S_2O_3^{2-}$		Nd^{3+}; Gd^{3+}	
				Dy^{3+}; Tb^{3+}	
				$[La^{3+}]$; Pr^{3+}	$Cu(CN)_2^-$
		ClO_3^-		Lu^{3+}; $[Y^{3+}]$	
					$Hg(CN)_4^{2-}$
10^8			Fe^{2+}		$Cd(CN)_4^{2-}$
$< 10^8$	H_2F_2		Mn^{2+}	Er^{3+}	

The differences in the reaction rates are due to the effects exerted by the substituents on the electron density distribution in the aromatic molecule [106].

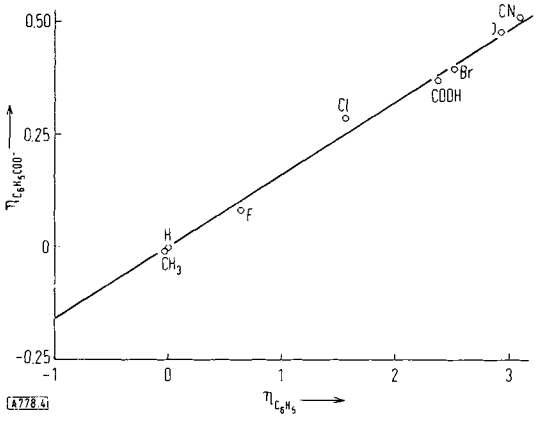


Fig. 4. Rates of the reactions of hydrated electrons with substituted benzoic acids and substituted benzenes [106].
$\eta_{C_6H_5COO^-} = \log (k_{X-C_6H_4CO_2^-} + e_{aq}^-)/(k_{C_6H_5CO_2^-} + e_{aq}^-)$;
$\eta_{C_6H_6} = \log (k_{X-C_6H_5} + e_{aq}^-)/(k_{C_6H_5} + e_{aq}^-)$.

[107] *M. Anbar* and *E. J. Hart* [11], p. 79.

[108] *W. V. Sherman*, J. Am. Chem. Soc. *88*, 1567 (1966).

[109] a) *C. L. Greenstock*, *M. Ng*, and *J. W. Hunt* [11], p. 397; b) *G. Scholes*, *P. Shaw*, *R. L. Wilson*, and *M. Ebert* [20], p. 151; c) *G. Scholes* in *G. Stein*: Radiation Chemistry of Aqueous Systems. Interscience, New York 1968, p. 259.

[110] a) *W. M. Garrison*, Curr. Top. Radiat. Res. *4*, 43 (1968); b) *R. Braams*, Radiat. Res. *27*, 319 (1966) and [20], p. 171; c) *P. Neta* and *R. W. Fessenden*, J. Phys. Chem., *74*, 2263 (1970).

substituents or the sulfur atom. *Fessenden* and *Neta* [110c] have shown that protonated amino groups are readily deaminated by hydrated electrons.

$$^{+}NH_3-CH_2-CO_2^- + e_{aq}^- \rightarrow NH_3 + {}^{\cdot}CH_2-CO_2^- \quad (25)$$

The resulting carboxylatoalkyl radicals have been detected with the aid of ESR spectroscopy [110c].

Peptides react with electrons faster than their constituent amino acids. On the other hand, the rate of the reactions between electrons and proteins is determined by the partial reactivities of their various components [110b]. All these examples clearly show that several reactive centers in the molecules must be considered for the attack by hydrated electrons. The purine and pyrimidine bases involved in nucleic acids are highly reactive with respect to hydrated electrons. The pH-dependence of the reactivity of pyrimidines (Table 5) points to a preferential addition of electrons to the carbonyl group (keto-enol tautomerism). It is not yet clear whether the absorption spectra observed in pulse-radiolytic investigations are to be attributed to radical anions of substituted pyrimidines or to the protonated products of these [109c]. Probably the C=N and the C=O groups are responsible for the preferential electron addition in purines.

4.1.3. Reactions between Solvated Electrons and Inorganic Compounds

Investigations of the reactivity of hydrated electrons toward a few hundred inorganic compounds have revealed a great variety in this respect, the rate constant varying from $k > 10^{10}$ l mole^{-1} s^{-1} for diffusion-controlled cases to $k_{11} = 16$ l mole^{-1} s^{-1} for the "slow" reaction with water. It has not yet been possible to classify these reactions as systematically as in the case of organic reactants. The product formed by electron transfer (2) is often thermodynamically unstable and reacts further, by protonation, dissociation, disproportionation, or charge transfer.

Neutral Molecules (Table 6)

The reactions with oxygen (12), CO_2 (13), and I_2 (26) [112] lead to the relatively stable electron addition products O_2^-, CO_2^-, and I_2^-. The absorption spectra and the chemical properties of these radical anions have been studied.

$$e_{aq}^- + I_2 \rightarrow I_2^-; \quad k_{26} = 5.1 \times 10^{10} \text{ l mole}^{-1} \text{ s}^{-1} \quad (26)$$

The reaction between electrons and hydrogen sulfide (27) leads to SH^- and S^- in a ratio of 1.9:1 *via* an intermediate that has not yet been intercepted [113].

$$e_{aq}^- + H_2S \rightarrow (H_2S)^- \begin{cases} \rightarrow SH^- + H \\ \rightarrow S^- + H_2 \end{cases} ; k_{27} = 1.35 \times 10^{10} \text{ l mole}^{-1} \text{ s}^{-1} \quad (27)$$

The high electron affinity of sulfur hexafluoride, which is otherwise chemically stable, has recently been utilized to capture electrons in solutions, as has been done with N_2O (28) [39].

$$e_{aq}^- + SF_6 \rightarrow SF_6^-; \quad k_{28} = 1.65 \times 10^{10} \text{ l mole}^{-1} \text{ s}^{-1} \quad (28)$$

The radical anion SF_6^- decomposes into SO_4^{2-}, H_3O^+, and F^- anions *via* a number of oxidizing intermediates. A value of $G_{e_{aq}^-} = 2.76$ has been obtained for reaction (28) by the determination of the fluoride formed [39].

Ions (Table 6)

Hydrated electrons react relatively slowly ($k \leqslant 10^7$ l mole^{-1} s^{-1}) or not at all with anions having a noble gas configuration (F^-, Cl^-, Br^-, I^-, CN^-, CNO^-, N_3^-, and OH^-), and with the oxygen-containing anions of nonmetallic elements in their highest oxidation state ($B_4O_7^{2-}$, CO_3^{2-}, HCO_3^-, ClO_4^-, PO_4^{3-}, HPO_4^{2-}, and SO_4^{2-}). Alkali metal phosphates and borates can be used as buffer additives to adjust the pH, owing to their lack of reactivity toward hydrated electrons. By contrast, the strongly oxidizing oxygen-containing anions of metals (MnO_4^- and CrO_4^{2-}) are very reactive. The anions NO_2^- and NO_3^- and the oxygen-containing anions of halogens also give fast and practically diffusion-controlled reactions with hydrated electrons. However, little is known as yet of the properties of the products formed in these reactions.

Hydrated electrons do not react with alkali metal and alkaline earth metal cations, but – as expected on the basis of their negative reduction potential (Table 3) – they do react with a number of metal ions that can be reduced by one valence state according to reaction (2) [114]. Some cations are thus reduced to the metallic state ($Ag^+ \rightarrow Ag^\circ$ [114]; $Au^+ \rightarrow Au^\circ$ [115]), while others are reduced to unstable oxidation states. Thus radiolytic reduction of the divalent cations of Cr, Mn, Fe, Co, Ni, Cu, Zn, and Cd yields the corresponding monovalent cations with a very short lifetime [114]. The monovalent cations of Mn, Co, Ni, Zn, and Cd give an absorption maximum at 310 nm, indicating that these cations are loose electron addition products (*e.g.* $Mn^{2+} \cdot e_{aq}^-$) [114].

There is a connection between the redox potential of trivalent lanthanide cations and their reactivities toward hydrated electrons [112]; Eu^{3+}, Yb^{3+}, Sm^{3+}, and – to a smaller extent – Tm^{3+} give stable divalent cations, and their reduction by hydrated electrons is faster by one order of magnitude than the corresponding reduction of the other lanthanide ions. Pr^{3+}, Tb^{3+}, and Dy^{3+}, which are relatively easily oxidized, react with

[111] *M. Anbar*, Quart. Rev. (London) *22*, 578 (1968).

[112] *J. K. Thomas*, *S. Gordon*, and *E. J. Hart*, J. Phys. Chem. *68*, 1524 (1964).

[113] *G. Meissner* and *A. Henglein*, Ber. Bunsenges. Phys. Chem. *69*, 3 (1965).

[114] *J. H. Baxendale*, *E. M. Fielden*, and *J. P. Keene*, Proc. Roy. Soc. (London) *A 286*, 320 (1965).

[115] *A. S. Ghosh-Mazumdar* and *E. J. Hart* [12], p. 193.

hydrated electrons particularly slowly. Since the 4f orbital in La^{3+}, Gd^{3+}, and Lu^{3+} is not half- or fully occupied, these cations have a relatively stable electron configuration, and therefore show a low electron affinity [112].

Rates of Reactions between Hydrated Electrons and Metal Complexes

Many inorganic compounds are reduced by electrons in a practically diffusion-controlled reaction [111]. This holds particularly for some metal complexes [107], in the case of which the ability of the ligand to transfer electrons to the central atom follows the order $OH^- < CN^- < NH_3 < H_2O < F^- < Cl^- < I^-$ (Table 6). The electron density distribution at the central atom is so modified by some ligands that orbitals accessible to electrons appear. An attempt has recently been made [107] to compare the experimental results with the values calculated from the Debye equation (29) for diffusion-controlled ionic reactions [84].

$$k_{diff} = \frac{4\pi N_A (D_{e^-_{aq}} + D_X)(r_{e^-_{aq}} + r_X) Q}{e^Q - 1} \qquad (29)$$

$$Q = \frac{-Z_X e^2}{\varepsilon kT (r_{e^-_{aq}} + r_X)}$$

The rate constant k_{diff} is expressed here in terms of the summed diffusion coefficients of the ions ($D_{e^-_{aq}} + D_X$), the summed effective ionic radii ($r_{e^-_{aq}} + r_X$), and the product of the ionic charges (Z_X and e^-). (ε is the dielectric constant, N is Avogadro's number, k is Boltzmann's constant, and T is the absolute temperature.)

The experimental rate constants and the values calculated from eq. (29) agree well for a series of complexes of divalent and trivalent cobalt and chromium [107]. The calculations were carried out with the $D_{e^-_{aq}}$ values [61] found from independent measurements, and with the effective ionic radius ($r_{e^-_{aq}}$) [23] of the hydrated electrons (Table 1). In a series of metal complexes, the reaction rates were faster (for $[CoO(CN)_5]_2^{5-}$, FeF_6^{3-}, and $Cr(CN)_6^{3-}$) or slower (for $[CoO(NH_3)_5]_2^{5+}$) than the corresponding calculated value. It must be assumed in these cases that not all the gegenions of the complex salts are dissociated, and therefore a smaller or a greater effective total charge must be taken for the complex.

4.2. Activation Energy and the Mechanism of Electron Transfer

The activation energy E_a involved in the reactions with hydrated electrons has been determined pulse-radiolytically [116] and by the method of competition kinetics [117]; it has been found to be 3.5 ± 0.4 kcal/mole for about 20 reactions differing in their reduction rate constants by 10^4. This suggests that the observed activation energy must be ascribed to the diffusion of the hydrated electrons, which is feasible in view of the energy needed for the dipole orientation of water (4 kcal/mole) [117].

The first product formed in the electron transfer is not yet known, but it is assumed to be the radical anion in an excited vibrational or electronic state, whose transition into a stable state is associated with a gain in free energy. There is yet no experimental proof to support the concept that this energy gain and the energy requirement for the orientation of the donor and the acceptor species into the electron transfer complex [*] (Frank-Condon condition) are a measure of the probability of a reaction [117].

4.3. Reactions of Electrons in Glasses Formed from Polar and Nonpolar Solutions [21, 119–123]

Optically transparent glasses are obtained by the rapid cooling of highly concentrated aqueous solutions, alcohols, and some hydrocarbons. The solutes are assumed to be uniformly distributed in the resulting glasses (except for polar and readily associating molecules in nonpolar hydrocarbons [51]). The reactions of electrons in these glasses can be described as follows. The localization of thermalized electrons e^-_m in electron traps T according to reaction (30) competes with the reactions with acceptors (1–3).

$$e^-_m + T \rightarrow e^-_t \qquad (30)$$

Thermally or photochemically delocalized electrons can react similarly

$$e^-_t \xrightarrow{\Delta, h\nu} e^-_m + T \qquad (31)$$

Apart from a few cases where resonance stabilization must be assumed, the radical anion intermediate A^- formed in (1) is not stable in protonic glasses, on account of the rapid protonation (23) that proceeds even at low temperatures. The secondary radicals R· can be detected in reactions (3) between electrons and halogen-substituted organic substances. It is characteristic of these reactions in glasses that the intensity of the optical absorption spectra and the ESR spectra of stabilized electrons decreases with increasing concentration of added electron acceptors (10^{-3} to 10^{-1}

[116] *B. Cercek* and *M. Ebert*, J. Phys. Chem. *72*, 766 (1968).

[117] *M. Anbar*, *Z. B. Alfassi*, and *H. Bregman-Reisler*, J. Am. Chem. Soc. *89*, 1263 (1967).

[*] The reactions of hydrated electrons differ from the classical electron transfer between a donor and an acceptor in two points:

1) the electron wave-function, which extends over several molecules and even outside the solvation shell, is very sensitive to changes in the orientations in the liquid; and

2) the number of reactants is decreased by one when the hydrated electron is captured by the acceptor [118].

[118] *R. A. Marcus* [11], p. 138.

[119] *L. Kevan* [109c], p. 21.

[120] *L. Kevan*, Actions Chim. Biol. Radiations *13*, 56 (1969).

[121] *B. G. Ershov* and *A. K. Pikaev* [12], p. 1.

[122] *D. M. Brown* and *F. S. Dainton*, Radiat. Res. Rev. *1*, 241 (1968).

[123] *D. Schulte-Frohlinde* and *K. Vacek*, Curr. Top. Radiat. Res. *5*, 39 (1969).

mole/l), and that the absorption and the ESR spectra contain new bands, attributable to the radicals A^-, AH, or $M^{(n-1)+}$. The course of the competing reactions (1)–(3) and (30)–(31) is determined by the range of the thermalized electrons in the medium and by the electron affinities of the acceptors A, M^{n+}, and RX. The concentration which decreases the yield of stabilized electrons to one half can be taken as a measure of the relative reactivity of electron acceptors. In glassy NaOH this concentration is 10^{-1} and 10^{-2} mole/l for chloroacetic acid [124] and for sodium nitrate [119], respectively.

4.3.1. Pure Ice and Neutral Aqueous Glasses

In comparison with the yield of OH radicals (G_{OH} = 0.8 [126]), the yield of detectable electrons in crystalline ice [42, 125] at −196 °C is very low ($G_{e_s^-} = 5\times10^{-4}$). Pulse-radiolytic measurements on ice [29, 127, 128] between −2 and −160 °C have shown that, as the temperature decreases, the yield of optically detectable electrons decreases (from $G_{e_s^-}$ 0.5 at −5 °C to 10^{-3} at −160 °C), and the lifetime increases by several orders of magnitude ($t_{1/2}$ is 2×10^{-5} s at −5 °C and 10^{-1} s at −130 °C) [29].

The disappearance of the light absorption is a kinetically complex process due probably to the inhomogeneous distribution of electrons in the crystal. The decrease in the electron yield with a decrease in the temperature is explained by the combination of charge carriers according to (32) or (33) [29].

$$e_m^- + H_3O^+ \rightarrow H + H_2O \quad (32)$$

$$e_m^- + H_2O^+ \rightarrow H_2O \quad (33)$$

Owing to the high mobility of the excess protons formed in ice [*] in accordance with reaction (34), and the low concentration of suitable electron traps T, reaction (32) is so much preferred that most of the thermalized electrons react before they are stabilized [29].

$$H_2O^+ + H_2O \xrightarrow{\approx 10^{-14}\,s} H_3O^+ + OH \quad (34)$$

Doping of ice crystals with H_2F_2, which increases the H_3O^+ concentration, leads to a further decrease in the electron yield [127].

Unlike the ice crystals, to which electrons impart only a pale blue color [42], the condensates of water irradiated in the vapor phase [43] show a deep blue color and strong ESR singlet signals. The electrons produced can presumably influence the orientation of the water molecules into the ice structure during condensation, for no electrons can be stabilized on subsequent irradiation of condensates produced from pure water vapor. The addition of electron scavengers $C(NO_2)_4$ and $(CD_3)_2SO$ to the gaseous mixture attenuates the blue color of the condensates, while the ESR spectra point to the formation of the radicals NO_2 and CH_3 [43].

The above-mentioned influence of the structure is particularly conspicuous in the glasses formed from highly concentrated salt solutions (> 5 mole/l), in which electrons can be stabilized in differing yields [119] ($G_{e_t^-}$ is 0.5, 0.6, and 2.0 for $NaClO_4$, LiCl, and K_2CO_3 respectively). Aqueous solutions of glycerol, ethylene glycol, and some hydrocarbons also form glasses in which electrons can be stabilized by irradiation [119, 120]. The absorption maximum exhibits a blue shift with respect to that of pure ice, indicating that the distribution of the electron traps is influenced by solvated ions.

4.3.2. Acid Glasses [122, 123]

Rapid cooling of aqueous solutions of phosphoric acid, sulfuric acid, perchloric acid, and sodium hydrogen sulfate (in a concentration of more than 5 mole/l) leads to the formation of glasses. Although the ESR spectroscopic examination of these "acid glasses" after irradiation at −196 °C reveals not electrons but hydrogen atoms [129], electrons should be regarded as the precursors of these hydrogen atoms in accordance with reaction (32). A direct proof is afforded by the formation of reduced metal cations, which occurs by reaction (3) when *e.g.* Mn^{2+}, Co^{2+}, or Cd^{2+} is added. This process is accompanied by a drop in the yield of hydrogen atoms [25].

4.3.3. Alkali Metal Hydroxide Glasses

Much work has been done on stabilized electrons in glasses formed by freezing of alkali hydroxide solutions with a concentration of over 5 mole/l [26, 119]. According to the absorption spectra and the ESR signals (Table 2), the alkali metal exerts no particular effect, but the solvent does, and this excludes the possibility that the electrons are stabilized in the immediate vicinity of the alkali metal cations [9]. The yield of stabilized electrons depends on the alkali concentration, and is $G_{e_t^-} = 2.0 \pm 0.2$ for a glass obtained from 10 N NaOH [26, 119]. By capturing the electrons with a nitrate, *Ershov* and *Pikaev* [121] have found $G_{e_t^-} = 3.0$. The acceptor-free glass evidently stabilized only two-thirds of the thermalized electrons according to reaction (30).

Kevan et al. [130a] have measured a photoelectric current in the bleaching of stabilized electrons, and have thus demonstrated that the optical transition from the

[124] *D. Schulte-Frohlinde* and *K. Eiben*, Atomstrahlung Med. Tech. *1964*, 265; *K. Eiben*, Kernforschungszentrum Karlsruhe *293* (1965).

[125] *O. F. Khoshaev, B. G. Ershov*, and *A. K. Pikaev*, Isv. Akad. Nauk SSSR, Ser. Khim *7*, 246 (1968).

[126] *F. E. Gunter*, J. Chem. Phys. *46*, 3818 (1967).

[127] *G. Nilsson, H. C. Christensen, F. Fenger, P. Pagsberg*, and *S. O. Nielson* [12], p. 71.

[128] *V. N. Shubin, V. A. Zhigunov, V. J. Zolotarevsky*, and *V. J. Dolin*, Nature *212*, 1002 (1966).

[*] On the other hand, we can neglect the low concentration of protons formed in ice by the dissociation of water.

[129] *R. Livingstone, J. Zeldes*, and *E. H. Taylor*, Discussions Faraday Soc. *19*, 166 (1955).

[130] a) *I. Eisele, R. Lapple*, and *L. Kevan*, J. Am. Chem. Soc *91*, 6504 (1969); b) *J. Zimbrick* and *L. Kevan*, *ibid. 89*, 2483 (1967); c) *L. Kevan, D. R. Renneke*, and *R. J. Friauf*, Solid State Commun. *6*, 469 (1968).

ground state is to a nonbonding conduction-band-like state.

According to recent work, dielectrons can be stabilized in alkali metal hydroxide glasses, similarly to the F'-centers in ionic crystals [130b]. These dielectrons arise in the photochemical bleaching of the blue color, or in irradiation with very high doses (> 10 Mrad), when the electrons e_m^- react with stabilized electrons as shown below:

$$e_m^- + e_t^- \rightarrow e_t^{2-} \xrightarrow{h\nu'} e_m^- + e_t^- \qquad (35)$$

Dielectrons, which are characterized by spin coupling, diamagnetism, and a broad absorption band ($\lambda_{max} \approx 900$ nm), can dissociate into singly occupied centers on annealing or photo-bleaching in the IR region [second step of reaction (35)] [130c].

Among the electron acceptors dissolved in alkali glasses [119], chloroacetic acid and chloroform react in accordance with (3) to yield chloride ions. Acetone [25], acrylamide [131], and aromatic carboxylic acids [135] form radical anions A^-, which are identified by their absorption spectra and sometimes also by their ESR spectra. The transfer of the photochemically remobilized electrons (31) onto aromatic carboxylic acids in accordance with reaction (1) is reversible. When the sample is exposed to monochromatic light, the absorption band of the radical-anion formed decreases, and the absorption band of the stabilized electrons increases [135].

4.3.4. Organic Glasses [21, 71]

The transfer of electrons induced by ionizing radiation has been studied in glasses formed from alcohols, methyltetrahydrofuran, or simple hydrocarbons, the electron acceptors being olefins, aliphatic and aromatic ketones, alkyl-substituted and vinyl-substituted aromatic compounds, aryl halides [71a], alkyl halides [71], and sulfur compounds [132]. In methyltetrahydrofuran and hydrocarbons such as pentane and 3-methylpentane, electron transfer (1) yields stabilized radical-anions, which can be detected optically and by ESR spectroscopy [71]. They are identical with the radical anions formed in ammoniacal and ethereal solutions of sodium [133].

Only the radical-anions of biphenyl [71] and of some aromatic carboxylic acids [135] have been identified in alcohol glasses. The electron adducts of benzene and naphthalene rapidly react further with the solvent (23) or with alkoxonium ions (24) [134].

Like the excess protons in water and ice [reaction (33)], the alkoxonium ions are produced in the transfer of protons to the alcohol cations *(8)*.

$$\begin{aligned} &R{-}CH_2{-}OH^+ + R{-}CH_2{-}OH \rightarrow \\ &\qquad R{-}CH_2{-}OH^+ + R{-}CH_2{-}O^\bullet \\ &R{-}CH_2{-}OH^+ + R{-}CH_2{-}OH \rightarrow \\ &\qquad R{-}CH_2{-}OH^+ + R{-}\dot{C}H{-}OH \end{aligned} \qquad (36)$$

They represent the gegenions to the solvated electrons, and are presumably also mobile in alcohol glasses, on account of proton migration.

Thermal and photochemical generation of electrons give different reactions in irradiated alcohol glasses [120]. Electrons remobilized by warming undergo reaction (24) [*] with alkoxonium ions, and can also be scavenged by the electron acceptors according to reactions (1)–(3). In the case of photochemically delocalized electrons, on the other hand, these reactions have not been observed; instead, the pseudo-first order photochemical reaction (37) leads quantitatively to hydroxyalkyl radicals with a quantum yield of 0.06.

$$e_t^- + CH_3OH_2^+ \xrightarrow[(\lambda = 540\ nm)]{h\nu} {}^\bullet CH_2OH + H_2 \qquad (37)$$

The formation of dielectrons, involved in reaction (35), has not been observed in alcohol glasses.

The author wishes to thank Prof. Dr. D. Schulte-Frohlinde, Prof. Dr. U. Schindewolf, and Dr. K. W. Böddeker for stimulating and valuable discussions.

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Translated by Express Translation Service, London

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[135] *H. Wieczorek* and *K. Eiben*, to be published.

[*] The hydrogen atoms formed in reaction (24) react at low temperatures *via* dimerization but not *via* hydrogen abstraction from the alcohol.

$Ru_3(CO)_9H(C_6H_5CC_6H_4)$: A μ-Hydridocarbonyl Metal Cluster Derivative of Diphenylcarbene[1]

By *A. W. Parkins, E. O. Fischer, Gottfried Huttner*, and *Dieter Regler*[*]

During our studies on the formation of carbene complexes of trinuclear metal carbonyl complexes we treated dodecacarbonyl-*triangulo*-triruthenium with one equivalent of phenyllithium in tetrahydrofuran at low temperatures. Chromatography of the products gave a very low yield of red crystals, m.p. 139–142 °C, total analysis of which gave the composition $Ru_3C_{22}H_{10}O_9$:

$$Ru_3(CO)_{12} \xrightarrow[2.\ H_3PO_4/CH_3OH]{1.\ LiC_6H_5/THF} Ru_3C_{22}H_{10}O_9$$

In accord with this composition the mass spectrum (50 eV; Atlas CH4) showed a peak for the molecular ion at $m/e = 730$ (referred to ^{104}Ru)[2]. The osmometric molecular weight in benzene was determined as 726. The mass-spectral fragmentation of the compound indicated the presence of nine CO ligands, which appeared in the IR spectrum (cyclohexane solution) as seven ν_{CO} absorptions — at 2097 m, 2071 s, 2041 vs, 2032 vs, 2018 s, 2006 s, and 1990 m cm^{-1}, which indicated terminal positions for these ligands; further, for KBr disks there were four strong C—C deformation vibrations of aromatic rings — at 767, 757, 723, and 703 cm^{-1}, which could indicate the presence of two differently bound phenyl groups. The ^1H-NMR spectrum (CS_2 solution) showed a strongly split group of signals for phenyl protons at $\tau = 2.5$–3.0 and a very sharp signal at $\tau = 30.2$ with relative intensities $\approx 10 : 1$, which, together with the diamagnetism of the compound, indicated a bridging H atom bound to metal.

These findings do not suffice to prove a structure, which was finally established (see Figure) by X-ray analysis.

The compound crystallizes in the triclinic system, space group $P\bar{1}$ with cell constants: $a = 9.38 \pm 0.01$, $b = 13.51 \pm 0.02$, $c = 9.75 \pm 0.01$ Å, $\alpha = 95.50 \pm 0.08$, $\beta = 90.02 \pm 0.08$, $\gamma = 110.70 \pm 0.06°$, $V = 1150 \pm 6$ Å^3, $d_{calc} = 2.08 \pm 0.01$, $d_{obs} = 2.06 \pm 0.02$ g · cm^{-3}, $Z = 2$.

4962 independent non-zero diffraction intensities in the range $0 < \sin\theta/\lambda \leq 0.845$ were collected for two crystals on a Weissenberg diffractometer (manufactured by Stoè) using $Mo_{K\alpha}$ radiation ($\lambda Mo_{K\alpha} = 0.71069$ Å). The structure was solved by Patterson, Fourier, and least-squares methods, the present value of R_1 being 0.071[3].

The ruthenium atoms form a three-membered ring. The bond distances Ru¹—Ru² and Ru²—Ru³ are equal within experimental error and appreciably shorter than the distance between Ru¹ and Ru³ which are joined by a H bridge (Table, Fig.). Three carbonyl groups are bonded to each ruthenium atom, two of which are approximately equatorial with respect to the plane formed by the metal atoms. The three remaining carbonyls occupy approximately axial positions on one side of the Ru ring.

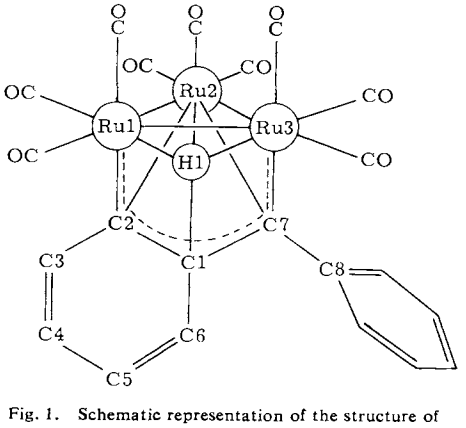


Fig. 1. Schematic representation of the structure of $Ru_3(CO)_9H(C_6H_5CC_6H_4)$.

Bond distances (in Å).

Ru¹—Ru²	2.776 ± 0.004	C¹—C²	1.46 ± 0.01
Ru¹—Ru³	2.914 ± 0.004	C²—C³	1.42 ± 0.01
Ru²—Ru³	2.773 ± 0.004	C³—C⁴	1.36 ± 0.02
Ru¹—C²	2.10 ± 0.01	C⁴—C⁵	1.42 ± 0.01
Ru³—C⁷	2.08 ± 0.01	C⁵—C⁶	1.36 ± 0.02
Ru²—C¹	2.36 ± 0.01	C⁶—C¹	1.43 ± 0.01
Ru²—C²	2.32 ± 0.01	C¹—C⁷	1.43 ± 0.01
Ru²—C⁷	2.26 ± 0.01		

The other side of the three-membered metal ring is occupied by the organic ligand system. This system can be derived formally from diphenylcarbene; it is, however, coordinated to all three metal atoms of the cluster in a quite unusual way. The average length of the bonds Ru¹—C² and Ru³—C⁷ (2.09 ± 0.01 Å) is only 0.18 Å greater than the mean Ru—C_{CO} bond length (1.91 ± 0.01 Å), so the former appear to have marked double-bond character. A double-bond contribution to these bonds is in line with the coplanarity of the atoms Ru¹, Ru³, C¹···⁶, and C⁷ which provide the skeleton of an extended mesomeric heterocyclic system that is stabilized by the π-bonding of the allyl fragment C²—C¹—C⁷ to Ru². The C—C bonds of the phenyl ring C¹···⁶ that is involved in the mesomeric system show clear alternation in length in accordance with the valence scheme illustrated in the Figure (cf. Table). The carbon atom C⁸ of the second phenyl group is in the plane of the heterocyclic system, but the ring itself does not take part in complex formation and lies perpendicular to that plane.

Experimental

LiC_6H_5 (0.85 mmole) is added rapidly to a suspension of $Ru_3(CO)_{12}$ (500 mg, 0.78 mmole) in tetrahydrofuran (100 ml) at −30 °C. The deep red mixture is evaporated to dryness in a vacuum at −30 °C and the red residue is taken up in 20% aqueous methanol precooled to −30 °C. The resulting red solution is acidified with 85% H_3PO_4 (0.75 ml) and at once extracted with pentane at −30 °C. This extract is dried over Na_2SO_4, filtered, and concentrated to 20 ml. The product is chromatographed at 10 °C on a silica gel (Merck) column (2 × 55 cm) prepared in pentane. Elution with 2.5–5% benzene/pentane gives unchanged $Ru_3(CO)_{12}$; then elution with 7.5–10% benzene/pentane gives a yellow oil that has not yet been examined; a third fraction, obtained by using 12.5–15% benzene/pentane, contains the new complex. The third fractions of four batches are collected and chromatographed once again by the same procedure. On recrystallization from pentane we obtained the product in 1% yield (25 mg).

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[1] Transition-metal-Carbene Complexes. Part 24. – Part 23: *E. O. Fischer, H. J. Kollmeier, C. G. Kreiter, J. Müller*, and *R. D. Fischer*, J. organometallic Chem. *22*, C 39 (1970).

[2] Measurements by Dr. *J. Müller*, München.

[3] We thank the Leibniz-Rechenzentrum of the Bayerische Akademie der Wissenschaften for computing time, and the Deutsche Forschungsgemeinschaft and the Royal Society, London (*A. W. P.*) for support of this investigation.

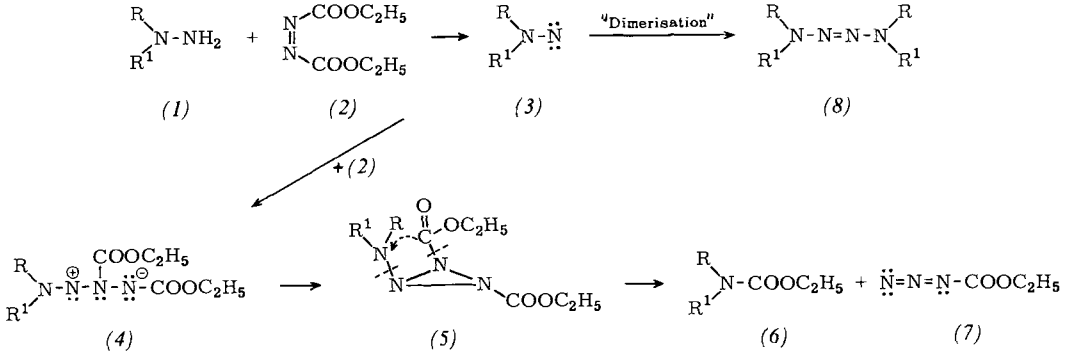
Aminoazimines by Addition of Aminonitrenes to α-Carbonylazo Compounds[1,2]

By *Karl-Heinz Koch* and *Egon Fahr* [*]

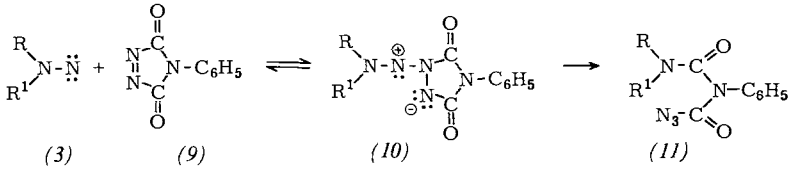
Reaction of the unsymmetrically substituted hydrazines *(1a)* to *(1c)* [3] with diethyl azodicarboxylate *(2)* leads to the formation of the aminonitrenes *(3)* and hydrazodicarboxylate. The aminonitrenes *(3)* add a second molecule of *(2)* to give the aminoazimines *(4)* [4], which then decompose — presumably *via* compound *(5)* — into the urethanes *(6)* and ethyl azidoformate *(7)*. The intermediary formation of the aminonitrenes *(3)* is supported by the following findings:

a) In the reaction, as in other reactions of aminonitrenes [5], some tetrazene *(8)* is formed.

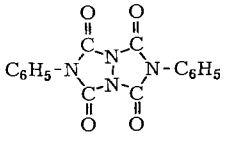
b) When compound *(1) is added to (2)*, the aminonitrene *(3)* is intercepted by *(2)* with formation of much *(6)* and *(7)*, the yield of tetrazene *(8)* being low [*(1a)*:*(6a)* 80 %, *(7)* 80 %, *(8a)* 5 %; *(1b)*: *(6b)* 70 %, *(7)* 70 %, *(8b)* < 2 %; *(1c)*: *(6c)* 75 %, *(7)* 80 %, *(8c)* < 2 % [6]]. If, however, *(2) is added to (1)* under the same conditions then the yield of tetrazene increases considerably and the yields of *(6)* and *(7)* are lower [*(1a)*: *(6a)* 30 %, *(7)* 30 %, *(8a)* 20 %; *(1c)*: *(6c)* 30 %, *(7)* 30 %, *(8c)* 50 % [6]].



(1) *(2)* *(3)* *(8)* *(4)* *(5)* *(6)* *(7)*



(3) *(9)* *(10)* *(11)*



(12)

(a), R = R¹ = CH_3
(b), R = R¹ = C_2H_5
(c), R-R¹ = $(CH_2)_5$
(d), R = R¹ = C_6H_5-CH_2
(e), R = R¹ = C_6H_5
(f), R = CH_3, R¹ = C_6H_5

(10)	Yield (%)	M.p. (°C) [a]	λ_{max} (nm) [b]	E_{mol} [b]
(a)	60	133—134	387	14450
(b)	66	123—124	388	11700
(c)	54	131—133	387	11900
(d)	44	144—145	389	13200
(e)	86	140—141	435	18600

[a] The substances melt with decomposition.
[b] Region 380—450 nm. toluene.

If the cyclic α-carbonylazo compound *(9)* is used instead of *(2)*, the reaction sequence *(4)* → *(5)* → *(6)*/*(7)* is so hindered by the rigidity of the C=O group in *(9)* that the aminoazimines can be isolated. Their structure is based, in addition to elemental analysis and molecular weight determination, on the following findings:

a) Their absorption maximum between 387 and 435 nm (see Table) excludes unequivocally a triaziridine structure [corresponding to the formulation *(5)*].

b) On reduction with dithionite four H atomes are taken up per molecule with formation of *(1)* and phenylurazole.

c) On warming in an apolar solvent, cleavage into the azo compound *(9)* [identified as the thermal decomposition product *(12)* [7]] and the aminonitrene *(3)* [trapped with *(2)* as *(6)*/*(7)*] takes place alongside the rearrangement to *(11)*.

d) The "element list" [carried out for *(10a)* [8]] determined for the molecular ion and 12 fragments by mass spectrometry also proves the suggested formulation.

e) The aminoazimines *(10)*, like triazenes [9], exhibit a hindered rotation of the R_2N grouping that can be studied by NMR spectroscopy; *e.g. (10d)*: $\Delta G_c^{\ddagger} \approx 14.5$ kcal/mole, $T_c \approx 25\,^{\circ}C$ [10].

f) Gentle warming in ethanol results in rearrangement to *(11)*, which corresponds to the formation of *(6)*/*(7)* from *(2)* and *(1)* [*(11a)*: m.p. 58—60 °C, yield 40 %].

General preparation of aminoazimines (10)

A solution of compound *(9)* (10 mmoles) in anhydrous toluene (250 ml) is added at room temperature to a solution of *(1)* (5 mmoles) in anhydrous toluene (20 ml) and the mixture is allowed to stand for 12 hours. The phenylurazole formed is then removed from the reaction mixture by suction and the filtrate, in the case of *(10b)*—*(10d)*, is concentrated to 10—15 ml; in the case of *(10a)* and of *(10e)* the filtrate is evaporated to dryness. The aminoazimines are precipitated from the filtrates of *(10b)*—*(10d)* when the latter are allowed to stand with ice-cooling. *(10a)*, *(10d)*, and *(10e)* can be recrystallized from alcohol-free glacial acetic acid, and *(10b)* and *(10c)* from toluene (take care: tendency to decompose).

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[1] α-Carbonylazo Compounds, Part 5. Part 4: *J. Markert* and *E. Fahr*, Tetrahedron Letters *1970*, 769.

[2] Part of dissertation by *K. H. Koch*, Universität Würzburg 1969.

[3] The reactions of *(1a)–(1f)* with *(2)* are complex. Here, tetrazene formation and decomposition of *(3)* with evolution of N_2-accompany the aminonitrene addition to *(2)*.

[4] The name "azimines" for the system isomeric to the triaziridine ring was suggested by *R. Huisgen*, Angew. Chem. *75*, 604 (1963); Angew. Chem. internat. Edit. *2*, 565 (1963).

[5] See *e.g. C. G. Overberger* and *L. P. Herin*, J. org. Chemistry *27*, 417 (1962).

[6] The yields for the reaction of *(1)* with *(2)* (molar ratio 1:2) at room temperature in CCl_4 were given. Since the yields [*(6)* and *(8)* determined by gas chromatography, *(7)* by IR spectroscopy] depend on the absolute concentrations and on the rate of mixing of the reactants they have been rounded off.

[7] For the structure see *T. J. Kealy*, J. Amer. chem. Soc. *84*, 966 (1962).

[8] Drawn up by Dr. *K. Habfast* by computerized evaluation of the mass spectrum (Equipment: SM 1-B by Varian MAT) (deviation between measured and calculated masses, 0.1 to 1.7×10^{-3} mass units).

[9] *N. P. Marullo, C. B. Mayfield*, and *E. H. Wagener*, J. Amer. chem. Soc. *90*, 510 (1968).

[10] In dimethylformamide. An accurate determination is difficult because of the tendency to decompose. The measurments were carried out in collaboration with Doz. Dr. *A. Mannschreck*, Heidelberg.

An Investigation of the Nitrile Oxide-Isocyanate Rearrangement[1] [**]

By *Christoph Grundmann* and *Peter Kochs* [*]

The thermal isomerization of nitrile oxides to isocyanates has been known for more than sixty years [1a].

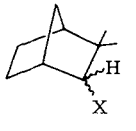
$$R-C\equiv\overset{\oplus}{N}-O^{\ominus} \rightarrow R-N=C=O$$

A recent INDO-calculation of the fulminate-cyanate rearrangement [2] indicates an oxazirinyl anion as cyclic transition state (or intermediate).

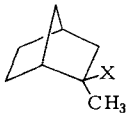
If the nitrile oxide-isocyanate rearrangement proceeds *via* separated ions, and if R in R—CNO is a group of demonstrated propensity toward carbon skeleton rearrangement

$$R-C\equiv\overset{\oplus}{N}-\overset{\ominus}{O} \rightarrow R^{\oplus} + C\equiv\overset{\ominus}{\underset{}{O}}\!\!\rightarrow N \rightarrow R-N=C=O$$

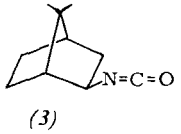
under conditions in which cationic carbon is thought to be involved, then the ionic mechanism should lead to carbon skeleton rearrangement. Such systems R are, *e.g.*, the camphenilyl group *(1)* and the *endo*-2-methyl-2-norbornyl group

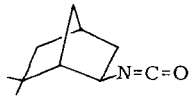


(1a), X = CH=N⁓OH
(1b), X = CNO
(1c), X = N=C=O

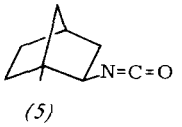


(2a), X = CH=N⁓OH
(2b), X = CNO
(2c), X = N=C=O
(2d), X = CO_2H

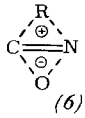


(3) + 

(4)



(5)



(6)

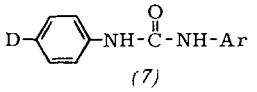
(2), which were chosen since the precursors for the required nitrile oxides were easily accessible.

The dehydrogenation of a mixture of *endo-* and *exo-(1a)* [3,4] yielded the unstable nitrile oxide *(1b)* which partly rearranged to the isocyanate *(1c)* on being heated to 110 °C in xylene solution, while most of the material dimerized to the corresponding furoxane.

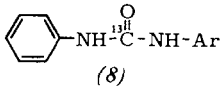
The isocyanate, isolated as the symmetrical urea derivative, showed a mass-spectrographic disintegration pattern compatible only with the unrearranged carbon skeleton structure *(1c)*; structures *(3)* and *(4)* are definitely ruled out [5]. Furthermore, we were not able to detect a rearrangement of *endo-(1b)* to *exo-(1b)*.

We investigated then the nitrile oxide *(2b)*, easily available from *(2a)* [6], and also found no products derived from a Wagner-Meerwein rearrangement, *e.g. (5)*, such as are formed in carbonium ion reactions [7]. The isocyanate *(2c)* was also synthesized independently by Curtius degradation of the known acid *(2d)* [8], and found identical with that obtained from the nitrile oxide. Both compounds were compared as the corresponding symmetrical urea derivatives.

To support the evidence for an intramolecular, rather than an intermolecular, mechanism we rearranged *p*-deuteriobenzonitrile oxide in the presence of [α-^{13}C]benzonitrile oxide. These compounds should rearrange at approximately the same rate, so that, if the reaction were to any extent intermolecular, the product should contain some *p*-deuterio-[α-^{13}C]phenyl isocyanate. We isolated the phenyl isocyanate as the unsymmetrical urea by reaction with *o*-toluidine. Only the singly labeled products *(7)* and *(8)* could be detected by mass spectrometry [9].



(7)



(8)

Ar = *o*-CH_3-C_6H_4

This intramolecular rearrangement [10], in which bond breaking and bond making are essentially synchronous, can be visualized as proceeding *via* an activated transition complex *(6)*. A consequence of such a mechanism is that the group R migrating from carbon to nitrogen should do so with retention of configuration when the point of attachment is a center of optical asymmetry.

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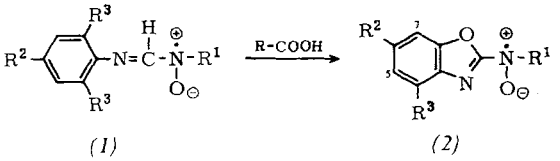
An Unusual Reaction of Azomethine Nitroxide Radicals with Carboxylic Acids[**]

By *Hans Günter Aurich* and *Klaus Kabs*[*]

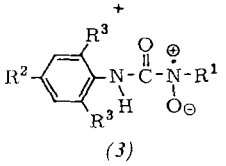
Dedicated to Professor K. Dimroth on the occasion of his 60th birthday

We have found that *N*-alkyl-*N*-aryliminomethyl nitroxides *(1)* are converted into *N*-alkyl-*N*-benzoxazolyl nitroxides *(2)* and *N*-alkyl-*N*-arylcarbamoyl nitroxides *(3)*, with retention of the nitroxide group, by treatment with carboxylic acids.

If small amounts of glacial acetic acid are added, in the absence of oxygen, to the violet solutions of the radicals *(1a)* to *(1f)*[1] in benzene, which are then frozen, pale red radicals *(2)* are formed immediately; their ESR spectra differ significantly from those of the initial radicals *(1)*. Analysis of the ESR spectra showed that the H atom attached to the central C atom and one of the two *o*-H atoms of the phenyl had been replaced during the reaction. Treatment of 2-chlorobenzoxazole with *N*-*tert*-butylhydroxylamine and *N*-isopropylhydroxylamine, respectively, and subsequent oxidation of the reaction solution yielded radicals whose ESR spectra were identical with those obtained on reaction of *(1a)* and *(1b)*.



(1) *(2)*



(3)

	R^1	R^2	R^3
(a)	$C(CH_3)_3$	H	H
(b)	$CH(CH_3)_2$	H	H
(c)	$C(CH_3)_3$	$C(CH_3)_3$	H
(d)	$CH(CH_3)_2$	$C(CH_3)_3$	H
(e)	$C(CH_3)_3$	$C(CH_3)_3$	D
(f)	$CH(CH_3)_2$	$C(CH_3)_3$	D

Coupling constants of the radicals *(1)* and *(2)* (in gauss):

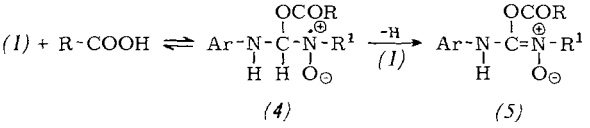
	$a_{N(NO)}$	$a_{N(-N=C)}$	$a_{H(H-C^{\diagup})}$	$a_{H(R^1)}$	$a_{H(R^2)}$	$a_{H(R^3)}$	$a_{H(meta)}$
(1a)	8.3	3.5	1.4	–	0.9	0.9	0.45
(1b)	7.85	3.8	not assigned				
(1c)	8.3	3.6	1.5	–	–	1.0	0.45
(1d)	7.8	3.9	not assigned				
(1e)	8.3	3.6	1.5	–	–	–	<0.5
(1f)	8.1	3.9	1.9	2.5	–	–	<0.5

	$a_{N(NO)}$	$a_{N(-N=C)}$	$a_{H(R^1)}$	$a_{H(R^2)}$	$a_{H(R^3)}$	$a_{H(5\text{ and }7)}$
(2a)	8.85	2.55	–	0.95	0.95	<0.5
(2b)	8.3	2.7	2.5	1.1	1.1	<0.5
(2c)	8.75	2.6	–	–	0.9	0.3 (1 H) <0.3 (1 H)
(2d)	8.4	2.75	2.75	–	1.2	<0.5
(2e)	8.75	2.6	–	–	–	<0.5
(2f)	8.3	2.75	2.6	–	–	<0.5

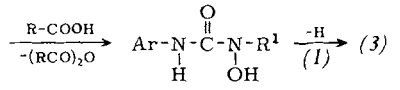
Surprisingly, the radicals *(1)* react with acetic acid much more slowly at room temperature (solution not frozen). Under such conditions the radicals *(2a)* and *(2b)* can no longer be detected; only after several hours do *(1c)*–*(1f)* afford *(2c)*–*(2f)* and *(3c)*–*(3f)* [superposed ESR spectra: *(3c)* and *(3e)*: triplet $a_{N(NO)}$ = 10.25 G; *(3d)* and *(3f)*: six-line spectra, $a_{N(NO)}$ = 9.9 G, $a_{H(R^1)}$ = 3.3 G. The C=O group in such radicals[2] imposes a barrier to delocalization of the unpaired electron and the Ar–NH group consequently has practically no effect on the spectrum].

We prepared the radicals *(3)* independently by oxidation of *N*-hydroxy-*N*-*tert*-butyl-*N'*-arylureas and *N*-hydroxy-*N*-isopropyl-*N'*-arylureas *(6)*, respectively. Mixtures of solutions of these radicals with solutions of *(2)* gave the same superposed ESR spectra as were obtained during the slow radical reaction at room temperature.

From experiments with substituted phenylacetic acids and substituted benzoic acids we have found that the rate of conversion at 25 °C increases with the strength of the carboxylic acid. We therefore assume that the first step of the highly complex reaction involves addition of the carboxylic acid to the C=N double bond. The fact that intermediates of the radical conversion are dehydrogenated by unreacted *(1)* suggests the following reaction route for the formation of *(3)*:



(4) *(5)*



(6)

The mode of formation of the benzoxazolyl nitroxides *(2)* is not yet clear. Since *(6)* is not converted into *(2)* under the reaction conditions, formation of *(2)* from *(4)* or *(5)* in several reaction steps appears likely.

If the conversion of *(1c)* by acetic acid is followed by means of the decrease in concentration, the reaction occurring on freezing is seen to be accelerated by a factor of 300 to 1700, depending on the concentration of acetic acid, compared with that at 25 °C. Experiments with other solvents and solvent mixtures indicate that this acceleration is caused by a freezing out of the solvent and concentration of the reactants in the liquid regions[3].

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Anomalous Spin States of Iron(II) in $[Fe(phen)_3](ClO_4)_2 \cdot 2H_2O$ [**] [1]

By *J. Ensling, B. W. Fitzsimmons, Philipp Gütlich*, and *K. M. Hasselbach* [*]

The Mössbauer spectrum of the complex $[^{57}Co^{II}(phen)_3](ClO_4)_2 \cdot 2H_2O$ [1,2] (symmetry D_3; as source) is temperature dependent (absorber: ^{57}Fe-enriched $K_4[Fe(CN)_6] \cdot 3H_2O$ at room temperature); in the range 4.2—296 °K, only iron(II) was observed in the decay product of the labeled cobalt compound.

The spectrum recorded at 296 °K gave the same values for the isomer shift (δ = 0.40 ± 0.02 mm/s) and the quadrupole splitting (ΔE_Q = 0.30—0.04 mm/s) of the resonance lines as Mössbauer measurements on the synthesized complex $[Fe^{II}(phen)_3](ClO_4)_2 \cdot 2H_2O$ as absorber (δ = 0.38 mm/s relative to $K_4[Fe(CN)_6] \cdot 3H_2O$ and ΔE_Q = 0.27 mm/s) [3–5]. Accordingly, the magnetic properties of the iron, occurring in the lattice of the strongly paramagnetic cobalt compound (μ_{eff} = 4.70 μ_B at 300 °K [2]) by nuclear disintegration (K capture), are not influenced by the high-spin (hs) character of the surrounding Co^{II} ions (S = 3/2); the iron exhibits the same magnetic behavior, *i.e.* low-spin (ls) character, as in the corresponding synthesized Fe^{II} complex (S = 0).

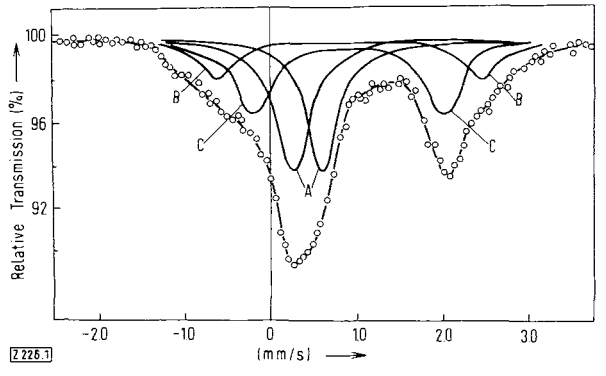


Fig. Mössbauer spectrum of $[^{57}Co(phen)_3](ClO_4)_2 \cdot 2H_2O$ at 4.2 °K relative to $K_4[Fe(CN)_6] \cdot 3H_2O$ (296 °K).

The spectra recorded at or below 223 °K, however, contain alongside the quadrupole doublet of the ls form of $[Fe(phen)_3](ClO_4) \cdot 2H_2O$, new resonance lines whose intensity increases with decreasing temperature. The Figure shows *e.g.* the spectrum at 4.2 °K; least-squares analysis using an appropriate computer fit program yields a superposition of three quadrupole doublets (A, B, C). The values for the Mössbauer parameters of all measured spectra are given in the Table.

The doublets B and C occurring at low temperature differ in magnitude of splitting by a factor of about 2 and in this respect are very different from A. As the lattice surroundings of the iron originating from ^{57}Co disintegration may be assumed to be the same in each case the different magnitudes of quadrupole splitting for A, B, and C must be chiefly ascribed to different arrangements of valence electrons. This would result in different valence electron contributions to the electric field gradient at the Fe^{II} nucleus in the species corresponding to A, B, and C. The valence electron contribution to the field gradient in the case of the ls form A is known to be zero, since the d electron configuration about the nucleus is spherically symmetrical. (The small quadrupole splitting of 0.3 mm/s is due to the trigonal distortion of the octahedron; this is also true for the species B and C.) On the basis of ligand field theory (splitting of the d orbitals [6] and occupation of the three most stable $3d^6$ electron configurations in a ligand field of D_3 symmetry according to the strong field approximation) we suggest the excited electron configurations $a_1^2 e_2^3 e_1^1$ with S = 1 for the doublet C, $a_1^2 e_2^2 e_1^2$ with S = 2 for the doublet B, and configuration $a_1^2 e_2^4$ with S = 0 for the stable ls form (A). The observed value of δ = 1.08 ± 0.06 mm/s for the isomer shift of the species B and C is in agreement with this suggestion; it is characteristic of paramagnetic Fe^{II} compounds.

A further indication of the occurrence of the "anomalous" spin states S = 1 (C) and S = 2 (B) follows from the valence electron contributions to the field gradient calculated according to *Ingalls* [7]: the factor of 2 between the values of $-2/7 \langle r^{-3} \rangle$ and $-4/7 \langle r^{-3} \rangle$ for C and B is in good agreement with the observed difference in the quadrupole splittings for C and B.

From the average lifetime of the 14.4 keV level of the ^{57}Fe nucleus and the lifetime of excited electron states along with the consideration of permitted and forbidden d—d transitions there follows an average lifetime for the "anomalous" spin states B and C of $10^{-9} < \tau \lesssim 10^{-8}$ s at room temperature and $\tau \gtrsim 10^{-8}$ s at $T \leq 223$ °K. The temperature dependence of τ can readily be understood on the grounds of the (likewise temperature dependent) spin lattice relaxation.

Table. Chemical isomer shift (δ), quadrupole splitting (ΔE_Q), intensity (I), and half-width (Γ_{exp}) of the resonance lines of $[^{57}Co(phen)_3](ClO_4)_2 \cdot H_2O$ as a function of temperature (A, B, and C refer to various spin states of Fe^{II}).

T (°K)	δ(A) (mm/s)	ΔE_Q(A) (mm/s)	δ(B) = δ(C) [a] (mm/s)	ΔE_Q(B) (mm/s)	ΔE_Q(C) (mm/s)	I(A)	I(B)	I(C)	Γ_{exp} (mm/s)
296	0.40 ± 0.02	0.30 ± 0.04	—	—	—	1.00 ± 0.05	0	0	0.56 ± 0.04
223	0.44 ± 0.02	0.28 ± 0.04	1.05 ± 0.06	3.0 ± 0.1	1.70 ± 0.08	0.86 ± 0.05	0.08 ± 0.05	0.06 ± 0.05	0.53 ± 0.04
78	0.46 ± 0.02	0.27 ± 0.04	1.10 ± 0.06	3.0 ± 0.1	1.68 ± 0.08	0.65 ± 0.05	0.15 ± 0.05	0.20 ± 0.05	0.56 ± 0.04
4.2	0.44 ± 0.02	0.26 ± 0.04	1.08 ± 0.06	3.0 ± 0.1	1.86 ± 0.08	0.49 ± 0.05	0.16 ± 0.05	0.35 ± 0.05	0.56 ± 0.04

[a] The isomer shifts of species B and C are, within the limit of error, equal.

The above observations indicate the "anomalous" spin states as resulting from various kinds of processes in the highly excited electron shell immediately following the nuclear transformation.

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Cyclooctatriene Complexes with Fluctuating Ligands

By *Rudolf Aumann*[*] and *Saul Winstein* (deceased)

Reaction of $C_8H_9Fe_2(CO)_6^+BF_4^-$ [1] with nucleophiles N was found to give specifically substituted 1,3,5-cyclooctatriene complexes $C_8H_9NFe_2(CO)_6^+BF_4^-$ *(1)* [N = pyridine *(1a)*, $P(C_6H_5)_3$ *(1b)*] and $C_8H_9NFe_2(CO)_6$ *(2)* [N = N_3^- *(2a)*, CN^- *(2b)*, H^- *(2c)*, D^- *(2d)*]. In the complexes *(1)* and *(2)* the π-electron system of cyclooctatriene is distorted to such an extent that an isolated double bond, a π-allyl system, and a two-center bond between a C atom and an Fe atom can be distinguished as new structural features [2] (Fig. 1).

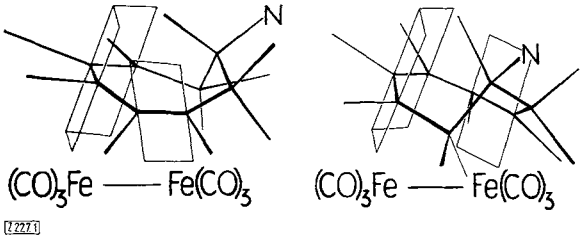
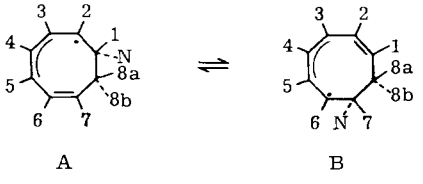


Fig. 1. Enantiomers A and B of the complexes *(1)* and *(2)*.

Both *(1)* and *(2)* were obtained as racemates. On the basis of ^{1}H-NMR measurements, we were able to demonstrate for *(1)* a mutual rearrangement of the enantiomers A and B *via* a 1,3 shift of the substituent N and a simultaneous migration of the vinyl system from 6,7 to 1,2; the allyl system $H^{3,4,5}$ remains fixed during the process.



The NMR spectrum of the pyridine adduct *(1a)* at 37 °C shows three sharp groups of signals for H^4, H^{8a}, and H^{8b}, and a broad signal (with little structure at a field of 60 MHz) for the other protons which undergo an exchange of magnetic environment and whose resonance frequencies are therefore averaged in pairs $H^1 \rightleftharpoons H^7$, $H^2 \rightleftharpoons H^6$, $H^3 \rightleftharpoons H^5$. At −20 °C the lifetime of the enantiomers is sufficiently high to give a non-averaged spectrum corresponding to the racemate *(1a)*.

The triphenylphosphine adduct *(1b)* is considerably more rigid than *(1a)* and shows a non-averaged spectrum at 37 °C. However, in this case we were able to demonstrate interconversion of the enantiomers ($t_{1/2}$ = 1.7 at 37 °C) using the double resonance- (relaxation-) method developed by *Hoffman* and *Forsén* [3].

Like *(2c)* and *(2d)*, the neutral azide- and carbonitrile complexes *(2a)* and *(2b)* are configurationally stable on the NMR time scale up to 50 °C; however, in *(2c)* and *(2d)* rapid isomerization of the valence tautomers C and D (Fig. 2) occurs; they are the only members of the series to exhibit such behavior.

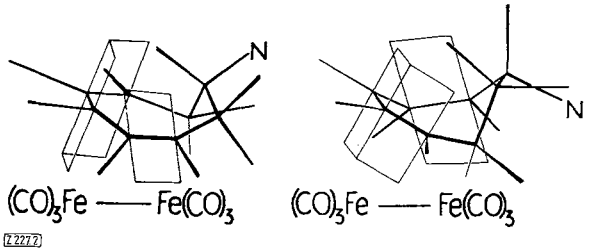


Fig. 2. Valence tautomers C and D of the complexes *(1)* and *(2)*.

C and D differ in the position of the allyl system and the isolated double bond on the one hand, and in the relative arrangements of the substituents N (in C pseudoequatorial, in D pseudoaxial) on the other. At −90 °C the spectrum of *(2c)* corresponds to structure C or D [2]; on stepwise increase in the temperature, averaged resonance frequencies are observed as a result of increasingly rapid interconversion of the valence tautomers (Fig. 3). In contrast to the rearrangement of the enantiomers described above, exchange of the magnetic environments of $H^4 \rightleftharpoons H^5$, $H^3 \rightleftharpoons H^6$, $H^2 \rightleftharpoons H^7$, $H^{1a} \rightleftharpoons H^{8a}$, $H^{1b} \rightleftharpoons H^{8b}$ occurs (cf. Table).

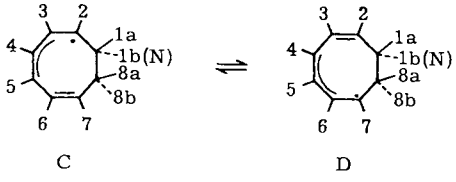


Table: ^{1}H-NMR spectrum of *hexahapto*-1,3,5-cyclooctatrienehexacarbonyldiiron(Fe—Fe) *(2c)* in $CHCl_2F$ (TMS as internal standard; 100 MHz). Comparison of the resonance frequencies (τ values) measured at 37 °C with values calculated by averaging the relevant resonance frequencies observed at −90 °C.

	measured	calculated
$H^{4,5}$	5.51	5.52
$H^{3,6}$	6.13	6.15
$H^{2,7}$	7.37	7.32
$H^{1a,8a}$	8.08	8.12
$H^{1b,8b}$	8.52	8.50

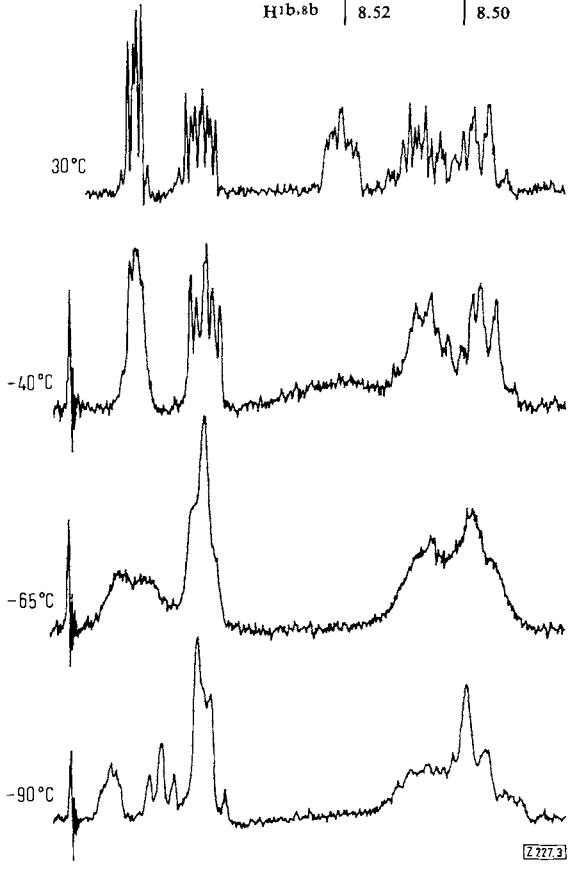


Fig. 3. ^{1}H-NMR spectrum of *(2c)* at various temperatures (10% $CHCl_2F$ solution; reference signal CH_2Cl_2 = 4.70 τ; 60 MHz).

A common feature of the complex NMR spectra of the compounds *(1)* and *(2)* is the H^3—H^4—H^5 allyl system (protons numbered as in C) with $J_{3,4} \approx J_{4,5}$ = 6—7 Hz, as is also the isolated vinyl system of the protons H^6 and H^7 with a vicinal coupling constant of 8—9 Hz; as expected, the signal of H^2 always appears at high field (τ = 7.9—8.5).

The coupling constants $J_{1a,2}$, $J_{1a,8a}$, $J_{1a,8b}$, $J_{7,8a}$, $J_{7,8b}$ of *(2a)* and *(2b)* can be explained by the Karplus equation[4], paying attention to the group electronegativity[5] of the substituents N[6], and the allyl coupling can be interpreted satisfactorily in terms of a relationship given by *Garbisch*[7]. It can be assumed with a high degree of certainty that N is fixed exclusively *cis* to the $Fe_2(CO)_6$ group, thus suggesting that the attacking nucleophile is transferred onto the ring by the agency of the metal.

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A New Octamolybdate: $(NH_4)_6Mo_8O_{26}(OH)_2 \cdot 2\,H_2O$

By *Oskar Glemser*, *Gebhard Wagner*, and *Bernt Krebs*[*]

If an almost saturated aqueous solution of ammonium heptamolybdate (0.20 to 0.25 M) is allowed to stand for several weeks slow formation of almost colorless needle-like crystals occurs; they may be filtered off and dried in air without undergoing any change in composition. Analysis showed the crystals to have the composition $(NH_4)_6Mo_8O_{27} \cdot 3\,H_2O$; the IR and Raman spectra differ markedly from those of solid ammonium heptamolybdate $(NH_4)_6Mo_7O_{24} \cdot 4\,H_2O$ and ammonium octamolybdate $(NH_4)_4Mo_8O_{26} \cdot 4\,H_2O$.

IR (cm^{-1}): 480w, 570w, 670w, 700w, 790m, 845vs, 865m, 885vs, 900sh, 912m, 935vs, 1405vs, 1625m, 3020m.

Raman (cm^{-1}): 45m, 78m, 106w, 123w, 136m, 154w, 185m, 208m, 307w, 338m, 360m, 393w, 706m, 826w, 857s, 875s, 886s, 918s, 945vs.

Weissenberg and precession photographs recorded for a single crystal of about 0.1 mm in length show the compound to crystallize in the space group $P2_1/c$ with lattice constants $a = 9.50 \pm 0.03$, $b = 11.30 \pm 0.03$, $c = 15.00 \pm 0.04$ Å; $\beta = 109.5 \pm 0.5°$. Assuming $Z = 2$, the value $d_{pyk} = 3.01 \pm 0.05$ g cm^{-3} determined in benzene and in carbon tetrachloride gives a molecular weight of 1376 (value calculated for $(NH_4)_6Mo_8O_{27} \cdot 3\,H_2O = 1362$).

Since the general point distribution is fourfold in the space group $P2_1/c$, the octameric structural unit must possess a center of inversion. According to the rules for aggregation of polywolframates and polymolybdates[1], a centrosymmetric octamolybdate containing an odd number of oxygens, *i.e.* having one oxygen at the center, cannot consist entirely of MoO_6 octahedra. The structure of the compound must therefore contain an even number of oxygen atoms which may not exceed 28[1]. Moreover, the symmetry of the space group permits only an even number of molecules of water of crystallization. The new octamolybdate with two OH groups should therefore be formulated $(NH_4)_6Mo_8O_{26}(OH)_2 \cdot 2\,H_2O$. In order to distinguish between the two octamolybdates we designate the known compound "octamolybdate A" and the new one "octamolybdate B".

The Z^* value[2] of octamolybdate B (1.25) is higher than that of heptamolybdate (1.14), but lower than that of octamolybdate A (1.50). We also found that formation of solid octamolybdate B ceases when 60—70 % of the heptamolybdate has reacted; NH_3 is liberated in the process.

$$48\,NH_4^+ + 8\,Mo_7O_{24}^{6-} + 18\,H_2O \rightarrow 7\,(NH_4)_6Mo_8O_{26}(OH)_2 \cdot 2\,H_2O + 6\,NH_3$$

The new isopolymolybdate can form a solid ammonium salt only as a result of its lower solubility. Formation of an alkali-metal salt of this type would yield OH^- ions, which would effect immediate disaggregation.

Ammonium octamolybdate B dissolves slowly in water with hydrolysis

$$10\,(NH_4)_6Mo_8O_{26}(OH)_2 \cdot 2\,H_2O \rightarrow 8\,Mo_7O_{24}^{6-} + 3\,Mo_8O_{26}^{4-} + 60\,NH_4^+ + 30\,H_2O$$

to form heptamolybdate and octamolybdate A. X-ray structure analysis of octamolybdate B is in progress.

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[2] The Z^* value denotes the ratio of reacted H^+ to reacted MoO_4^{2-}.

Cleavage of σ Bonds between Transition Metals and Carbon by Carbon Disulfide

By *Ekkehard Lindner*, *Rudolf Grimmer*, and *Helmut Weber*[*]

CS_2-insertion reactions of organometallic compounds leading to dithiocarboxylato derivatives have so far been encountered only with main group metals[1–3]. We have now observed the first cleavage of σ bonds between the transition metal and carbon in organometal carbonyls of Group VII A elements, a reaction requiring a great deal of energy, under pressure at 90—150 °C.

$$R{-}M(CO)_5 + CS_2 \xrightarrow{CS_2} RC(S)SM(CO)_4 + CO$$

M \ R	CH_3	C_6H_5	p-$CH_3C_6H_4$	p-ClC_6H_4	$C_6H_5CH_2$	$(C_6H_5)_3C$
Mn	*(1a)*	*(1b)*	*(1c)*			
Re	*(2a)*	*(2b)*	*(2c)*	*(2d)*	*(2e)*	*(2f)*

The reaction, in which CS_2 also functions as solvent, is of a general nature, the only exceptions being perfluorinated organometal carbonyls. The diamagnetic products *(1a)–(2f)*, whose colors vary between yellow and deep red depending on the substituent R, can be sublimed and are soluble in almost all organic solvents. The rhenium derivatives *(2)*, unlike those of manganese *(1)*, are stable towards oxygen and heat.

Composition and structure of *(1a)–(2f)* result from elemental analyses, molecular-weight determinations, IR, Raman, ^1H–NMR, and mass spectra, as well as from X-ray studies[4]. In the terminal CO region the IR spectra show four sharp absorption bands of irreducible representation $2\,A_1 + B_1 + B_2$ (*e.g.* for *(2a)* in *n*-hexane: 2110m, 2011vs, 2000s, 1963 cm^{-1} s-vs). The ν_{as} and ν_s (CS_2) vibrations observed in the Raman spectrum lie in the ranges 1270—1140 and 620—600 cm^{-1} re-

pectively (*e.g.* for *(2a)* in CCl_4: $\nu_{as}(CS_2)$ = 1146vw, $\nu_s(CS_2)$ = 619 cm^{-1} vs). Spectroscopic and X-ray data indicate pseudo-octahedral environment of the metal in *(1a)*–*(2f)* with (pseudo)-C_{2v} symmetry. The ^1H–NMR spectra indicate in particular that an isomeric mixture containing *(2e)* and a tolyldithiocarboxylato derivative is only formed on reaction of $C_6H_5CH_2Re(CO)_5$ with CS_2.

The dithiocarboxylato complexes described above are reactive. For instance, *(2b)* loses CO on reaction with $P(C_6H_5)_3$ at 80 °C in benzene to give the stable orange compound *cis*-$C_6H_5C(S)SRe(CO)_3P(C_6H_5)_3$ (dec. pt. 190 °C).

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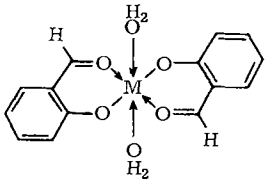
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Oxidation of the Salicylaldehyde Ligand in Cobalt(II)- and Nickel(II) Complexes[**]

By *Hans G. Biedermann* and *Karl E. Schwarzhans* [*]

Bis(salicylaldehydato)diaquocobalt(II) *(1a)* reacts with pyridine[1] and several other unsaturated heterocycles[2] with substitution of the two *trans* water molecules in the pseudo-octahedral complex.



(1a), M = Co^{II}
(1b), M = Ni^{II}

In the corresponding reaction with an excess of morpholine under an inert gas atmosphere (N_2) the neutral ligands are likewise exchanged and a deep-red 1:2 adduct is formed. If, however, the reaction is not carried out under inert gas the color of the reaction solution changes from deep-red to red-brown; this change of color takes place much more rapidly when the reaction mixture is heated to about 120 °C in air, and when only morpholine is present as solvent. An examination of the susceptibility of such a solution by *Evans*' method[3] shows, however, that no oxidation of the central metal ion takes place. The magnetic moment of the starting complex and of the isolated end product was determined as μ_{eff} = 4.8 μ_B. If the reaction of *(1a)* with morpholine is carried out in $CHCl_3$ solution at room temperature in an open vessel 3.4 moles of water are liberated (H_2O determination by K. Fischer method) and 0.7–0.8 mole oxygen is taken up per mole of *(1a)* over a period of 48 hours (oxygen uptake measured volumetrically). Decomposition of the oxidation product with 6 N HCl yields salicylic acid morpholide; hydrolysis with 6 N KOH followed by cleavage with 6 N HCl gives salicylic acid in yields of up to 40 % [referred to *(1a)*]. The product complex bis(salicylmorpholidato)bis(morpholine)cobalt(II) was identified, as was the secondary product arising from its degradation, by elemental analysis, determination of melting point or decomposition point, and by ^1H–NMR and IR spectra.

The remarkable ease of oxidation of the aldehyde function in complex *(1a)* by atmospheric oxygen can be explained by the fact that a very high spin density is present even on the aldehyde group as a result of delocalization of the unpaired electrons of the central metal ion in the ligand. The ^1H-NMR spectrum of bis(salicylaldehydato)bis(pyridine)cobalt(II) shows *e.g.* the C(O)H signal at −365 ppm relative to TMS[4]. If an excess of morpholine is added to a solution of this complex and the mixture shaken in presence of air, the signal of the proton is no longer detectable in the NMR spectrum. NMR spectroscopy, therefore, can give information about reactive centers in such complexes. Analogous compounds having similar NMR parameters ought to show the same reaction. We have already been able to confirm this in the case of bis(salicylaldehydato)diaquonickel(II) *(1b)*.

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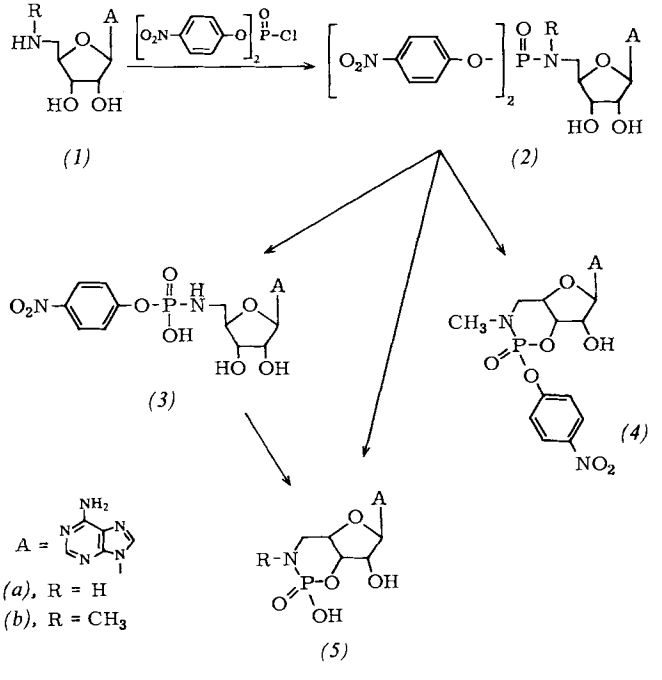
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Synthesis of 5′-Amido Analogs of Adenosine (3′-5′)-Cyclophosphates

By *Akira Murayama*, *Bernd Jastorff*, and *Hans Hettler* [*]

Adenosine (3′-5′)-cyclophosphate plays a key regulatory role at various levels of organization, *e.g.* it acts as "chemical messenger" in the production of blood sugar by the liver, as aggregation initiator of slime fungi, and as a kind of "second messenger" for more than a dozen hormones found in mammals, including humans[1,2]. Here we report on the synthesis of its 5′-amido analogs, 5′-amino- *(5a)* and 5′-*N*-methylamino-5′-deoxyadenosine (3′-5′)-cyclophosphoramidate *(5b)*.

5′-Amino- *(1a)*[3] and 5′-*N*-methylamino-5′-deoxyadenosine *(1b)*[4] are converted into the diester amides *(2a)* and *(2b)*,



(1) *(2)* *(3)* *(4)*

A =

(a), R = H
(b), R = CH_3

(5)

respectively, in about 50 % yield by reaction with di(*p*-nitrophenyl) phosphorochloridate[5].

Whereas *(5b)* is obtained directly (55 % yield) on treatment of *(2b)* with 1 N NaOH/methanol (1:1) in 100 h at room temperature, *(5a)* can only be synthesized stepwise. As first step, one *p*-nitrophenol group is removed by ammonia/pyridine/water (5:2:1); *(3)* is isolated in 80 % yield by preparative layer chromatography and cyclized according to *Borden*[6] by treatment with 1 M potassium *tert*-butoxide/*tert*-butanol in dimethyl sulfoxide (15 min, 10 °C) to give the cyclophosphate analog *(5a)* which is isolated in 65 % yield after separation on a DEAE cellulose column. Ring closure of *(2b)* to *(5b)* proceeds *via* the unusual cyclic diester amide: after 1 h it was possible to isolate compound *(4)*.

All the compounds gave correct analyses and spectroscopic data. Compounds *(5a)* and *(5b)* are currently being tested in conjunction with other research teams for biological activity.

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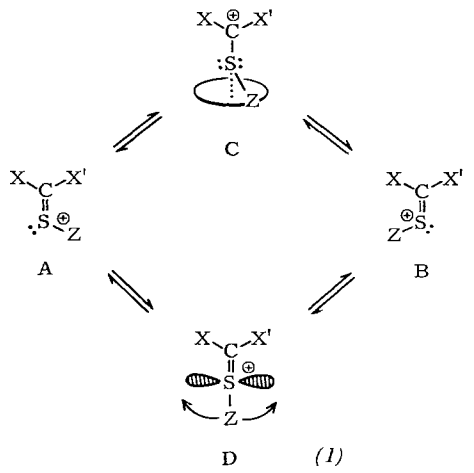
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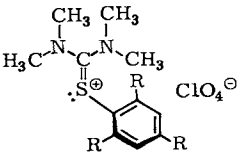
syn-anti-Isomerism at the Carbon-Sulfur Double Bond in Isothiouronium Salts [1] [**]

By *Horst Kessler* and *Hans-Otto Kalinowski*[*]

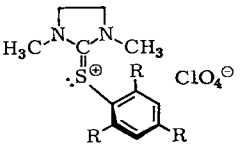
While the *syn-anti* isomerism at the C=N double bond in imines is well known, the possibility of *syn-anti* isomerism (A, B) at the isoelectronic C=S double bond in thioketonium ions *(1)* has not yet been reported on. In an NMR spectroscopic examination of the isothiouronium salt *(1)* (X=X' = $N(CH_3)_2$; Z = aryl, alkyl) at low temperature, we have been able to detect and "freeze" the equilibrium A ⇌ B[2]. The isomerization could be effected by rotation about the partial CS double bond (transition state C) or by inversion at the sulfur (transition state D)[3]. A differentiation is possible by studying the influence of *ortho* substituents on the isomerization of the *S*-aryl substituted compounds *(2)* and *(3)*.



(1)



(2)



(3)

The rotation is hindered[4,5] by large groups R, which must rotate past X. In contrast the steric hindrance in the transition state of the inversion (D) is less than in the ground state — hence, the rate of inversion ought to increase with increasing size of R[3].

The free enthalpies of activation determined in the case of isothiouronium perchlorates *(2)* and *(3)* are given in the following table.

Table. NMR parameters for the *syn-anti* isomerization of *S*-aryliso-thiouronium perchlorates *(2)* and *(3)*. T_c = coalescence temperature. The coalescence of the methyl signal is used for the evaluation [4].

	R	Solvent	Δν (Hz)	T_c (°C)	$\Delta G_c^{\neq}$ (kcal/mole)
(2a)	H	CH_2Cl_2	57	− 83	9.1 [a]
			10	− 92	9.3 [a]
(2b)	CH_3	CH_2Cl_2	67	− 64	10.0 [a]
			13	− 73	10.2 [a]
(2c)	*i*-C_3H_7	CH_2Cl_2	40	− 29	12.0 [b]
(2d)	*t*-C_4H_9	$(CD_3)_2SO$	50	+ 89	17.9 [b,d]
(3a)	H	CH_2Cl_2	—	<−115	<7.6 [c]
(3b)	CH_3	CH_2Cl_2	46	−107	8.0 [d]
(3c)	*i*-C_3H_7	CH_2Cl_2	55	− 80	9.3 [d]
(3d)	*t*-C_4H_9	TCB [e]	75	+106	18.5 [d]

[a] The error is ± 1 kcal/mole because the simultaneous "freezing-in" of the CN rotation interferes with the evaluation; the first results are w. r. t. the coalescence of the outer singlets, the second to the two inner singlets.
[b] Splitting to a doublet; the CN rotations are only "frozen-in" at lower temperature. [c] Calculated for an assumed splitting of 40 Hz. [d] Error ± 0.2 kcal/mole. [e] 1,2,4-Trichlorobenzene.

The distinct increase of the $\Delta G^{\neq}$ values on going from the phenyl compounds *(2a)* and *(3a)* to the sterically much hindered tri-*tert*-butylphenyl compounds *(2d)* and *(3d)* proves that the *syn-anti* isomerization at the partial CS double bond is *via* rotation (transition state C) and not by inversion, as in the corresponding process in the guanidines[3]. A minimum value of the activation barrier for the inversion at doubly bonded sulfur is obtained at the same time: it must be greater than 18.5 kcal/mole [= the value for *(3d)*]. In compounds with less strongly electron repelling groups X on the thiocarbonyl system, inversion at the sulfur atom ought — according to findings in the imine system[3] — to be very much less probable. The high barrier to inversion should make a separation of such *syn-anti* isomers at room temperature possible. This is at present under investigation.

The compounds *(2a)*—*(2c)* and *(3a)*—*(3c)* can be prepared from chloroformamidinium chloride and thiophenols[6]. *(2d)* and *(3d)* were not prepared *via* thiophenol but *via* the lead or thallium salt.

1,1,3,3-Tetramethyl-2-(2,4,6-tri-tert-butylphenyl)-isothiouronium perchlorate (2d)

Thallium 2,4,6-tri-*tert*-butylthiophenolate (4.5 g) was added with stirring to a solution of tetramethylchloroformamidinium chloride[7] (1.5 g) in anhydrous acetonitrile (50 ml). After three hours' stirring the reaction mixture was filtered and the filtrate treated with a solution of $NaClO_4$ (1.15 g) in aceto-

nitrile (20 ml). After refiltration the solvent was evaporated off and the residue recrystallized from ethanol [yield of *(2d)*, 25 g (64 %); m.p. 214–215 °C].

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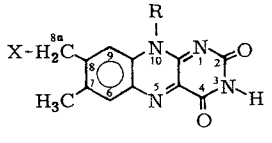
The Synthesis of Succinate-Dehydrogenase Riboflavin

By *Sandro Ghisla, Ursula Hartmann*, and *Peter Hemmerich* [*]

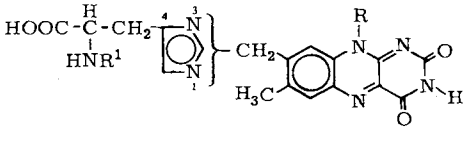
Singer and *Kearney* [1], in their early studies, recognized that the flavocoenzyme of mitochondrial succinate dehydrogenase ("SD-flavin") [**] was a derivative of flavin-adenine-dinucleotide which was covalently bound to the protein. In cooperation with Dr. *Singer*'s team [***], we have attempted to elucidate the structure of this coenzyme. In the first preliminary communication [2], we concluded from the hyperfine structure of electron spin resonance (ESR) spectra of partially purified SD-riboflavin (obtained from SD-FAD-peptide mixtures by total hydrolysis in 6 N HCl) that

a) SD-riboflavin is irreversibly converted into riboflavin *(1a)* by reduction and

b) the bond between the leaving group "X" [cf. *(1)*] and the heteroaromatic flavin nucleus is connected through position 8α.



(1a), X = H, R = Ribityl
(1b), X = Morpholino, R = CH_3
(1c), X = Br, R = Tetraacetyl-ribityl



(2a), R = Tetraacetyl-ribityl, R^1 = C_6H_5CO
(2b), R = Ribityl; R^1 = H

The light absorption of neutral SD-riboflavin is hardly different from that of riboflavin *(1a)* (λ_{max} 445 nm), but the near UV spectrum of the oxidized cation differs more drastically (Fig. 1, λ_{max} shifted from 395 [2] to 373 nm). Most characteristic is the pH-dependence of the fluorescence obtained with SD-riboflavin (Fig. 2) and, as mentioned above, the ESR hyperfine structure of the red radical cation (Fig. 3). Since these ESR results could be interpreted unequivocally [2] in terms of 8α-substitution of the flavin nucleus, we have synthesized 8α-substituted flavin derivatives [3], *e.g. (1b)*, which mimic the light absorption as well as the fluorescence properties of SD-riboflavin closely. This work enabled us to predict that the characteristic quenching of SD-riboflavin fluorescence with p*K* 4.4 (Fig. 2) originates from a secondary or tertiary nitrogen function in position 8α. Subsequently, *Walker* and *Singer* [4] succeeded in identifying the X-fragment obtained from reductive cleavage of the flavin-X-bond as *histidine*.

We have now synthesized SD-riboflavin *(2b)* as follows: Riboflavin *(1a)* is peracetylated in pyridine-acetic anhydride and then monobrominated in position 8α with an 80 % yield by refluxing 40 min with an 1.3-fold excess of Br_2 and catalytic amounts of dibenzoyl peroxide in dioxane. The yield is estimated from the decrease of the C(8)CH_3-peak in the NMR spectrum (δ = 2.45 ppm).

In addition to the C(8)CH_2Br-signal (δ = 4.7 ppm), the product of bromination *(1c)* shows only a trace of C(8)$CHBr_2$-signal (δ = 7.0 ppm [6]), indicating the presence of dibrominated analog [6]. The dibrominated product is obtained quantitatively upon heating with a larger excess of bromine in

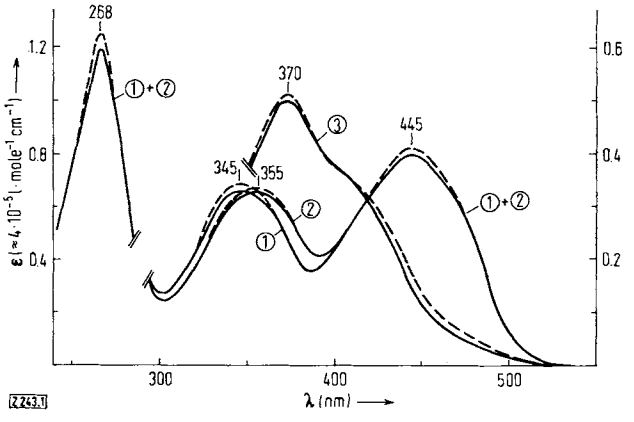


Fig. 1. Electronic spectra of native (---) and synthetic (—) SD-riboflavin.
① Neutral SD-riboflavin, pH 7, λ_{max} = 445, 355, 268, 221 nm.
② SD-riboflavin monocation protonated in the imidazole ring, pH 3, λ_{max} = 445, 345, 268, 221 nm.
③ Dication, 6 N HCl, λ_{max} = 405 (S), 373, 265, 221 nm.

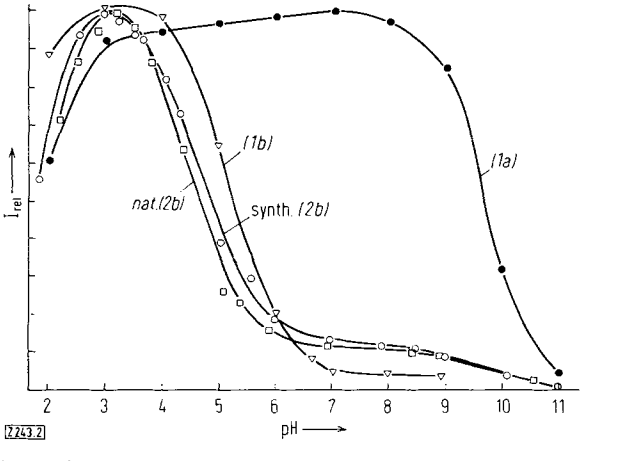


Fig. 2. Dependence of the relative intensity of fluorescence I_{rel} on the pH of unbuffered solutions of native and synthetic SD-riboflavin *(2b)*, riboflavin *(1a)*, and the model compound *(1b)*.

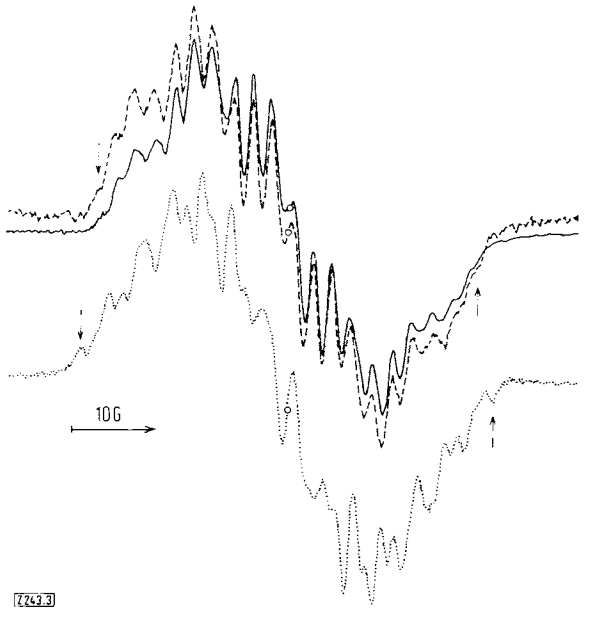


Fig. 3. Hyperfine structure of the ESR of SD-riboflavosemiquinone cation in 6 N HCl obtained by reduction with $TiCl_3$. The arrows indicate the outermost lines of the spectrum. Riboflavin *(1a)* shown for comparison, exhibits 2 more ESR active 8α-protons than SD-riboflavin *(2b)* since. in contrast to the 8-methyl group in riboflavin *(1a)*, the bulky histidyl-CH_2 group in *(2b)* is not free to rotate. (An analogous situation, for instance, exists with 5-methyl- and 5-benzylflavosemiquinone [5].) All ESR spectra have been recorded at a modulation amplitude of 0.5 gauss and 25 mW power in an anaerobic flat cell with a Varian E3 spectrometer. ———: native SD-riboflavin, —: synthetic SD-riboflavin, ····: riboflavin.

presence of pyridine[6]. The monobromide *(1c)* was heated for 15 hours at 90 °C in absolute dimethylformamide (without addition of a basic catalyst) with a 2.5-fold excess of N_α-benzoylhistidine. The resulting flavin mixture was shaken in aqueous buffer of pH 7. The aqueous phase contains the 8α-histidyl flavin *(2a)* which can be separated from the unreacted histidine by extraction with chloroform at pH 3 after saturation of the aqueous phase with ammonium sulfate. Finally, *(2a)* is hydrolyzed to *(2b)* by refluxing in 6 N HCl for 2 hours (overall yield 35 %).

The ESR and light absorption spectra of the resulting 8α-(*N*-histidyl)riboflavin are identical with those of authentic native material[4] (Figs. 1, 3). The pH derived from quenching of fluorescence (Fig. 2) of the synthetic product is slightly less clear cut than that of the native material. We conclude from this that the synthesis leads to a mixture of isomers because the imidazole nitrogens are chemically not equivalent. The native and synthetic products appear homogeneous and identical in thin layer chromatography on silica gel. The chromatographic separation of the presumed isomers and their structural assignment is presently under investigation.

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[**] The general term "flavin" denotes all species having formula *(1)* with any groups R and X, but not R = H.

[***] This work has been supported by the Deutsche Forschungsgemeinschaft. – A prerequisite for our work was the intense cooperation with Drs. *E. B. Kearney*, *T. P. Singer*, and *W. H. Walker* (San Francisco) to whom we are greatly indebted for the authentic sample of native SD-riboflavin.

[1] *T. P. Singer*, *J. Hauber*, and *E. B. Kearney*, Biochem. Biophysic. Res. Commun. *9*, 146 (1962); *E. B. Kearney*, J. biol. Chemistry *253*, 865 (1960).

[2] *P. Hemmerich*, *A. Ehrenberg*, *W. H. Walker*, *L. E. G. Eriksson*, *J. Salach*, *P. Bader*, and *T. P. Singer*, FEBS-Letters *3*, 37 (1969).

[3] *S. Ghisla* and *P. Hemmerich*, unpublished.

[4] *W. H. Walker* and *T. P. Singer*, J. biol. Chemistry, in press.

[5] *F. Müller*, *P. Hemmerich*, *A. Ehrenberg*, *G. Palmer*, and *V. Massey*, Europ. J. Biochem. *14*, 185 (1970).

[6] *D. B. McCormick*, J. heterocyclic Chem. *7*, 447 (1970).

CONFERENCE REPORTS

Protein Mapping in Polyacrylamide and its Application to Genetic Analysis in Plants

By *Hermann Stegemann*[*]

At present, the best separations of charged macromolecules are accomplished in gels of crosslinked polyacrylamide (PAA) as carrier. In PAA electrophoresis the migration is determined by both the charge and the size of the molecule; the extent of migration is a function of time.

In an electrofocusing run (in PAA gel with ampholines®) the site of the focused ampholyte is constant after equilibration of the pH gradient (in practice, a slight cationic migration of the ampholines® is observed); the proteins, nucleic acids *etc.* separate according to their isoelectric values.

If proteins are focused in a PAA rod, which is then placed horizontally on the 3 mm front edge of a 13 cm×18 cm PAA plate, proteins having the same charge start to migrate in the gel matrix and separate according to molecular size. This technique of separation, which is called "mapping", for it provides a "map" of protein spots, is probably the most rapid and efficient method for the separation and characterization of such mixtures. The lower limit of detection is 0.5 μg protein or fractions of a nanogram phosphorylase. In an apparatus designed for PAA layers between 1 and 16 mm, which will soon be available commercially, sample mixtures of up to 1 g can be analyzed. The molecular weight of proteins in PAA are determined according to *Maizel*'s method, and loading with dodecyl sulfate is carried out in a new continuously operating microdialysis apparatus.

The main proteins in potato tubers have molecular weights between 20000 and 25000, the distribution of charge and molecular weight is genetically fixed (thus permitting a diagnosis of type). The mapping method also affords a means of differentiating very closely related hybrids.

Lecture at Bonn, May 26, 1970 [VB 242 IE]
German version: Angew. Chem. *82*, 640 (1970)

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Use of Pulse Radiolysis in Elucidation of the Mechanisms of Complex Organic and Inorganic Reactions

By *Arnim Henglein*[*]

Free OH radicals and hydrated electrons in known concentration can be generated in aqueous solution by passage of a microsecond pulse of high-energy ionizing radiation. Reac-

tions of these species with dissolved organic and inorganic substances can be followed by electronic registration of optical absorption and electrical conductivity as a function of time. Some typical applications are described below.

Hydrates of aromatic nitroso compounds: These compounds were hitherto unknown. They are formed by reduction of a nitro compound by the hydrated electron; in acid solution the anion formed then picks up a proton and disproportionates:

$$2\,XC_6H_4NO_2H \rightarrow XC_6H_4N(OH)_2 + XC_6H_4NO_2$$

The hydrates, whose spectra were recorded in a number of cases, give up water within 10^{-4} to 10^{-2} s, depending upon the nature of the substituent X and the pH of the solution. The dehydration proceeds in two steps:

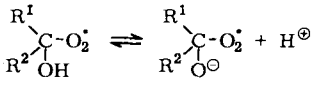
$$XC_6H_4N(OH)_2 + H^{\oplus} \underset{K}{\rightleftarrows} XC_6H_4N(OH)_2H^{\oplus} \xrightarrow[k_1]{-H_2O}$$

$$XC_6H_4\overset{\oplus}{N}OH \xrightarrow[k_2]{} XC_6H_4NO + H^{\oplus}$$

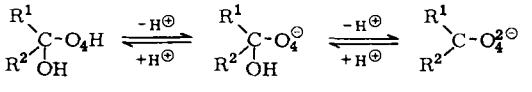
($k_2 \gg k_1$). The dissociation constants and the Hammet constants of the substituents X are related according to:

$$\log K/K_0 = 2.3 \times \sigma \quad (K_0 \text{ for } X = H).$$

Charged intermediates of autoxidation: Oxidation of many organic substances in aqueous solution (alcohols, ethers, olefins) in presence of O_2 proceeds *via* intermediate acids that can be detected by their conductivity. α-Hydroxyperoxyl radicals dissociate according to



The spectra of the acid and basic forms were recorded. The pK is 7.1 for the radical formed from methanol, 8.3 for that from ethanol, and 8.5 for that from isopropanol. Two hydroxyperoxyl radicals form a dibasic acid that disappears in accord with first order kinetics. The results can be quantitatively interpreted if a hydroxyhydrotetroxide structure is assigned to the acid:



The first pK value is about 4.5, the second is about 8 (for R^1 and R^2 = alkyl or H). Decomposition is attributed to the loss of O_2.

Unstable oxides and acids of nitrogen: Short-lived compounds of nitrogen in abnormal valence states are obtained by the action of OH radicals and hydrated electrons on dissolved nitrate- and nitrite ions and nitrogen monoxide. The absorption spectra of the unstable compounds were recorded and the rate constants of their reactions were determined.

The species H_2NO_3, $HNO_3^{\ominus}$, and $NO_3^{2\ominus}$, and also H_2NO_2, $HNO_2^{\ominus}$, and $NO_3^{2\ominus}$ are in protolytic equilibrium. All pK values were determined and the decomposition of the various species to give NO_2 or NO was studied. It also proved possible to determine the equilibrium constants for

$$N_2O_4 \rightleftarrows 2\,NO_2$$

and

$$N_2O_3 \rightleftarrows NO_2 + NO$$

and the rate constants of hydrolysis of N_2O_4 and N_2O_3. The reaction of NO_2 and OH leads to pernitrous acid whose pK and rate constant for isomerization to HNO_3 were measured. Reduction of NO by the hydrated electron gives the species $NO^{\ominus}$, NOH, $N_2O_2^{\ominus}$, N_2O_2H, N_3O_3H, and $N_3O_3^{\ominus}$, of which the last two subsequently yield $(H)NO_2^{\ominus}$ and N_2O by spontaneous decomposition.

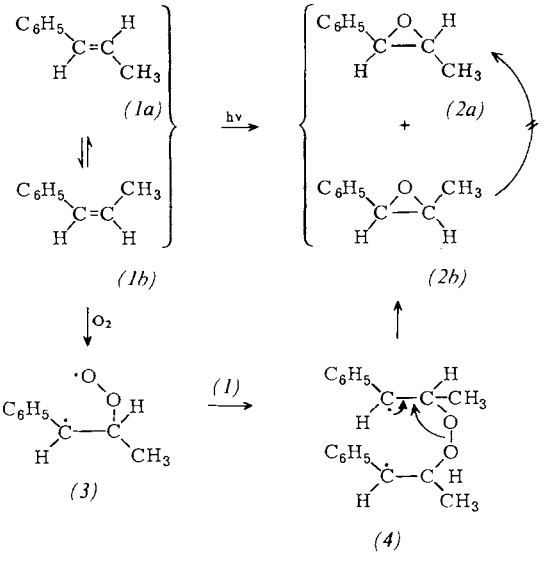
Lecture at Hannover on May 14, 1970 [VB 243 IE]
German version: Angew. Chem. *82*, 670 (1970)

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A Novel Photooxidation of Hydrocarbons Involving Triplet Oxygen

By *R. C. Petterson* [*]

A photooxidation of certain olefins has been discovered which is unusual in that reaction of a vibrationally excited ground state or twisted form of the hydrocarbon with triplet (ground state) oxygen appears to be involved, and the products are epoxides. 1,1-Diphenylpropene, *cis*- and *trans*-phenylpropenes *(1a)* and *(1b)*, and *trans*-stilbene undergo the reaction when irradiated (in contact with air) with light of wavelength 3000–4000 Å (16-8 W lamps) in 0.1 M benzene or heptane solution at 35 °C for 72 hours. Neat 1,1-diphenylpropene also is thermally oxidized (110 °C) to 1,1-diphenylacetone, undoubtedly *via* the epoxide; in this case a vibrationally excited ground state or twisted state must be involved.



The *cis* and *trans* forms of olefin *(1)* rapidly interconvert photochemically, but the epoxide isomers *(2a)* and *(2b)* do not, and the predominance (*ca.* 30/1) of *trans* epoxide *(2a)* over the *cis* form *(2b)* in the products suggests the existence of an intermediate which can rotate to give the thermodynamically more stable epoxide isomer.

The photooxidation of *(1)* can be sensitized with triphenylene and thus may go through a triplet state, but whether directly or only after crossing to a vibrationally excited ground state or twisted state is not clear.

By-products from oxidative cleavage, *e.g.* benzaldehyde from *(1)*, are always found in small amounts. While these may have been products of reaction of singlet oxygen, it was shown that singlet oxygen, produced *in situ* by irradiation of photo-

sensitizers such as rose bengal with visible light, does not oxidize these olefins to epoxides. It is interesting that singlet oxygen type by-products were not increased in the triphenylene sensitization experiment.

A mechanism is tentatively proposed in which the excited olefin collides with a triplet oxygen molecule forming a dioxy diradical molecule or a complex *(3)* of the type previously postulated by *G. O. Schenck*[1]. *(3)* then attacks a further olefin molecule to give the diradical *(4)*, which could give either 2 molecules of epoxide or one epoxide plus an oxy radical.

Lecture at Darmstadt (Germany) May 4, 1970 [VB 247 IE]
and at Mülheim/Ruhr (Germany) May 11, 1970
German version: Angew. Chem. *82*, 671 (1970)

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[1] *K. Gollnick* and *G. O. Schenck*, Pure appl. Chem. *9*, 507 (1964).

SELECTED ABSTRACTS

The oxidation kinetics of iron carbides have been studied by *J. Freel*, *B. R. Wheeler*, and *A. K. Galway*. Starting materials were a) a cementite with low surface area and small carbon excess, prepared by treatment of reduced magnetite with hydrocarbon vapor at 350 °C; b) a cementite with high surface area and large carbon excess from pyrolysis of basic iron mellitate; c) the reaction product of iron with CO and H_2 consisting of 76% Fe_5C_2, 8% Fe_3O_4, and 9% "free" carbon, besides catalyst residues. The reaction rates were monitored by observation of CO_2 evolution; the activation energies of oxidation of all three preparations were equal within the limits of error (102 kJ mole^{-1} at 240—500 °C). Both free and carbidic carbon were oxidized to CO_2, the primary solid product was always Fe_3O_4; Fe_2O_3 appears only in an advanced period of the reaction. It is concluded that the oxidation proceeds in the same manner as that of metallic iron: the rate determining step is diffusion of cations across the boundary between metallic phase (metal or carbide) and the primary product Fe_3O_4. / Trans. Faraday Soc. *66*, 1015 (1970) / —Hz. [Rd 204 IE]

Diffusion coefficients of alkali atoms in flames are measured by *A. F. Ashton* and *A. N. Hayhurst* by a new technique. A metal atom "point-source" is realized as follows: the gas mixture for the flame ($H_2 + O_2 + N_2$ under atmospheric pressure) flows through an array of 270 thin tubes and a metal salt solution is supplied in aerosol form *via* a single central tube. The intensity of the resonance emission of the metal measured at different points of the flame is used as a measure of concentration. The diffusion coefficients of sodium atoms were measured with an accuracy of ±7% in the temperature range 1920—2520 °K. They are in the range 10^{-3} m^{2}s^{-1}, are proportional to T^n with $n = 2.1$—2.2, and are larger in fuel-rich than in stoichiometric flames. In addition, the rate of thermal ionization of sodium atoms was determined in the hottest flames: in a stoichiometric flame at 2520 °K it was 105 s^{-1}, in a flame with $H_2 : O_2 = 2.5 : 1$ at 2480 °K, 58 s^{-1}. / Trans. Faraday Soc. *66*, 824, 833 (1970) / —Hz. [Rd 207 IE]

The photochemistry of the well-known uranyl oxalate actinometer has been thoroughly investigated by *L. J. Heidt*, *G. W. Tregay*, and *F. A. Middleton, jr.* For solutions with an uranyl ion concentration not less than 10^{-3} M and with an oxalate: uranyl ratio of 2 or greater the quantum yield of oxalate decomposition is 0.6 (±3%) at 208 to 436 nm. This value is constant for initial pH values between 1 and 5; outside this range it decreases. The photolysis always consumes acid. For each mole of oxalate consumed, approximately 1 mole of CO_2 is formed, which, depending on the pH, partly remains in solution. The quantum yield of CO formation amounts to nearly unity at pH 0; it drops rapidly with increasing pH. At pH 6 no CO was detected. The uranium(IV) yield increases with pH to a maximum of 10% of the oxalate consumed. The following mechanism is proposed for interpretation of the results: an electron is transferred from oxalate to uranium by light absorption; the primary products are U(V) and 1 mole of CO_2. With a proton from water, the U(V) intermediate is converted to a "hot" uranyl formate complex. At low pH CO is evolved from this complex, at higher pH formate is conserved. As a side reaction, the U(V) intermediate can disproportionate to U(VI) and U(IV). / J. physic. Chem. *74*, 1876 (1970) / —Hz. [Rd 208 IE]

Homogeneous nucleation in supersaturated vapors of *n*-alkanes was studied by *J. L. Katz*. A cloud chamber was used for measurement of critical supersaturation ratios. A thin layer of liquid hydrocarbon is spread on a horizontal thermostated metal plate and its vapor diffuses upward through a light carrier gas (H_2, He, Ne) to a second, cooler metal plate. The pressure and the temperature gradient between the two plates are chosen so that condensation will take place at about 80% of the chamber height. Condensation is determined visually by scattering of light. Results on *n*-alkanes from hexane to nonane at 225—330 °K are in good agreement with predictions from a simple theory used for calculating the equilibrium distribution of nuclei in the vapor with the assumption that the free energy of a nucleus equals the free energy of the same number of molecules in the bulk of liquid plus the surface free energy of the nucleus considered to be a sphere and to have the density of the liquid. The size of the critical nucleus lies between 24 and 87 molecules, depending on molecular weight and temperature. / J. chem. Physics *52*, 4733 (1970) / —Hz. [Rd 209 IE]

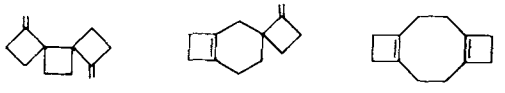
Radiation effects in NH_4HF_2 and $NaHF_2$ crystals following 1 MeV electron irradiation at 77 °K were studied by *L. J. Vande Kieft* and *O. R. Gilliam* by means of ESR and optical spectra. The crystals turn blue-green on irradiation, and the paramagnetic resonances developing can be interpreted to result from F_2^- ions in anion sites. Such defects arise from displacement of H atoms from their normal positions in the linear HF_2^- ions; however, only in NH_4HF_2 could the displacedH atoms themselves be detected. Annealing kinetics of the F_2^- ions in both crystals are of second order, as is to be expected for a recombination process. In certain sites of NH_4HF_2, the F_2^- ions appear to be tilted from the orientation of the original HF_2^- ion. This is interpreted as resulting from weaker N · · H · · F bonding to the F_2^- ions, since these are shorter and the N—H—F distance consequently larger than in the intact crystal. / Physic. Rev. [3] *B 1*, 2015 (1970) / —Hz. [Rd 210 IE]

Fine structure of fundamental bands in the IR spectrum of cyclobutane vapor at low pressures is interpreted by *J. M. R. Stone* and *I. M. Mills* as being due to the puckering motion of the C_4H_8 ring. The most conclusive results were derived

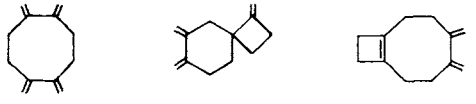
from sidebands on the 1453 cm^{-1} CH_2 scissoring mode: the side bands could be analyzed in terms of two slightly different puckering potential functions of the ground and the excited vibrational states. Barriers of inversion of 503 cm^{-1} ≙ 1.44 kcal $mole^{-1}$ in the ground state and 491 cm^{-1} in the excited state were calculated. The equilibrium dihedral angle of the C_4 ring is estimated to be about 35 °, in good agreement with electron diffraction data. A similar puckering structure of other IR and also Raman bands of C_4H_8 and C_4D_8 was observed; all observations are consistent with the same ground state puckering potential function. / Molecular Physics *18*, 631 (1970) / —Hz. [Rd 211 IE]

Internal electrolysis as an analytical method for uranium fission products was investigated by *F. Van Kote* and *J.-C. Catonne*. The electrolysis cell consists of a gold or platinum gauze cathode and a copper or zinc anode separated by a semipermeable cellulose diaphragm. If the cell is short-circuited across a suitable load resistance (*ca.* 1 ohm), the metals with more positive standard potentials than that of the anode metal are deposited on the cathode. With suitably selected anode materials and compositions of the electrolyte separations are feasible. The deposition of a few milligrams of Ag, Cd, and Te, alone and in the presence of each other from 5 M NaCl solution was followed with the aid of radioactive tracers, and the optimum conditions for electrolysis were established. Ag, Pd, Cd, and Sb were then deposited selectively by this method from a 5 M NaCl solution of fission products. Complete radiochemical purification, however, requires in addition conventional chemical methods. / Radiochim. Acta *13*, 139, 145 (1970) / —Hz. [Rd 212 IE]

1,2,5,6-Tetramethylenecyclooctane *(4)*, which is of interest as a model substance for the formation of polycyclic hydrocarbons by transannular photochemical ring closure, has been synthesized in a two-step process by *W. T. Borden, L. Sharpe*, and *I. L. Reich*. Benzophenone-sensitized photodimerization of 1,2-dimethylenecyclobutane in benzene afforded *(1)*—*(3)* as major products. Pyrolysis of the crude photoproduct at 330 °C affords a 3 : 2 mixture of *(4)* and *(5)* (85% yield based



(1) *(2)* *(3)*

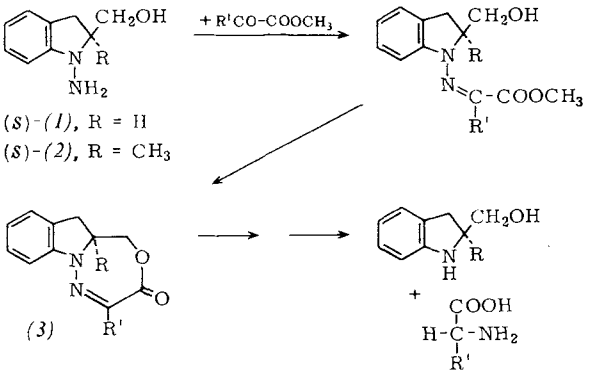


(4) *(5)* *(6)*

on 1,2-dimethylenecyclobutane), which can be separated on a preparative scale by gas chromatography. Direct photolysis of *(3)* leads solely to *(4)*; at 270 °C *(6)* is also detected. / Chem. Commun. *1970*, 461 / —Ma. [Rd 213 IE]

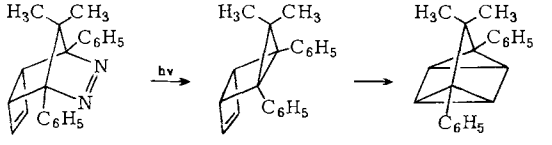
New protective groups for the phosphate residue on synthesis of deoxyribo oligonucleotides of defined sequence, namely 3-*p*-methoxyanilino-3-oxopropyl, 3-anilino-3-oxopropyl, benzylideneamino, and 3-benzylamino-3-oxopropyl groups, have been suggested by *S. A. Narang, O. S. Bhanot, J. Goodchild*, and *J. Michniewicz*. They can be removed by mild treatment with alkalis at room temperature — without simultaneous deamination. The protected di- and trinucleotides are isolated by chromatography on benzoylated DEAE cellulose and by Sephadex gel filtration. / Chem. Commun. *1970*, 516 / —Ma. [Rd 216 IE]

A new route for the asymmetric synthesis of α-amino acids with the chiral *N*-amino-2-hydroxymethylindolines *(S)-(1)* and *(S)-(2)* has been described by *E. J. Corey, R. J. McCaully*, and *H. S. Sachdev*. *(1)* and *(2)* are condensed with α-keto acids to give the chiral tricyclic compounds *(3)*. After reduction of the C=N group of *(3)* and hydrolysis of the N—N



bond and ester hydrolysis, the optically active amino acids can be isolated. D-Alanine and D-α-aminobutyric acid were prepared from pyruvic acid and α-ketobutyric acid in 80 and 90% purity respectively. / J. Amer. chem. Soc. *92*, 2476 (1970) / —Ma. [Rd 214 IE]

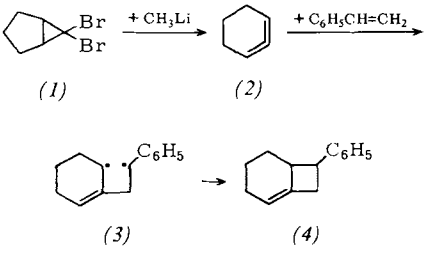
A novel rearrangement has successfully been employed by *L. A. Paquette* and *L. M. Leichter* to prepare a quadricyclane derivative *(3)* of the *trans*-tricyclo[4.1.0.$0^{2,5}$]hept-3-ene system *(2)*. The reaction can be regarded as an intramolecular capture of a 1,3-diradical by a cyclobutene ring. In the reaction of cyclobutadiene (liberated *in situ* from its tricarbonyl-iron complex) with 4,4-dimethyl-3,5-diphenyl-4*H*-pyrazole



(1) *(2)* *(3)*

the adduct *(1)* is formed which, on irradiation, is converted quantitatively into *(2)*. Compound *(3)* is obtained in quantitative yield when *(2)* is heated at 100 °C in tetrachloroethylene for four hours. This reaction can only proceed *via* a diradical. At 130 °C, *(3)* can be obtained directly from *(1)*. / J. Amer. chem. Soc. *92*, 1765 (1970) / —Kr. [Rd 218 IE]

Trapping of 1,2-cyclohexadiene *(2)* by styrene is reported on by *W. R. Moore* and *W. R. Moser*. *(2)*, which occurs as intermediate in the reaction of 6,6-dibromobicyclo[3.1.0]hexane *(1)* with methyllithium, reacts with the styrene to give *exo*- and *endo*-7-phenylbicyclo[4.2.0]oct-1-ene *(4)* (total yield



(1) *(2)*

(3) *(4)*

76%). The authors assume that the reaction of *(2)* with styrene proceeds in two steps *via* a diradical *(3)*. / J. org. Chemistry *35*, 908 (1970) / —Kr. [Rd 220 IE]

Electrochemical Processes in Fuel Cells. By *M. W. Breiter.* Vol. IX of the series "Anorganische und Allgemeine Chemie in Einzeldarstellungen". Springer-Verlag, Berlin-Heidelberg-New York 1969. 1st Edit., xi, 247p p., 98 figures, bound DM 48.—.

The present monograph deals exclusively with electrode processes in fuel cells; technological aspects are not discussed.

The material is presented concisely, and is more like a series of reviews than a textbook. The contents are therefore rather heavy, and not always easy for the non-expert to understand. For example, pages 39 to 59 of *Levich*'s book[1] have been condensed to only three pages. The problems on which the author has worked are discussed rather more fully. The depth in which the various questions are dealt with appears arbitrary. Thus the oxidation of ammonia is not even mentioned, and the reactions of hydrazine are touched on only briefly. The classification of fuel cells (p.3) includes a group b "organic electrolytes". This evidently refers to the biochemical fuel cells. However, these are not discussed further by the author.

After introductory chapters (definitions, thermodynamics, mass transfer, and electrode kinetics, 47 pp.), the adsorption of hydrogen on platinum metals and their alloys is discussed (37 pp.). This is followed by a very brief discussion of the anodic oxidation of hydrogen (11 pp.). Some results from investigations on oxygen surface films are described for platinum, nickel, silver, and carbon. The adsorption of hydrocarbons and the mode of action of the oxygen electrode in aqueous electrolytes and carbonate melts are dealt with in considerable length.

In Chapter X, on the anodic oxidation of fuels, the emphasis is placed on the study of methanol and formic acid. The book closes with some results on the properties of porous electrodes and their model treatment (30 pp.).

The present work provides a maximum of information for the number of pages available. References to the literature are very copious, though not complete. An author index would have been welcome in this respect.

The volume provides the electrochemist with a very valuable summary of a large number of investigations in a compact form. The printing and presentation of the book are excellent.

Wolf Vielstich [NB 881 IE]

Ullmanns Encyclopädie der technischen Chemie (Ullmann's Encyclopedia of Technical Chemistry). Chief editor: *W. Foerst.* Editor: *Hertha Buchholz-Meisenheimer.* Urban und Schwarzenberg, Munich-Berlin-Vienna.

Vol. 19: Zement bis Zwischenprodukte (Cement to Intermediates). 1969. 66 illustrations 418 pp., DM 120.—.

Complete Index for Vols. 1, 2/I, 2/II and 3 to 19 with references to the supplementary volume. 1969. 354 pp., DM 80.— price of the two volumes together DM 190.—.

Supplementary Volume: New Processes, New Products, Economic Developments. 1970, 175 illustrations + 846 pp., DM 198.—

19 years after work on the project began, the publication of these three volumes[*] completes the encyclopedia, which has a total of 16243 pages and 808 articles, with contributions from more than 1000 authors. The individual fields dealt with are as follows: organic intermediates and chemicals 16.2%, inorganic chemistry 11.2%, metals 8.7%, drugs, natural products (alkaloids, vitamins, hormones), cosmetics, and perfumes 8%, plastics, lacquers, and rubber 7.1%, physical methods in the laboratory 6.2%, construction of apparatus and process technology 6.1%, fuels and petrochemistry 6%, fibers, wood, cellulose 5%, food, fats, and foodstuffs 4.6%, dyes and dyeing 4.4%, production supervision 4.2%, ceramics, silicate chemistry, cement, other building materials, glass, enamels 2.9%, and miscellaneous (including fertilizers, pest control, nuclear energy, isotopes, and atomic structure) 9.4%. The work contains a unique assortment of material, giving a coherent picture of the whole field of technological chemistry including the economic principles of this branch of science, manifestly an enormous and bold undertaking in view of the rapid development of science and technology in the postwar period, which is clearly mirrored in the 22 volumes.

Volume 19 contains sections on intermediate products (147 pp.), zinc, zinc alloys, and zinc compounds (107 pp.), sugar and confectionery (62 pp.), cement (34 pp.), tin, alloys of tin, and tin compounds (31 pp.), zirconium and zirconium compounds (24 pp.), and flammables (9 pp.), with contributions from 22 authors, of whom 20 work in industry and 2 in universities. *H. Morchel*'s (Farbenfabriken Bayer) article on "Intermediates" deserves special attention. He concentrates on aromatic and heterocyclic intermediate products, tabulating in twenty subdivided synopses the methods of preparation for 1400 compounds arranged in order of precedence on the basis of the introduction of functional groups. The article gives detailed references to the original literature and to relevant sections in the encyclopedia. Dye chemists in particular will find this section useful, with its comprehensive coverage and novel way of classifying the material.

The index volume is of considerable importance to the complete work, and the editors have therefore devoted particular attention to it. Chemical technology is developing so rapidly that it is difficult to classify it on a systematic basis. Nor has it been possible to avoid overlapping in the case of this encyclopedia, where a lexical arrangement has been chosen for the articles which are of varying length and are in some cases presented in monographic form. Moreover, the later volumes have to take into account and incorporate progress made in the fields dealt with earlier. This means that any system for the classification of material of this type is far from perfectly practicable, and a comprehensive and reliable keyword index becomes all the more important. The present index volume contains 354 pages and about 30000 keywords, covering the whole field of technological chemistry. Important keywords are provided with comprehensive and subdivided textual references. For example, the keyword "rubber", is accompanied by 150 references covering such topics as recovery, use, grades, processes, and economic considerations. To facilitate the search for subjects the index also contains a number of titles arranged both as independent keywords and as subdivisions under main entries. Normal and bold type is used for quoting page references, the difference showing where more detailed treatments of the relevant topic can be found. It is easy to see that all the material contained in this encyclopedia can quickly be found by means of the index.

The supplementary volume is a useful and interesting addition to the complete work. This volume contains articles on organic intermediate products (131 pp.), plastics and plastics products (85 pp.), drugs (81 pp.), economic development and its importance in the chemical industry (78 pp.), petrochemical bases (53 pp.), fertilizers (41 pp.), metals (34 pp.), rubber (31 pp.), dyes and optical brighteners (28 pp.), fibers (25 pp.), nuclear energy (25 pp.), petroleum (21 pp.), and a number of shorter sections, with contributions from 177 authors. The subject matter of the book is varied and stimulating since the editors with the experience of the previous 21 volumes behind them and suitable contacts with specialists have gathered together new and interesting material from all fields. This volume can also be bought singly, and makes worthwhile reading independent of the encyclopedia. New fields like lasers, holography, and nuclear energy are described with

[1] *V. G. Levich:* Physicochemical Hydrodynamics. Prentice-Hall, Englewood Cliffs, N. J., 1962.

[*] See Angew. Chem. *81*, 472 (1969); Angew. Chem. internat. Edit. *8*, 465 (1969).

maximum clarity, but it has also been necessary to include reports on the revolutionary progress made in classic processes. We find, for example, that the ammonia process has changed fundamentally in the last decade. Petrochemical synthesis gas production has become established, new catalysts allow almost complete CO conversion at low temperatures, and with the development of the turbocompressor there has been a transition to a single-line plants with capacities of 1000 t/day.

In addition to the varied scientific and technical developments reported in this volume, particular mention should be made of the article on the development of science, which gives an impressive picture of the dynamics and importance of technological chemistry. The global chemical production has quintupled in the last twenty years, and will continue to increase at this exponential rate. The pipeline network for oil and petrochemical products amounts to 40 times the circumference of the earth and is increased by 15000 to 20000 km a year. Between the years 1958 and 1968 the world production of synthetic fibers increased ninefold. In contrast to other large industries, the chemical industry deals at the same time with the production of basic substances, intermediates, and consumer articles. Unlike any other industry, it acts both as a supplier and as a purchaser in all fields of the economy, and is thus perpetually involved in the development of human relationships and social life. With its abundant key figures, this article gives a clear survey of development trends.

In view of this dynamism one may well wonder to what extent a field subject to such far-reaching changes can be covered by an encyclopedia. In fact, the achievements and difficulties of our scientific and technological development are mirrored in the achievements and problems of the present Ullmann Encyclopedia. A characteristic of our time is that the quantity of information increases more quickly than it can be arranged and classified. New documentation systems are being developed so that we can remain masters of this situation and store information in readily available form. Electronic information services, however necessary and important they are, can only store material; they cannot sift through it, evaluate it or select what is important — they cannot process (reduce and compress) the information. The more quickly a field changes and grows the more important the condensation of material becomes, so that a survey of trends and developments is available. If there is no overall survey, contact and understanding between allied branches are lost and hence also the possibility of fruitful cooperation.

Furthermore, difficulties will be created if this welter of material is handed down in disorder to the next generation. There is little point in supplying students with the newest and most up-to-date information — it will be out of date by the time they are ready to use it — but there must be a comparative penetration of the material so that the essential principles, which will play a decisive role in development, can be worked out. A large number of our educational difficulties arise because we neglect the didactic processing and condensation of knowledge in the process of searching out new material. In the case of many students this leads not only to difficulties in understanding but also to misconceptions and highly undesirable attitudes to this complex of modern chemical practice which is so important for our very existence.

Ullmann can be considered as a comprehensive personal interpretation of chemical technology and the chemical industry; it is an example of the fact that abstract modern theory can successfully be shown to have relevance to the accepted for mulas already used in practice. It is written in such a way that anyone can obtain information on the main aspects of a related field in which he is not at home. Finally, therefore, we must thank the authors who have taken the time, for the most part in spite of pressing practical duties, to describe their work to a wider circle of colleagues, and in particular the management and editors who have managed to coordinate all this work and produce an encyclopedia which, as its name implies, deals coherently with the whole sphere of chemical and technological knowledge.

Hans Sachsse [NB 889 IE]

The Wave Mechanics of Atoms, Molecules and Ions. By *C. J. H. Schutte*, Edward Arnold (Publishers) Ltd., London 1968. 1st Edit., xiii + 502 pp., numerous figures, bound, 84 s.

Many of the modern textbooks devoted to the subject of wave mechanics and molecules suffer from the disadvantage, in particular as regards the chemistry student, of assuming either a very extensive or a very meager knowledge of mathematics on the part of the reader. Consequently, the understanding of the chemical bond is often inadequate.

The present book attempts to tread the middle path, and in fact the author does succeed in striking a happy medium between the two extremes.

The book consists of three main parts, the first of which deals with the principles of wave mechanics. Numerous examples are given starting with classical mechanics. Perhaps it was not entirely necessary to include *Bohr*'s postulates, which have now passed into history and which have been extended by wave mechanics. On the other hand, the reviewer finds it it highly sensible to present the fundamentals with the aid of operator algebra. The perturbation method is discussed at length.

The second part consists of a total of 11 sections in which the individual methods of quantum chemistry are dealt with: First of all a particle in simple potential fields, then the harmonic oscillator in its application to spectroscopy. Rotational and vibrational states are considered next. The 5th section deals with the hydrogen atom, and the 6th with polyelectronic atoms. Sections 7 and 8 are devoted to group theory and, finally, the last three sections are concerned with di- and polyatomic molecules and with a number of applications of the Hückel theory.

The third part of the book deals exclusively with spectroscopy. An introduction to the principles of spectroscopy is followed by a discussion of the spectroscopic behavior of rotational states, vibrational states, and finally, of complex compounds, including magnetic effects.

Exercises are given with each section, the solutions being collected at the end of the book. There is also an appendix on symmetry groups.

The book is clearly written, well illustrated, and provided with a very detailed subject index. It can be emphatically recommended to every student of chemistry. Even those who merely want to acquaint themselves with the field will find it to be an excellent introduction.

Heinzwerner Preuss [NB 886 IE]

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Recent Results on the Biochemistry of the Cell Wall Lipopolysaccharides of *Salmonella* Bacteria[**]

By Otto Lüderitz[*]

Lipopolysaccharides, which are located in the cell wall of gram-negative bacteria, are characterized by their biological versatility. They represent the O antigens of the bacteria, they are potent endotoxins, and they often function as the receptor sites for bacteriophages. The study of the mode of action of lipopolysaccharides and the search for structures in the macromolecules that are responsible for biological activity became promising when principles of the chemical fine structure of lipopolysaccharides were identified. The following review summarizes the results of recent investigations regarding the structure of lipopolysaccharides, their biosynthesis and its genetic determination.

1. Introduction[***]

The great achievement of *Fritz Kauffmann* is the Kauffmann-White scheme[1,2], in which hundreds of bacterial species belonging to the genus *Salmonella* are classified according to their serological and biochemical properties. This classification provided the starting point and has since served as a basis for all chemical and biochemical work on *Salmonella* lipopolysaccharides. This is illustrated in Table 1, which summarizes the results we obtained about ten years ago, together with *Kauffmann*, when we subjected a first series of *Salmonella* species to immunological and chemical study. At that time, our efforts were directed to the correlation of the serological classification of these species with the sugar composition of their surface antigens. The fourteen *Salmonella* species listed in Table 1 are representative of the groups A–E of the Kauffmann-White scheme, and it was at this point that it first became clear that the lipopolysaccharides of species belonging to the *same* serogroup contain identical sugar units. There exists a close relationship between the *serotype* of a species and the *chemotype*

Table 1. Serological and chemical classification of some *Salmonella* species: serotypes-chemotypes [3].

Species	Group	Antigen factors [a]	O-specific sugars in the lipopolysaccharides
S. paratyphi A	A	1, 2, 12	mannose, rhamnose, paratose
S. paratyphi B	B	*4*, 5, 12	mannose. rhamnose, abequose
S. typhimurium		*4*, 5, 12	mannose, rhamnose, abequose
S. abortus equi		*4*. 12	mannose. rhamnose, abequose
S. paratyphi C	C	*6*, 7	mannose
S. cholera suis		*6*, 7	mannose
S. montevideo		*6*, 7	mannose
S. typhi	D	*9*, 12	mannose, rhamnose, tyvelose
S. enteritidis		1, *9*, 12	mannose, rhamnose, tyvelose
S. sendai		1, *9*. 12	mannose, rhamnose, tyvelose
S. anatum	E	*3*. 10	mannose, rhamnose
S. newington		*3*, 15	mannose, rhamnose
S. minneapolis		(*3*),(15),34	mannose, rhamnose
S. senftenberg		1, *3*, 19	mannose, rhamnose

[a] Antigen factors represent a subdivision of the O antigens (for their structure see 5.2).

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[**] Taken from the F. I. Huddleson Memorial Lecture given at the Michigan State University, East Lansing, Oct. 23, 1968; see *O. Lüderitz*, Jahrb. Max-Planck-Ges. *1969*, 93.

[***] Abbreviations: Glc = Glucose, Gal = Galactose, Man = Mannose, Hep = L-Glycero-D-mannoheptose, KDO = 2-Keto-3-deoxyoctonic acid, Rha = Rhamnose, Fuc = Fucose, Abe = Abequose, Par = Paratose, Tyv = Tyvelose, GlcN = Glucosamine, GalN = Galactosamine, Ac = Acetyl, EtN = Ethanolamine, P = Phosphate groups.

[1] *F. Kauffmann*: Die Bakteriologie der Salmonella Species. Munksgaard, Copenhagen 1961.

[2] *F. Kauffmann*: The Bacteriology of Enterobacteriaceae. Munksgaard, Copenhagen 1966, 2nd Edit.

of its lipopolysaccharide. This was later shown to be true for the species of all *Salmonella* groups of the Kauffmann-White scheme [3].

Groups A–E contain approximately 500 species and the Kauffmann-White scheme includes about 45 groups. Each *Salmonella* species is characterized by the serological specificities of the heat-stable O antigen (lipopolysaccharide), and the heat-labile H (flagellar) antigen. By analogy, *E.coli* [4], *Shigella* [5], and other genera were classified later in a similar way. The designation of antigens as O and H has an historical origin and refers to flagellated and non-flagellated proteus strains. H comes from the German "mit *H*auch". O comes from "*o*hne Hauch", and both terms were meant to describe the morphological appearance of the cultures.

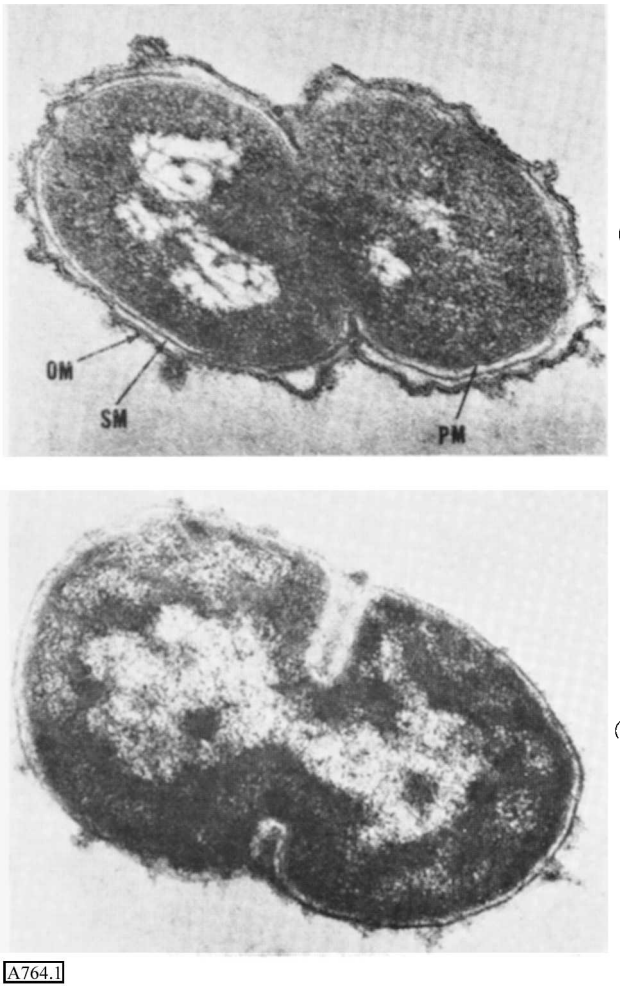
2. Isolation and Biological Properties of Lipopolysaccharides

Since the introduction of the classical extraction methods of *Boivin* and *Mesrobeanu* [6], *Morgan* [7], and *Goebel et al.* [8], a series of further methods has been developed for the isolation of lipopolysaccharides from gram-negative bacteria. Among these procedures the phenol/water method [9] has been widely adopted because of its wide range of applicability, and has been used in our laboratory for routine isolation of lipopolysaccharides.

Dried bacteria are heated at 68 °C for a short time in a mixture of phenol and water (45 : 55, v/v), whereupon the protein/lipid/lipopolysaccharide complexes of the cell wall dissociate and the components are released into the solution. The mixture which is monophasic at this temperature separates into two layers on cooling and centrifugation. The extracted cell residues appear at the bottom; the lower phenol phase contains lipids and proteins and the upper aqueous phase contains the desired lipopolysaccharide alongside nucleic acids and polysaccharides. After high speed ultracentrifugation (100000 g), the lipopolysaccharide is obtained as a sediment, and is finally lyophilized (1–4 % of the dry bacterial weight). The lipopolysaccharide thus extracted dissolves in water to give an opalescent solution.

Recently, a very mild extraction procedure has been worked out (PCP method) [10], which enables the isolation of exclusively R form lipopolysaccharides.

Electron-microscope studies carried out by *Bladen* and *Mergenhagen* [11] (Fig. 1) provide impressive evidence of the morphological changes on the bacterial cells after phenol/water extraction. Only the outer, plastic layer



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Fig. 1. Electron micrograph (approx. 75000× magnification) of *Veillonella* bacteria a) before and b) after extraction with phenol/water [11] OM = outer membrane, SM = solid membrane, PM = plasma membrane.

of the cell, the cell wall (OM, outer membrane), is dissolved away; the cell itself, surrounded by the plasma membrane (PM) and the rigid layer (SM, solid membrane), remains intact. These pictures show that lipopolysaccharides (complexed with proteins and lipids) are located on the surface of the bacterial cell, and it is likely that in this exposed state they play a special role in the interactions between bacterial cell and host organism in the course of an infection. The validity of this statement is supported by the fact that many of the endotoxic manifestations appearing during an infection can also be simulated when purified lipopolysaccharides are injected into animals.

Among the manifold endotoxic activities of lipopolysaccharides, their pyrogenicity is most remarkable (Fig. 2). Injection of 1 μg in man (and correspondingly smaller amounts in experimental animals) results, after a short latent period, in the development of fever, with body temperatures reaching up to 40 °C. Simultaneously, drastic changes occur in the white blood picture, *i.e.* leucopenia, followed by a pronounced leucocytosis. Many other biological manifestations of endotoxins can be observed, such as changes in blood pressure, fibrinolytic activity, complement activation, changes of resistance to infection, Shwartzman-activi-

[3] *F. Kauffmann, O. Lüderitz, H. Stierlin,* and *O. Westphal,* Zbl. Bakteriol., Parasitenkunde, Infektionskrankh. Hyg., I. Abt., Orig. *178,* 442 (1960).

[4] *F. Ørskov, I. Ørskov, B. Jann, K. Jann, E. Müller-Seitz,* and *O. Westphal,* Acta pathol. microbiol. scand. *71,* 339 (1967).

[5] *D. A. R. Simmons,* European J. Biochem. *11,* 554 (1969).

[6] *A. Boivin* and *L. Mesrobeanu,* Revue d'Immunologie *1,* 553 (1935).

[7] *W. T. J. Morgan,* Biochem. J. *31,* 2003 (1937).

[8] *W. F. Goebel, F. Binkley,* and *E. Perlman,* J. exp. Medicine *81,* 315 (1945).

[9] *O. Westphal, O. Lüderitz,* and *F. Bister,* Z. Naturforsch. *7b,* 148 (1952).

[10] *C. Galanos, O. Lüderitz,* and *O. Westphal,* European J. Biochem. *9,* 245 (1969).

[11] *H. A. Bladen* and *S. E. Mergenhagen,* J. Bacteriol. *88,* 1482 (1964).

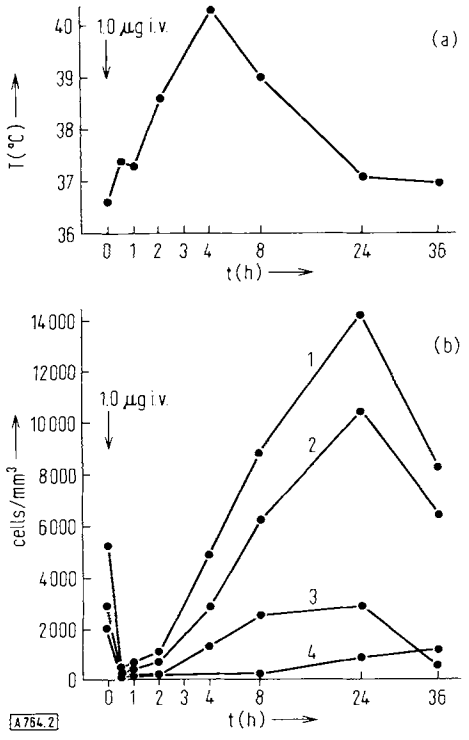


Fig. 2. Changes in the body temperature a) and white blood count b) following the injection of 1 µg of a *Salmonella* lipopolysaccharide into man. 1: Total number of leucocytes; 2: granulocytes; 3: stabs; 4: lymphocytes.

ty, adjuvant-activity and, with larger amounts of lipopolysaccharide, lethal toxicity [12–14].

In addition to these non-specific endotoxic reactions, which are more or less common to all lipopolysaccharides, highly specific processes are also stimulated. Lipopolysaccharides constitute the O antigens of bacteria, and their introduction into the organism induces production of specific antibodies that are directed against specific structures in the lipopolysaccharide molecule used for immunization.

Lipopolysaccharides frequently exhibit a further distinct activity. They function as the specific receptor sites on the cell for a number of phages [15,16]. Fig. 3a shows an electron micrograph by *Lindberg* [17] which was obtained after incubation of Felix O1-phages with lipopolysaccharide from an *S.minnesota* Ra mutant (see Table 6). It can be seen that the phages are fixed by their tails to the chains of aggregated lipopolysaccharide. The phages that have released their contents on contact are present as ghosts. The high degree of specificity underlying this interaction is demonstrated in Fig. 3b where the same phage has been incubated with lipopolysaccharide isolated from a different, but closely related, strain. This (Rb) lipopolysaccharide

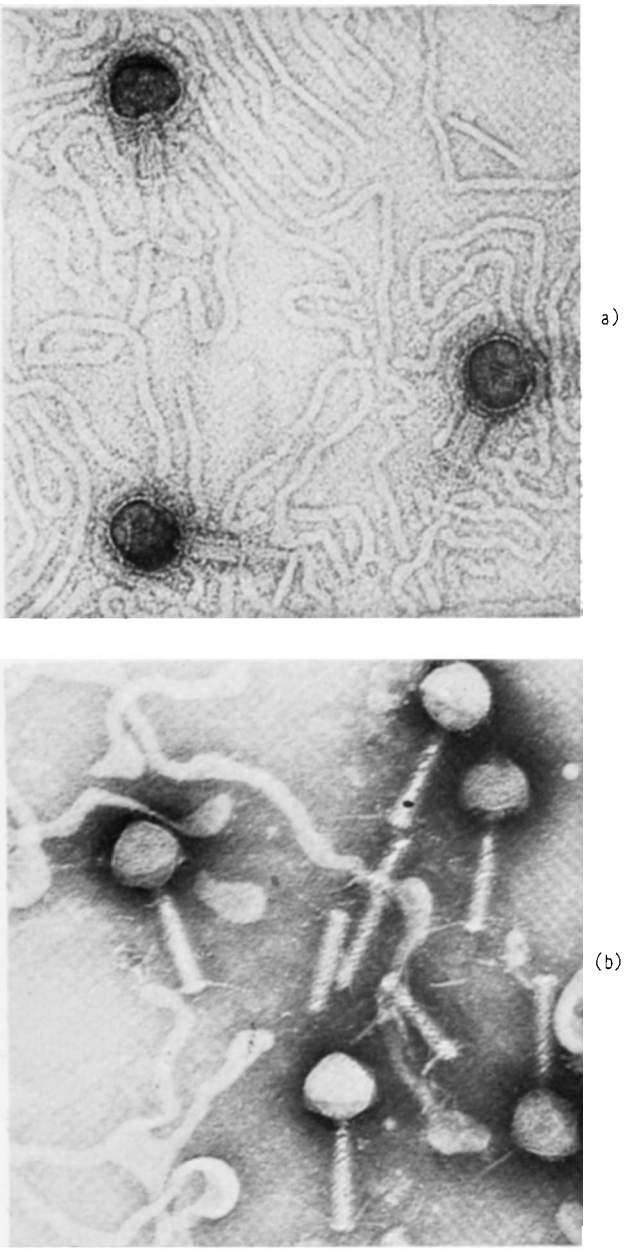


Fig. 3. Electron micrograph (approx. 400000 × magnification) of Felix 01 phages in admixture with lipopolysaccharides from a) *S. minnesota* Ra and b) *S. minnesota* Rb bacteria. The phages have reacted only with the Ra lipopolysaccharide [17].

differs from the preceding one only by the absence of *one terminal* sugar constituent, namely *N*-acetylglucosamine (see Table 6). This minor alteration in structure, however, causes a dramatic change in the specificity of the receptor, so that fixation of this phage, and its consequent inactivation, are no longer possible.

All the properties so far mentioned show clearly that the lipopolysaccharides of gram-negative bacteria represent a unique group of natural polymers, endowed with a great number of distinct biological activities. Inevitably a series of questions arises, regarding the structure of these substances, the mechanism of their action *in vivo*, as well as the question of the presence, in these macromolecules, of structural groupings or configurations which make it possible for them to act as antigens, endotoxins [12–14], or as phage receptors.

[12] *M. Landy* and *W. Braun*: Symposium on "Bacterial Endotoxins". Rutgers Univ. Press, New Brunswick 1964.

[13] *A. Nowotny*: Symposium on "Molecular Biology of Gram-Negative Bacterial Lipopolysaccharides", Ann. New York Acad. Sci. *133*, 279 (1966).

[14] *L. Chédid*: La Structure et les Effects Biologiques des Produits Bactériens provenants de Germes Gram-Négatifs. Coll. Intern. C.N.R.S., Paris, Oct. 24–26, 1967, Vol. *174*, (1969).

[15] *W. F. Goebel* and *M. A. Jesaitis*, J. exp. Med. *96*, 425 (1952).

[16] *W. Weidel* and *E. Kellenberger*, Biochim. biophysica Acta *17*, 1 (1955).

[17] *A. A. Lindberg*, J. gen. Microbiol. *48*, 225 (1967).

3. General Principles of Lipopolysaccharide Structure

As early as 1960, before structural chemical investigations had been undertaken, a series of analytical and biochemical results led to the assumption that lipopolysaccharides are built up according to a common general principle, and contain three regions of dissimilar structure. This concept (Fig. 4) has since proved to be correct.

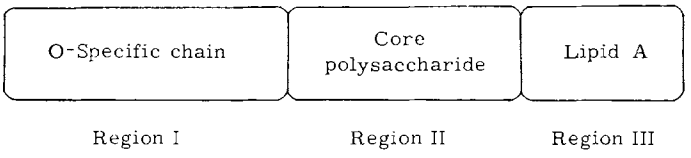


Fig. 4. The three structural regions and their sequence in lipopolysaccharides.

All lipopolysaccharides contain a lipid component, the so-called *lipid A* (region III), to which the *core polysaccharide* (region II) is bound. In closely related lipopolysaccharides, such as those of *Salmonella*, the structure of this core is identical or very similar. To region II are linked the *O-specific chains* (region I). It is by this part of the molecule that the lipopolysaccharides of different species are differentiated from one another. The type, sequence, as well as the nature of the linkages of the sugars in region I are specific for each individual lipopolysaccharide. Region I, which carries the serological specificity of each lipopolysaccharide, provides the close correlation that exists between the serological classification into serotypes and the chemical classification into chemotypes.

It should be emphasized that innumerable gram-negative species (serotypes) exist in nature, of which thousands have already been identified and characterized. Accordingly, thousands of serologically distinct lipopolysaccharides are in principle available, and in fact several hundreds have already been isolated in recent years. All lipopolysaccharides possess the general structure shown in Fig. 4. This large unique class of macromolecules constitutes an ideal subject for comparative investigations.

4. The Sugar Composition of *Salmonella* Lipopolysaccharides

The sugar units that have been identified in *Salmonella* lipopolysaccharides are shown in Table 2 [18,19]. The complexity of their structures is illustrated by the fact that they contain at least five, and some as many as nine, different sugar units. The 18 monosaccharides that have been found can be divided into two groups: the five "*basal sugars*" are common to all lipopolysac-

Table 2. *Salmonella* lipopolysaccharides: sugar composition and classification into chemotypes [3]. ● = basal sugar, ○ = specific sugar.

Chemotypes	3-Amino-3,6-dideoxyglucose	3-Amino-3,6-dideoxygalactose	2-Amino-2,6-dideoxyglucose	D-Mannosamine	D-Galactosamine	D-Glucosamine	2-Keto-3-deoxyoctonate	L-Glycero-D-mannoheptose	D-Galactose	D-Glucose	D-Mannose	L-Fucose	L-Rhamnose	D-Ribose	Colitose	Abequose	Paratose	Tyvelose	O Groups
I						●	●	●	●	●									V, X, Y
II					○	●	●	●	●	●									L, P, 51
III						●	●	●	●	●	○								C_1, C_4, H
IV					○	●	●	●	●	●	○								K, R
V						●	●	●	●	●		○							W
VI					○	●	●	●	●	●		○							G, N, U
VII						●	●	●	●	●			○						59
VIII					○	●	●	●	●	●			○						53,57
XXV						●	●	●	●	●				○					52
IX					○	●	●	●	●	●				○					56
X						●	●	●	●	●					○				O
XI					○	●	●	●	●	●					○				Z
XII					○	●	●	●	●	●	○	○							I
XIII						●	●	●	●	●	○		○						E, F, 54
XIV						●	●	●	●	●	○		○			○			B, C_2, C_3
XV						●	●	●	●	●	○		○				○		A
XVI						●	●	●	●	●	○		○					○	D_1, D_2
XXXIV				○		●	●	●	●	●									J
XXXV				○		●	●	●	●	●			○						T
XXXVI			○			●	●	●	●	●									58
XXXVII			○			●	●	●	●	●	○								S
XXXVIII		○			○	●	●	●	●	●									55
XXXII	○				○	●	●	●	●	●			○						M (28_1, 28_3)
XXXIX	○				○	●	●	●	●	●				○					M (28_1, 28_2)
XXXX	○				○	●	●	●	●	●	○	○							Q

[18] *O. Lüderitz, A. M. Staub,* and *O. Westphal,* Bacteriological Reviews *30*, 192 (1966).

[19] *O. Lüderitz, K. Jann,* and *R. Wheat* in *M. Florkin* and *E. H. Stotz*: Comprehensive Biochemistry. Vol. 26 A, Elsevier, Amsterdam 1968, p. 105.

charides; they constitute the core polysaccharide (region II) and will be discussed in Section 6. The "*specific sugars*" of the second group occur in various combinations. Each individual sugar combination denotes the chemotype of a lipopolysaccharide for which it is specific. While some sugars are widely distributed in natural products, others, such as those belonging to the stereoisomeric 3,6-dideoxyhexoses or the 2- and 3-amino-6-deoxyhexoses, were first found in lipopolysaccharides. The list of chemotypes is probably still incomplete and new sugars may yet be found in the various *Salmonella* lipopolysaccharides.

In lipopolysaccharides obtained from other genera additional sugars were found: 4-amino-6-deoxy-D-glucose and -D-galactose; 2-amino-6-deoxy-D-glucose, -D- and -L-galactose, -L-mannose; D-glycero-D-manno- and -D-galacto-heptose; 2-amino-D-glyceroheptose; 6-deoxy-L-talose; D-rhamnose; ascarylose; glucuronic acid; galacturonic acid (see [19,20]).

5. The O-Specific Chains (Region I)

5.1. The Structure of the O-Specific Chains in Some Lipopolysaccharides

The realization that the role of the specific sugars is concerned exclusively with the building up of the O-specific chains (region I) has considerably advanced research on this part of the lipopolysaccharides, and in some cases has led to complete elucidation of the structure. Credit for these results goes mainly to *Staub et al.* [18–20] and *Robbins et al.* [21], who were able to reconstruct the complete structure of region I by studying fragments from partial hydrolyzates of the lipopolysaccharides with the aid of immunochemical methods. Recently, the suggested structures were confirmed and supplemented by *Lindberg et al.*, who applied the latest methods of methylation analysis [22–24].

Partially methylated sugars obtained by hydrolysis of fully methylated polysaccharides are converted to the *O*-acetyl-*O*-methylalditols. They are then identified by a combination of GLC and mass spectrometry. Methods have been worked out for the localization of acetyl groups. These have the advantage of being independent of individually synthesized, partially methylated sugar standards. By undermethylation, all theoretically possible partially methylated derivatives can be obtained. After reduction and acetylation the components of such mixtures can be characterized by gas chromatography and mass spectrometry (retention times).

The results of these investigations showed that O-specific chains are made up of a series of identical oligosaccharides, the *repeating units*. As an example, the lipopolysaccharide of *S.newington* (3, 15) is shown in Fig. 5. In this case, the specific chains (region I) contain 10 to 20 trisaccharide units of mannose, rhamnose, and galactose. They are linked to the lipid A, *via* the core polysaccharide, to form the complete lipopolysaccharide.

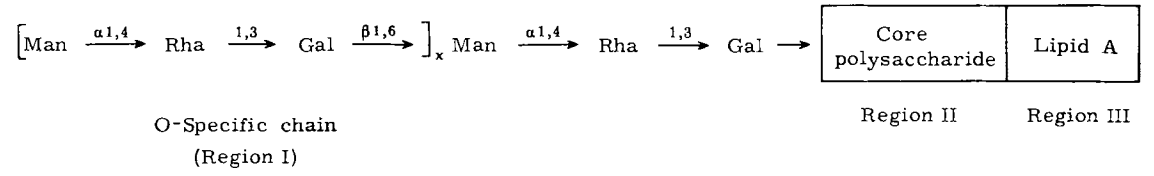


Fig. 5. Structure of the O-specific chains (region I) in the lipopolysaccharide of *S.newington* (3, 15) [21].

Table 3 shows the repeating units which constitute the O-specific chains of *Salmonella* serotypes belonging to groups B, D, and E [19–21,24]. They all contain a trisaccharide of mannose, rhamnose, and galactose, but are different with respect to their linkages and substituents.

Table 3. The "repeating units" of the O-specific chains in the lipopolysaccharides of *Salmonella* groups B, D, and E [18,21,23,24,24a].

Serogroup	O Factors	Repeating units
E_1	3, 10	6 → Man α1,4 → Rha 1,3 → Ac Gal α1 →
E_2	3, 15	6 → Man α1,4 → Rha 1,3 → Gal β1 →
E_3	(3),(15), 34	6 → Man α1,4 → Rha 1,3 → Glc ↓α1,4 Gal β1 →
E_4	1, 3, 19	6 → Man α1,4 → Rha 1,3 → Glc ↓α1,6 Gal α1 →
D_2	(9), 46	6 → Tyv ↓α1,3 Man α1,4 → Rha 1,3 → Gal α1 →
B	1, 4, 12	2 → Abe ↓α1,3 Man (β)1,4 → Rha 1,3 → Glc ↓α1,6 Gal α1 →
B	1, 4, 5, 12	2 → 2-Ac-Abe ↓α1,3 Man 1,4 → Rha 1,3 → Glc ↓α1,6 Gal α1 →
B	1, 4 12, 27	6 → Abe ↓α1,3 Man (β)1,4 → Rha 1,3 → Glc ↓α1,6 Gal α1 →
D_1	9, 12	2 → Tyv ↓α1,3 Man 1,4 → Rha α1,3 → 2-Ac-Glc ↓α1,4 Gal α1 →

Oligosaccharide units that were isolated from lipopolysaccharides of other *Salmonella* groups are shown in Table 4 [18,25]. As expected (see Table 2), these oligo-

[20] *O. Lüderitz, O. Westphal, A. M. Staub*, and *H. Nikaido* in *S. J. Ajl, G. Weinbaum*, and *S. Kadis*: Microbial Toxins. Academic Press, Vol. III, in press.

[21] *P. W. Robbins* and *T. Uchida*, Biochemistry *1*, 323 (1962).

[22] *H. Björndal, C. G. Hellerqvist, B. Lindberg*, and *S. Svensson*, Angew. Chem. *82*, 643 (1970); Angew. Chem. internat. Edit. *9*, 610 (1970).

[23] *C. G. Hellerqvist, B. Lindberg, S. Svensson, T. Holme*, and *A. A. Lindberg*, Carbohydrate Res. *8*, 43 (1968).

[24] *C. G. Hellerqvist, B. Lindberg, S. Svensson, T. Holme*, and *A. A. Lindberg*, Carbohydrate Res. *9*, 237 (1969).

[24a] *Note added in proof*: There was some confusion regarding the anomeric linkages of mannose in the lipopolysaccharides of groups B and E [56]. From recent results of the groups of *B. Lindberg* (Stockholm) and *F. Egami* (Tokyo) it is now clear that mannose in group B is α-linked and in group E β-linked. For technical reasons, Table 3 and Figures 6 and 9 were not changed. Only Fig. 16 contains the correct linkages of mannose.

[25] *N. Fuller, M. Etiévant*, and *A. M. Staub*, European J. Biochem. *6*, 525 (1968).

Table 4. Structure of the O-specific chains in the lipopolysaccharides of *Salmonella* groups L, G, N, U, C [18, 25].

Sero-group	O-Specific chain
L (21)	→ [Gal (↓) Gal —β 1,3→ GalNAc → GalNAc (↓α GalNAc)] →
G (13, 22)	→ [Gal —β 1,3→ Glc? GalNAc —1,3→ GalNAc → Fuc] →
N (30)	→ [Glc —β 1,3→ GalNAc (↓1,4 Glc) → Fuc] →
U (43)	→ [Gal (↓α 1,3 Gal) —β 1,3→ GalNAc —1,3→ GlcNAc —1,4→ Fuc] →
C (6, 7)	→ [Man —1,2→]$_2$ Man —1,2→ Man —1,3→ GlcNAc (↓1,3 Glc)] →

saccharides are considerably different in their sugar composition and structure from the structurally related oligosaccharides of Table 3.

The oligosaccharide units shown in Fig. 5 and Tables 3 and 4 not only provide some evidence of the great variety of possible lipopolysaccharide structures that are present in bacteria, but also contribute to the recognition of one fundamental principle, *i.e.*, that identical repeating units form the structural units of the O-specific chains.

The results described so far lead to a series of questions, which will be discussed in the subsequent Sections. The O-specific chains carry the serological specificities of the lipopolysaccharides: which chemical structures correspond to the serological determinants, *i.e.* the antigen factors of the Kauffmann-White scheme? How are the side chains synthesized in the cell and how is their biosynthesis genetically determined? We have seen that the building up of the side chains in lipopolysaccharides of different species can be very similar (Table 3); are there any genetic relationships present within these species? The answer to these questions has been an essential target in recent research.

5.2. Localization of Determinant Groups (O-Antigen Factors) in O-Specific Chains

Immunochemical investigations led *Staub* [18, 20] and *Robbins* [26] to the identification of concrete structures in the O-specific chains, the serological determinants, which carry the specificity of the O factors of the Kauffmann-White scheme. By precipitation inhibition tests the monosaccharide is determined which gives the highest inhibition of a factor/anti-factor system. The monosaccharide that possesses the highest affinity for the anti-factor antibody is called the *immunodominant sugar* [18] (abequose in the 4 anti-4 system, mannose in the 3 anti-3 system, and so on). Oligosaccharide fragments containing the immunodominant sugar are then similarly tested for precipitation inhibition. The oligosaccharide displaying the highest inhibition activity has the same structure as the O factor under test. Figure 6 features the structures of determinant groups and their location in the O-specific chains [18, 20].

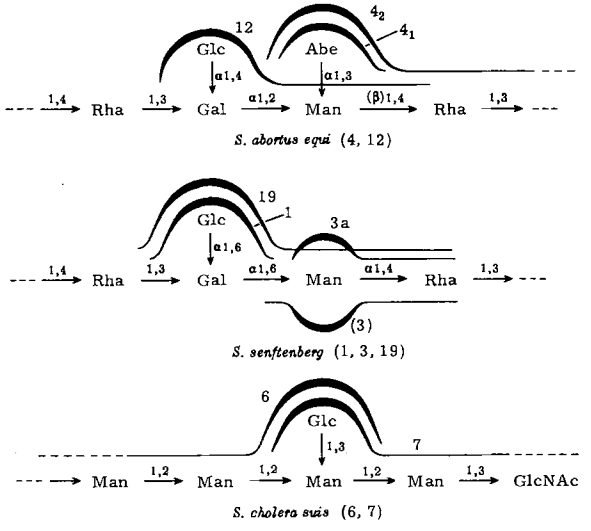


Fig. 6. Distribution of serologically determinant groups along the O-specific chains of lipopolysaccharides [18, 20, 24a].

These investigations have led to the following results [20]:

a) In theory, *each sugar unit* can function as immunodominant sugar.

b) The determinant structures *overlap* along the O-specific chain (*i.e.* factors 12 and 4, 19 and 3a).

c) *A family of antibodies* is produced against a single immunodominant sugar. These antibodies are directed against larger or smaller areas of the determinant groups. (*i.e.* factors 4$_1$, 4$_2$, and 1,19).

d) A determinant group commences with the immunodominant sugar and can extend to the right or to the left or in both directions to *neighboring sugars* (*i.e.* factors 6 and 7).

e) The Kauffmann-White scheme is an intentionally simplified one: many O factors can actually be differentiated into *subfactors* (*e.g.* factor 4 in 4$_1$, 4$_2$; factor 3 in (3), 3a).

5.3. Biosynthesis of the O-Specific Chains (Region I)

The reaction steps involved in biosynthesis of the O-specific chains are represented in Fig. 7 for *S.newington* (3, 15) as an example [27–30]. Throughout the biosynthetic pathway, the intermediate products are attached *via* a pyrophosphate bridge to the "Antigen Carrier Lipid" (ACL), a polyisoprenoid alcohol with 55 C atoms. In the first step the sugar residues, from the form of their activated derivatives (in the case of *S.newington* UDP-galactose, TDP-rhamnose, and GDP-mannose), are combined into a repeating unit by the

[26] *T. Uchida, P. W. Robbins,* and *S. E. Luria,* Biochemistry *2,* 663 (1963).

[27] *H. Nikaido,* Advances in Enzymol. *31,* 77 (1968).

[28] *M. J. Osborn, S. M. Rosen, L. Rothfield, L. D. Zeleznick,* and *B. L. Horecker,* Science (Washington) *145,* 783 (1964).

[29] *B. L. Horecker,* Annu. Rev. Microbiol. *20,* 253 (1966).

[30] *R. Losick* and *P. W. Robbins,* Sci. American *221,* 121 (1969).

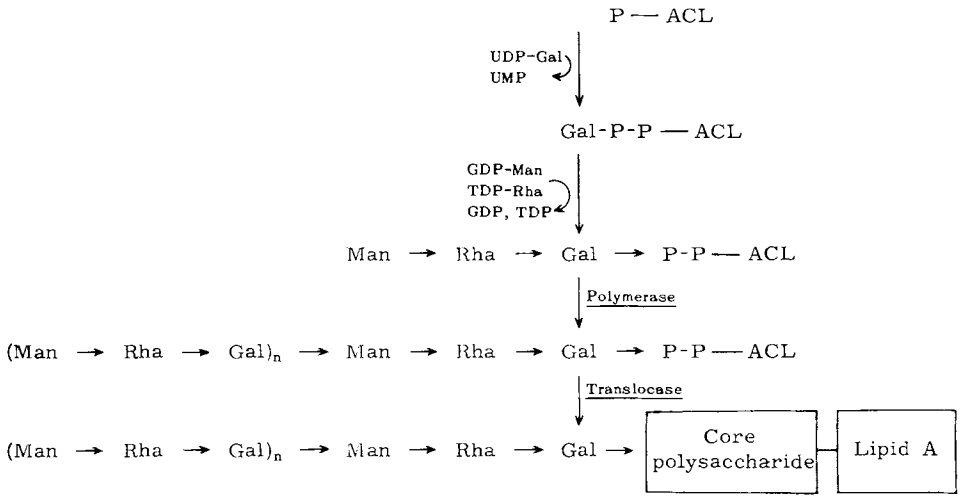
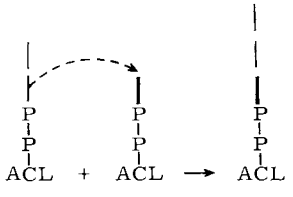


Fig. 7. Biosynthesis of the O-specific chains of the lipopolysaccharide of *S.newington* (3 15) [30] (see also [27]). ACL (antigen carrier lipid) = $H(CH_2-C(CH_3)=CH-CH_2)_{11}-O$.

action of specific transferases. These units are then polymerized by the enzyme polymerase, the side chain (which is attached to the antigen carrier lipid) being lengthened by one repeating unit in each growth step. Each freshly polymerized chain piece (– –) is transferred onto a new repeating unit (—), the chain thus growing at its reducing end [31].



In a final step the completed O-specific chain is transferred by the action of the enzyme translocase onto the core polysaccharide of the prefabricated lipid A-core polysaccharide unit. The individual steps of this biosynthesis have been studied *in vitro*. It was found that substituents such as glucosyl residues or acetyl groups (but not abequose or tyvelose) are transferred onto the O-specific chain *after* the lipopolysaccharide is completed [30].

It is believed that the ACL functions as an anchor to the cell membrane where biosynthesis of the specific chains proceeds, and that it serves as a transporting agent for the polysaccharides through the membrane. An analogous role could be attributed to lipid A during the synthesis of the core polysaccharide. The last step, the linkage of both polymers (region I and region II, III), probably takes place outside the cell membrane. Lipid carriers also play a role in the synthesis of other polysaccharides (*e.g.* murein synthesis [32]).

5.4. Genetic Determination of Biosynthesis of the Specific Side Chains: SR Mutants

The elucidation of the biosynthetic pathway of region I was accompanied by genetic investigations in the laboratories of *Stocker*, *Mäkelä*, and *Nikaido*. It was found that all the enzymes participating in the side chain synthesis are determined by a cluster of genes on the *Salmonella* chromosome near the *his* locus [33, 34, 34a]. This area of the chromosome, the O locus, is designated *rfb* (Fig. 8). Mutational changes in the *rfb* locus

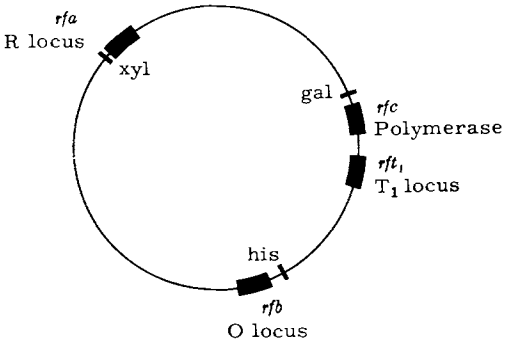


Fig. 8. The chromosome of *S.typhimurium* with the gene-regions of lipopolysaccharide biosynthesis [33].

and their effects on lipopolysaccharide synthesis will be discussed later (Section 6.3).

One exception, however, has been found. It concerns the enzyme polymerase (see Fig. 7), which maps at the *rfc* locus near the *gal* locus [35]. Mutations affecting the *rfc* locus lead to a defect in the synthesis of polymerase, resulting in the polymerization of the repeating units being blocked. In such mutants the sugar residues are assembled into *single* repeating units which are then transferred directly onto the core polysaccharide. The structure of an *rfc*⁻ lipopolysaccharide is shown in Fig. 9. In their bacteriological and serological proper-

[31] *P. W. Robbins, A. Wright*, and *J. L. Bellows*, Proc. nat. Acad. Sci. USA *52*, 1302 (1964).

[32] *J. M. Ghuysen, J. L. Strominger*, and *D. J. Tipper* in *M. Florkin* and *E. H. Stotz*: Comprehensive Biochemistry. Vol. 26 A, Elsevier, Amsterdam 1968, p. 53.

[33] *B. A. D. Stocker, R. G. Wilkinson*, and *P. H. Mäkelä*, New York Acad. Sci. *133*, 334 (1966).

[34] *B. A. D. Stocker* in: La Structure et les Effects Biologiques des Produits Bactériens provenants de Germes Gram-Négatifs, Coll. Intern. C.N.R.S., Paris, Oct. 24–26, 1967, Vol. *174*, 189 (1969).

[34a] *P. H. Mäkelä* and *B. A. D. Stocker*, Annu. Rev. Genetics *3*, 291 (1969).

[35] *Y. Naide, H. Nikaido, P. H. Mäkelä, R. G. Wilkinson*, and *B. A. D. Stocker*, Proc. nat. Acad. Sci. USA *53*, 147 (1965).

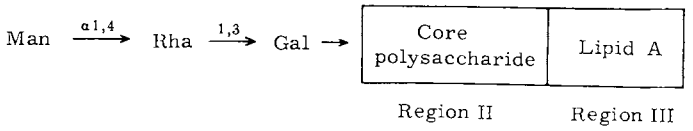


Fig. 9. Lipopolysaccharide structure of an SR mutant (*S.newington*) [24a, 35, 36].

ties, this class of mutants occupies an intermediate position between S forms and R mutants (see Section 6.1) and is, accordingly, termed semi-rough (SR).

5.5. Genetic Basis for Structural Relationships between Lipopolysaccharides of Different Species: Lysogenic Conversions

It has already been shown in Table 3 that different *Salmonella* species may show similarities with respect to the structure of their lipopolysaccharides, although they are not serologically related to one another (*e.g.* groups B and E). In many cases, the reason for such similarities may be traced back to a frequently occurring phenomenon: The so-called lysogenic conversion of *Salmonella* species brought about by the action of temperate (nonvirulent) phages. The credit for the elucidation of the chemical and biochemical principles underlying lysogenic conversions goes to *Staub* [18,20] and *Robbins* [26,30,36].

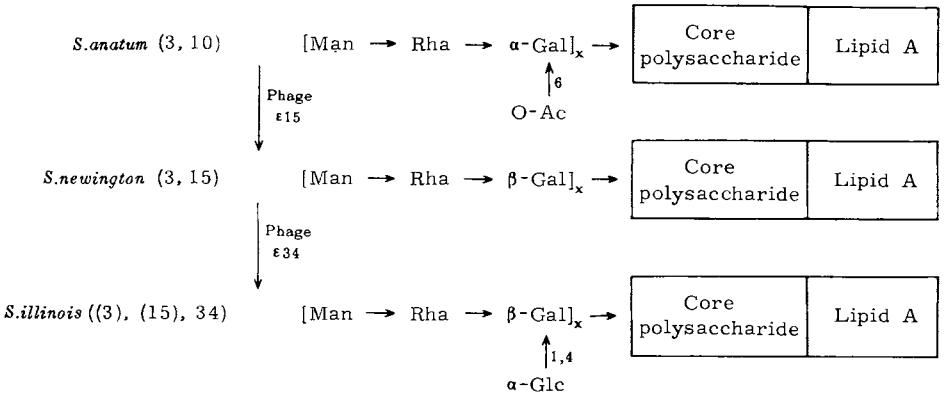


Fig. 10. Lysogenic conversions in *Salmonella* group E [26, 30].

An example of lysogenic conversions is given in Fig. 10 [30]: If *S.anatum* (3, 10) is infected with phage ε 15, it is converted into *S.newington* (3, 15). After superinfection of this species with phage ε 34, *S.illinois* ((3), (15), 34) is obtained. The serological changes (10 → 15 → 34) are paralleled by specific modifications in the structure of the O-specific chains of the respective lipopolysaccharides (Fig. 10). *S.anatum* contains α-linked acetylated galactosyl residues; in *S.newington*, galactose is β-linked but not acetylated, and in *S.illinois* the β-galactosyl residues carry a glucosyl side chain in position 4.

Although the complex mechanisms underlying lysogenic conversions are not fully understood, it is evident that the phage genome (phage nucleic acid), which is integrated into the chromosome of the host, influences and dictates new distinct steps of lipopolysaccharide biosynthesis. Thus, in the above example, some of the enzyme activities of the host are suppressed (acetylation and α-linking of galactose [37]), and new activities are introduced into the host (β-linking of galactose, and introduction of a glucosyl side chain). All cases of lysogenic conversion so far studied concern substituents of the O-specific chains or changes in the specificity of polymerases.

In the Kauffmann-White scheme (Table 1), factors 3 and 15 of *S.illinois* are placed in brackets ((3), (15)). This is to show that they cross-react with factors 3 and 15 of *S.newington*, but are not identical with them. In *S.illinois* the specificity of factor 34 is determined by glucose. At the same time glucose alters the specificity of the β-galactose to which it is bound. In contrast to the unsubstituted galactose with specificity 15, the substituted galactose determines the specificity (15), *i.e.* not all antibodies against the unsubstituted galactose "fit" onto the substituted galactose. Similarly, the mannose-determined specificity of factor 3 is influenced by the presence of glucose.

The constant unveiling of new conversion systems shows that many *Salmonella* species are genetically related. Inevitably, the question arises of the extent to which *Salmonella* serotypes are interrelated through lysogenic conversion, or, in other words, how many of the genes of the chromosome of a *Salmonella* are really its own or derive from prophages which were integrated during the course of evolution.

5.6. *Salmonella* Mutants with Atypical Specific Chains: T Forms

In 1956, two *Salmonella* strains that could not be typed with any of the known O sera were isolated in different hospitals in Europe. *Kauffmann* [1,2], to whom these two strongly cross-reacting strains were sent, hesitated to place them in a new *Salmonella* group. Further investigation revealed that, with respect to their flagellar antigens and their fermentative properties, the two strains were identical with *S.paratyphi* and *S.typhimurium*, respectively. From this, *Kauffmann* concluded that the new strains were mutants of the above mentioned species, in which the O antigens had been replaced by a new one which he termed T 1 antigen (T = transient, because T forms are relatively unstable and frequently undergo mutation into R forms). Later

[36] *R. Losick* and *P. W. Robbins*, J. molecular Biol. *30*, 445 (1967).

[37] *R. Losick*, J. molecular Biol. *42*, 237 (1969).

Schlosshardt found that many and perhaps all *Salmonella* species could in principle be converted into T1 forms [38]. However, T1 forms appear very seldom in nature.

In 1957, *Kauffmann* identified a T mutant derived from *S.bareilly* that was different from T1 and which he termed T2 [1,2]. Extraction of T1 and T2 forms with phenol/water yielded T1 and T2 lipopolysaccharides, which, like all *Salmonella* species, also contained the five basal sugars (Table 2). In addition, the T1 lipopolysaccharide also contained ribose and galactose in large quantities. Further examination showed that the O-specific chains, which are present in the wild forms, are replaced in the T1 lipopolysaccharide by T1-specific chains, which are also attached to the basal core polysaccharide in a similar way. These T1-specific chains are composed of ribose and galactose units. It was found that both sugars are present in the furanosidic form, *i.e.* in the five-ring structure [39,40]. A polysaccharide structure of this kind, which is rather rare in nature, is very acid-labile. For this reason it could not be established up to now whether T1 side chains are also made up of repeating units.

Mutation from the wild type into the T1 form proceeds in two steps (Fig. 11, see also Fig. 8): One mutation affects the O locus (leading to a block in the synthesis of the O-specific chains). A second mutation concerns the T1 locus, which determines the synthesis of

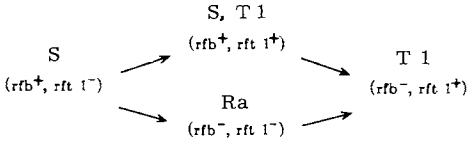


Fig. 11. The mutation steps leading from wild types to T1 mutants [41].

T1 chains [41]. Recently *rft1*+ mutants have been isolated with an intact *rfb* locus. As expected they synthesize simultaneously both O-specific and T1-specific lipopolysaccharides [42].

The biological significance of T1 mutants in nature (*e.g.* in pathogenicity) is not known. It is unlikely that *Salmonella* species possess a gene, *rft1*, which is never or very rarely brought into function.

6. The Core Polysaccharide (Region II)

6.1. The S → R Mutation

While the studies of O-specific chains (region I) could be performed with lipopolysaccharides of *Salmonella* wild forms (S forms), work on the basal core polysaccharide (region II) proved to be rather difficult, because in this case only a small internal region of the macromolecule was concerned. This difficulty was overcome by extending the studies to mutant strains, the so-called R forms. These mutants, which have been known for a long time [1,2], suddenly became of critical importance for biological and genetical studies on lipopolysaccharides when it was found that certain steps in their lipopolysaccharide biosynthesis are blocked.

Since R mutants occur spontaneously, they are frequently found in old cultures, from which their isolation is facilitated by their morphological properties. In contrast to the smooth-growing wild strains, the R mutants form rough colonies (hence *s*mooth = *S* form, *r*ough = *R* form). Parallel to these morphological changes, drastic serological changes take place: the O specificity of the parent strain is lost and new, R specificities become manifest.

6.2. Classification of R Mutants

It is possible to obtain a large number of R mutants from a single *Salmonella* species. The investigations discussed below were performed mainly with *S.minnesota* R mutants isolated by *Schlosshardt* [43]. Analogous series of R mutants were obtained from *S.typhimurium*, *S.ruiru*, and other *Salmonella* species.

Although R mutants do synthesize lipopolysaccharides, their sugar composition shows characteristic differences from that of the corresponding wild type lipopolysaccharides. All O-specific sugars are missing, and only all or some of the five basal sugars (see Table 2), which are also found in the wild form in addition to the specific sugars [18], are present. R (lipo)polysaccharides contain, besides ethanolamine and phosphate, *N*-acetyl-D-glucosamine, D-glucose, D-galactose, and two sugars that until now have been found exclusively in bacterial lipopolysaccharides: L-glycero-D-manno-heptose (first identified in *Shigella* [44]) and 2-keto-3-deoxy-D-mannooctonic acid (KDO) (first identified in *E.coli* [45]). Recently, a further sugar, 4-amino-L-arabinose, was found in R lipopolysaccharide preparations [45a]. It is not yet known whether it is a constituent of the lipopolysaccharide itself or of a contaminant.

In analogy to the chemotypes of the S forms (Table 2), comparative analysis of *S.minnesota* R forms led to a classification into R chemotypes (Ra, Rb, Rc, *etc.*) that is also based on the difference in sugar composition of the R lipopolysaccharides (Table 5, left-hand side) [43]. Ra mutants contain all five basal sugars. In Rb mutants, glucosamine is absent as a constituent of

[38] *J. Schlosshardt*, Zbl. Bakteriol., Parasitenkunde, Infektionskrankh. Hyg., I. Abt., Orig. *177*, 176 (1960).

[39] *R. H. Wheat, M. Berst, E. Ruschmann, O. Lüderitz*, and *O. Westphal*, J. Bacteriol. *94*, 1366 (1967).

[40] *M. Berst, C. G. Hellerqvist, B. Lindberg. O. Lüderitz, S. Svensson*, and *O. Westphal*, European J. Biochem. *11*, 353 (1969).

[41] *M. Sarvas* and *P. H. Mäkelä*, Acta pathol. microbiol. scand. *65*, 654 (1965).

[42] *M. Sarvas, O. Lüderitz*, and *O. Westphal*, Ann. Med. exp. Biol. fenn. *45*, 117 (1967).

[43] *O. Lüderitz, C. Galanos, H. J. Risse, E. Ruschmann, S. Schlecht, G. Schmidt, H. Schulte-Holthausen, R. Wheat, O. Westphal*, and *J. Schlosshardt*, Ann. New York Acad. Sci. *133*, 349 (1966).

[44] *M. A. Jesaitis* and *W. F. Goebel*, J. exp. Medicine *96*, 409 (1952).

[45] *E. C. Heath* and *M. A. Ghalambor*, Biochem. biophasic. Res. Commun. *10*, 340 (1963).

[45a] *W. A. Volk, C. Galanos*, and *O. Lüderitz*, FEBS Letters *8*, 161 (1970).

Table 5. Chemical and serological classification of lipopolysaccharides from *S.minnesota* R mutants [43]

Chemotype	*S.minnesota* strain	Sugar composition of lipopolysaccharides (%)							Serological cross reactions [a]						
									Antisera against the strains						
		Lipid A	KDO	Hep	Glc	Gal	GlcN (PS)[b]	GalN	S form	R60	R345	R5	R7	R3	R595
II	S form	25	5	3	4	13	10	17	+	+					
Ra	R60	45	5	7	6	8	6			+					
	R555	45	9	11	3	6	2			+					
	R708	47	10	11	4	6	2			+					
Rb	R345	50	5	10	4	9					+				
	R2	50	7	14	3	4					±				
Rc	R5	55	10	11	4						±	+			
	R8	55	8	6	5						±	+			+
Rd_1	R7	58	9	13									+		
Rd_2	R3	63	9	7										±	
	R4	65	8	7										±	
Re	R595	65	16												+
	R613	64	17												+

[a] Hemagglutination inhibition test. [b] (PS) = determined in the polysaccharide after removal of lipid A.

the core polysaccharide (glucosamine is present in all *lipo*polysaccharides as a constituent of lipid A). In Rc mutants the only hexose present is glucose, while in Rd mutants no hexose at all is present. In the last group, Re, hexoses as well as heptose are absent, leaving KDO as the only sugar bound to lipid A (region III). The various R classes differ from one another also with respect to their R specificity (Table 5, right-hand side) [43]. Finally, each R class is characterized by an individual phage pattern [46]. Hence the classification of the R mutants into R chemotypes corresponds to a classification into R serotypes and R phage types.

6.3. Ra-Mutants: Defects and Genetics

Ra mutants hold a key position in the class of R mutants and their study has contributed extensively to the understanding of the mechanisms which underly S → R mutation [18, 27, 29].

Ra lipopolysaccharides contain the five basal sugars but are devoid of all O-specific sugars of the parent strain. These findings led to the conclusion that in Ra mutants the synthesis of the O-specific chains (region I) is blocked. Analysis of Ra mutants actually showed that whenever a defect was identified it was always associated with an enzyme that participates in the biosynthesis of region I. Thus an Ra mutant of *S.minnesota* has lost the capacity of the parent strain to synthesize *N*-acetylgalactosamine (UDPGlcNAc —|→ UDPGalNAc). Similarly, *S.typhimurium* R mutants have been identified defective in the synthesis of rhamnose (TDPGlc —|→ TDPRha), abequose (CDPGlc —|→ CDP Abe), or mannose (Glc-6-P —|→ Man-6-P). The block of a *single step* in the biosynthesis of region I renders the cell incapable of synthesizing specific chains (see Fig. 7). Lipopolysaccharide synthesis in Ra mutants therefore stops at that point where the specific side chains are normally transferred onto the core polysaccharide-lipid A unit. Consequently, Ra mutants synthesize a lipopolysaccharide composed merely of regions II and III.

Genetic investigations by *Stocker* on Ra mutants have shown that the defect concerns the O locus (*rfb* region) [34] whose genes govern the synthesis of the enzymes necessary for the biosynthesis of the specific chains. Ra mutants may differ with regard to their genotype, *i.e.* according to the genetic defects of their O locus. Phenotypically, however, they are identical: they synthesize the intact core polysaccharide (region II), bound to lipid A (region III).

6.4. Rb to Re Mutants: Defects and Genetics

While in Ra mutants the synthesis of the O-specific chains is blocked, in Rb to Re mutants defects are present which lead to a more or less incomplete core structure. As seen in Table 5, remarkable differences in sugar composition are found in lipopolysaccharides synthesized by mutants of the various R classes. The synthesis of the core polysaccharide in these mutants proceeds normally up to the point of defect, and there the synthesis is interrupted [in contrast to the usual "all or nothing" principle underlying the synthesis of the specific chains (see Fig. 7)]. Defects in Rb to Re mutants may be concerned with the synthesis of the sugar units and/or their transfer.

Genetic studies by *Stocker*, *Mäkelä*, and *Nikaido* have led to the identification of the R locus [27, 34]. This part of the chromosome, which is designated *rfa*, controls many enzymes that catalyze the synthesis of the core polysaccharide. It is far removed from the O locus (Fig. 8).

Besides R-specific lipopolysaccharides, the majority of Rb to Re mutants synthesize a polysaccharide containing the O-specific sugars of the parent strain but none of the core-specific sugars (heptose, KDO) and no lipid

[46] *G. Schmidt* and *O. Lüderitz*, Zbl. Bakteriol., Parasitenkunde, Infektionskrankh. Hyg., I. Abt., Orig. *210*, 381 (1969).

A[47]. This so-called "specific hapten" consists of free O-specific chains (region I). Since the *rfb* locus in *rfa*-defective mutants is intact, the synthesis of the specific chains can proceed unimpeded also after mutation. Because of the high acceptor specificity of the translocase (see Fig. 7), the chains are not transferred onto the incomplete core polysaccharide. They accumulate in the R cells, probably bound to the antigen carrier lipid. The extremely labile pyrophosphate bridges are broken down during phenol/water extraction and the specific hapten is found in the supernatant after ultracentrifugation, whereas the R lipopolysaccharide sediments.

6.5. Chemical Structure of the Core Polysaccharide

Fig. 12 shows the structure of the *S.minnesota* core polysaccharide (region II) as obtained by combining the part-structures identified in Ra to Re lipopolysaccharides. It consists of two oligosaccharides, one of which contains hexoses and the other heptose and KDO.

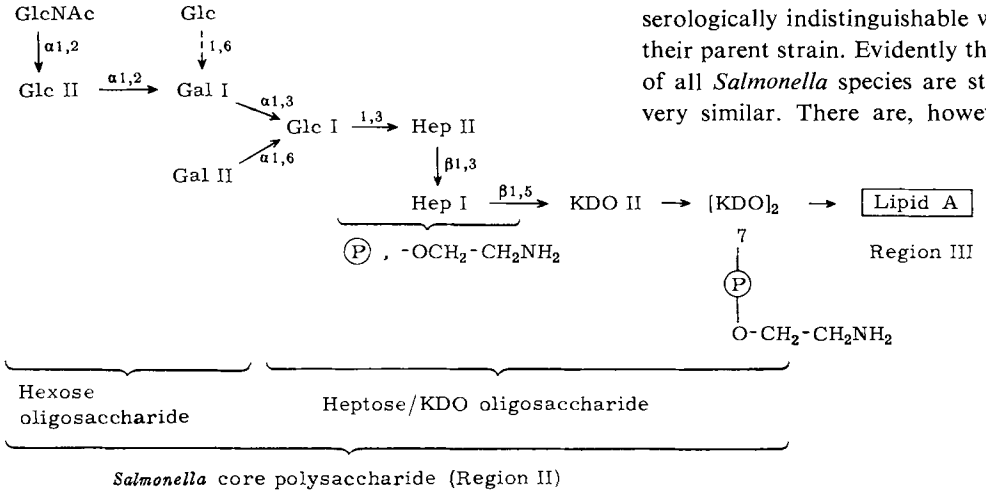


Fig. 12. Structure of *Salmonella* Ra lipopolysaccharides: The core polysaccharide (region II) [18, 29].

The structure of the hexose oligosaccharide resulted from analysis of fragments obtained by partial hydrolysis of Ra and Rb lipopolysaccharides[18,29]. According to more recent findings by *Nikaido*[48] and *Hämmerling et al.*[56], the O-specific chains are linked to the glucose II residue in wild type lipopolysaccharides.

In the heptose/KDO pentasaccharide, whose structure has been elucidated by analysis of Rc to Re lipopolysaccharides[49,49a], the three ketosidically-linked KDO residues are present as a branched trisaccharide, with the reducing end bound ketosidically to lipid A[54]. In the core polysaccharide, therefore, two KDO units are present in the main chain, while the third KDO unit forms a branch, carrying a phosphorylethanolamine group in position 7[49a]. One of the heptose residues[49b], probably heptose I[49c], is substituted in position 4 by a pyrophosphorylethanolamine group.

From the formula of Fig. 12, a molecular weight of about 2000 can be calculated for the core polysaccharide chain. The type of linkage of the phosphate groups, which are obtained as heptose phosphate after hydrolysis, is not known. The clarification of this matter could be of importance for the entire architecture of the lipopolysaccharide molecule. It is presumed that some of the phosphate groups form diester bridges to the neighboring chains. This would lead to a considerable enlargement of the molecule. A further question arises as to how many of the core polysaccharide units in an S form lipopolysaccharide are occupied by O-specific chains: Do all, a few, or just one core unit carry a specific chain?

Salmonella Ra lipopolysaccharides are chemically and serologically indistinguishable whatever the species of their parent strain. Evidently the core polysaccharides of all *Salmonella* species are structurally identical or very similar. There are, however, many indications that the lipopolysaccharides of other genera possess very different core structures. Thus, *Simmons* has isolated a pentasaccharide from a *Shigella flexneri* Ra lipopolysaccharide[50], which, although it has certain similarities to the pentasaccharide isolated from *Salmonella* (glucosamine as the non-reducing and glucose as the reducing end groups), is different with respect to the sequence of sugars and their substituents (Fig. 13). Even more contrasting differences are apparent in *Xanthomonas* species, whose lipopolysaccharides, according to *Volk*, contain KDO and galacturonic acid phosphate, but no heptose or galactose[50a,50b,50c].

[47] *I. Beckmann, T. V. Subbaiah,* and *B. A. D. Stocker,* Nature (London) *201,* 1299 (1964).

[48] *H. Nikaido,* J. biol. Chemistry *244,* 2835 (1969).

[49] *W. Dröge, O. Lüderitz,* and *O. Westphal,* European J. Biochem. *4,* 126 (1968).

[49a] *W. Dröge, V. Lehmann, O. Lüderitz,* and *O. Westphal,* European J. Biochem. *14,* 175 (1970).

[49b] *M. J. Osborn,* Annu. Rev. Biochem. *38,* 501 (1969).

[49c] *V. Lehmann et al.,* to be published.

[50] *J. H. Johnston, R. J. Johnston,* and *D. A. R. Simmons,* Biochem. J. *105,* 79 (1967).

[50a] *W. A. Volk,* J. Bacteriol. *95,* 980 (1968).

[50b] *G. Schmidt, B. Jann,* and *K. Jann,* European J. Biochem. *10,* 501 (1969).

[50c] *G. Schmidt, B. Jann,* and *K. Jann,* European J. Biochem., in press.

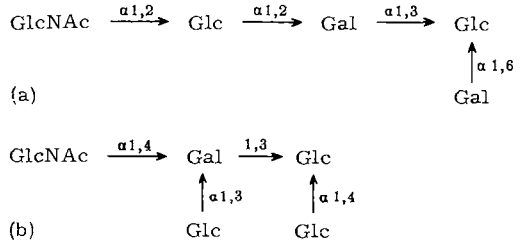


Fig. 13. Comparison of the hexose oligosaccharides in the core polysaccharides of a) *Salmonella* [18] and b) *Shigella flexneri* [50].

The elucidation of the detailed structure of core polysaccharides from as many bacterial groups as possible is of utmost importance for questions of evolution and taxonomy.

6.6. Structure of Core Defective Lipopolysaccharides: Possible Biosynthesis of the Core Polysaccharide

The entire structure of the core polysaccharide of *Salmonella* has been reconstructed from partial structures appearing in core-defective liposaccharides of the R classes Rb to Re. The structures ascribed to these lipopolysaccharides are summarized in Table 6 [19].

Table 6. Structure of the lipopolysaccharides of core-defective mutants: The biosynthetic pathway of *Salmonella* core polysaccharide [18].

Chemotype	Lipopolysaccharide
Re	$(KDO)_3 \rightarrow$ lipid A
Rd_2	Hep → $(KDO)_3 \rightarrow$ lipid A
Rd_1P^-	Hep → Hep → $(KDO)_3 \rightarrow$ lipid A
Rd_1P^+	Hep → Hep → $(KDO)_3 \rightarrow$ lipid A; Ⓟ, EtN
RcP^-	Glc → Hep → Hep → $(KDO)_3 \rightarrow$ lipid A
RcP^+	Glc → Hep → Hep → $(KDO)_3 \rightarrow$ lipid A; Ⓟ, EtN
Rb	Glc → Gal → Glc → Hep → Hep → $(KDO)_3 \rightarrow$ lipid A; Gal; Ⓟ, EtN
Ra	GlcNAc → Glc → Gal → Glc → Hep → Hep → $(KDO)_3$ → lipid A; Gal; Ⓟ, EtN

While the majority of the isolated mutants show a defect in sugar *synthesis* or in sugar *transfer*, some (P^-) mutants have been obtained whose defect concerns the transfer of phosphate groups to heptose. Biosynthetic experiments *in vitro* showed that ATP functions as a phosphate donor for the transfer of phosphate and it could be demonstrated that the presence of these heptose phosphate groups is necessary for the later transfer of galactose [51, 52].

The incompleteness of lipopolysaccharides from core defective mutants is the result of failure in certain biosynthetic steps. On the grounds of this concept the structures shown in Table 6 may be looked upon as intermediate products in the biosynthesis of lipopolysaccharides. Accordingly, two heptose residues are sequentially added to the Re lipopolysaccharide (which is now often termed glycolipid since it is rather a lipo-"oligosaccharide" than a lipo-"polysaccharide"). These heptose residues are then phosphorylated in a subsequent biosynthetic step. The incorporation of ethanolamine also takes place at this stage. *In vitro* transfer of heptose could not yet be carried out because the activated precursor of heptose (as well as its biosynthesis) is still unknown. However, *Osborn* and *Rothfield* and their co-workers have been successful in the *in vitro* synthesis of Ra from RdP^+ lipopolysaccharide by sequential incorporation of glucose, galactose, glucose, and finally *N*-acetylglucosamine [28, 29]. The sequence of incorporation of these sugars is determined by the high specificity of the transferases for acceptor and nucleotide sugars. The results from these biosynthetic studies are in good agreement with the results of structural investigations on the hexose oligosaccharide. They also show that the biosynthesis of the core polysaccharide and of the O-specific chains are based on fundamentally different principles.

6.7. Biological Properties of R Mutants

The mutants of all R classes are immunogenic and induce production of antibodies. The terminal nonreducing sugar residues of defective lipopolysaccharides act as immunodominant sugars, as was shown in precipitation inhibition studies (see Table 5). The corresponding homologous systems are thus inhibited by *N*-acetylglucosamine, glucose, heptose, and KDO, respectively.

R lipopolysaccharides also represent specific receptors for a series of phages. The phage Felix 01 reacts only with lipopolysaccharides which contain *N*-acetylglucosamine in the core polysaccharide (from S and Ra strains), but not with lipopolysaccharides of other R classes (*e.g.* from Rb strains) (see Fig. 3) [17].

Many *Salmonella* species are pathogenic. They are capable of entering the organism where they can multiply, thus flooding the system with endotoxin. *S.typhi*, *S.paratyphi*, and *S.enteritidis* are some of the well known pathogens. Although R lipopolysaccharides are also toxic, R forms are not pathogenic This is due to the action of macrophages which phagocytize R mutants and render them harmless. The S forms, on the other hand, are protected from this fate because of the presence of the long O-specific polysaccharide chains on their cell surface which prevent the contact between bacterial cell and macrophage that is necessary for subsequent phagocytosis. It can be demonstrated also *in vitro* that the hydrophilic specific chains of the S forms protect the cell against lytic enzymes, antibiotics, and adverse environmental conditions such as heat, a protection which the R forms lack [53a].

[51] *P. Mühlradt, H. J. Risse, O. Lüderitz*, and *O. Westphal*, European J. Biochem. *4*, 139 (1968).

[52] *P. Mühlradt*, European J. Biochem. *11*, 241 (1969).

[53] *O. Westphal* and *O. Lüderitz*, Angew. Chem. *66*, 407 (1954)

[53a] *S. Schlecht* and *O. Westphal*, Zbl. Bakteriol., Parasitenkunde, Infektionskrankh. Hyg. I. Abt. Orig. *213*, 356 (1970).

7. Lipid A (Region III)

7.1. Structure of Lipid A

By mild acid hydrolysis of (S and R) lipopolysaccharides the labile ketosidic linkage of the KDO residue, which links the core polysaccharide to lipid A, is broken down and lipid A is liberated in the form of a water-insoluble precipitate. Lipid A is a phospholipid with an uncommon structure. Instead of glycerol phosphate (lecithine, cephaline) it contains D-glucosamine-phosphate as the hydrophilic polyhydroxy compound. The amino groups of the glucosamine residues are occupied by D-β-hydroxymyristic acid, while the available OH groups are esterified with long-chain fatty acids, mainly lauric, myristic, palmitic, and β-hydroxymyristic acids [53].

For the elucidation of the glucosamine "backbone" of lipid A, the glycolipid from *Salmonella* Re mutants has proved to be most suitable as starting material because it contains only KDO and lipid A. On cleavage of the long-chain fatty acids by hydrazinolysis and subsequent partial hydrolysis, four main fractions (besides free KDO) could be identified by electrophoresis [54]. Their isolation and analysis led to the structures shown in Fig. 14. Fraction −5, glucosaminyl-β-1,6-glucosamine, represents the basic structure whose derivatives

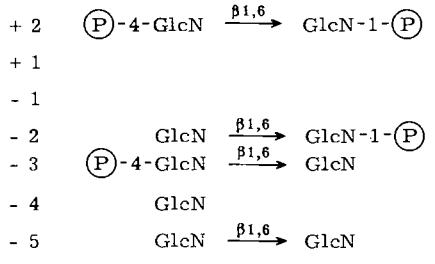


Fig. 14. Electropherogram of the partial hydrolyzate of a Re glycolipid after hydrazinolysis [54]. 40 V/cm, 150 mA, pH = 5.3.

carry one (fractions −3 and −2) and two (fraction +2) phosphate residues in positions 1 and, probably, 4′. When the product of hydrazinolysis was analyzed directly the corresponding phosphorylated derivatives of a KDO-containing pentasaccharide could be obtained. These derivatives could then be transformed into the (KDO)$_3$-glucosaminyl-β-1,6-glucosamine by phosphatase treatment or into the disaccharide glucosaminyl-β-1,6-glucosamine (and free KDO) by partial hydrolysis.

Lipid A therefore consists of phosphorylated β-1,6-linked glucosamine disaccharide units, whose hydroxyl and amino groups are acylated (Fig. 15). A KDO oligosaccharide which is linked to one of the hydroxyl groups of the non-reducing glucosamine residue effects the linkage of core polysaccharide and lipid A in S and R lipopolysaccharides.

It is quite probable that several glucosamine disaccharide units are linked together by phosphate bridges

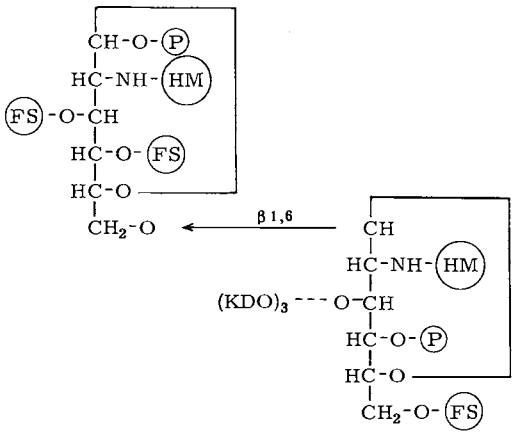


Fig. 15. Structure of a lipid A unit with a KDO oligosaccharide [54]. FS = long-chain fatty acids; HM = β-hydroxymyristic acid.

(1–4′) in the intact lipid A. This would mean a substantial increase in the size of the lipopolysaccharide molecule and could be of importance to the general design and organization of the cell wall.

7.2. The Endotoxic Region in the Lipopolysaccharide Molecule

The isolation and identification of a series of R classes and the study of their lipopolysaccharides and glycolipids has opened up new possibilities for the identification of regions in the lipopolysaccharide that are responsible for endotoxic activity. What has been postulated for a long time could now be confirmed, *i.e.* that the O-specific chains and the hexoses and heptoses of the core polysaccharide do not contribute to the toxic effects of the molecule and are, in this respect, non-essential. In many laboratories it has been shown that the glycolipids of Re mutants, which contain only KDO and lipid A, are just as active endotoxins as the lipopolysaccharides of the corresponding wild types [13, 14]. Lipopolysaccharides in which the lipid A component has been deacylated by either specific amoeba enzymes or by treatment with alkali are no longer toxic [55]. This and other results show that lipid A is responsible for the endotoxic activity of lipopolysaccharides.

8. Summary and Discussion

Fig. 16 shows the complete structure of the lipopolysaccharide from *S.typhimurium* [18, 23, 54, 56]. It is made up of the three regions shown in Fig. 4: the O-specific polysaccharide chains; the core polysaccharide; and lipid A.

The physicochemical properties of lipopolysaccharides are determined by the simultaneous presence of hydrophilic, strongly polar polysaccharidic regions, on one

[54] *J. Gmeiner, O. Lüderitz,* and *O. Westphal,* European Biochem. *7,* 370 (1969).

[55] *D. Malchow, O. Lüderitz, B. Kickhöfen, O. Westphal,* and *G. Gerisch,* European J. Biochem. *7,* 239 (1969).

[56] *G. Hämmerling, O. Lüderitz,* and *O. Westphal,* European J. Biochem. *15,* 48 (1970).

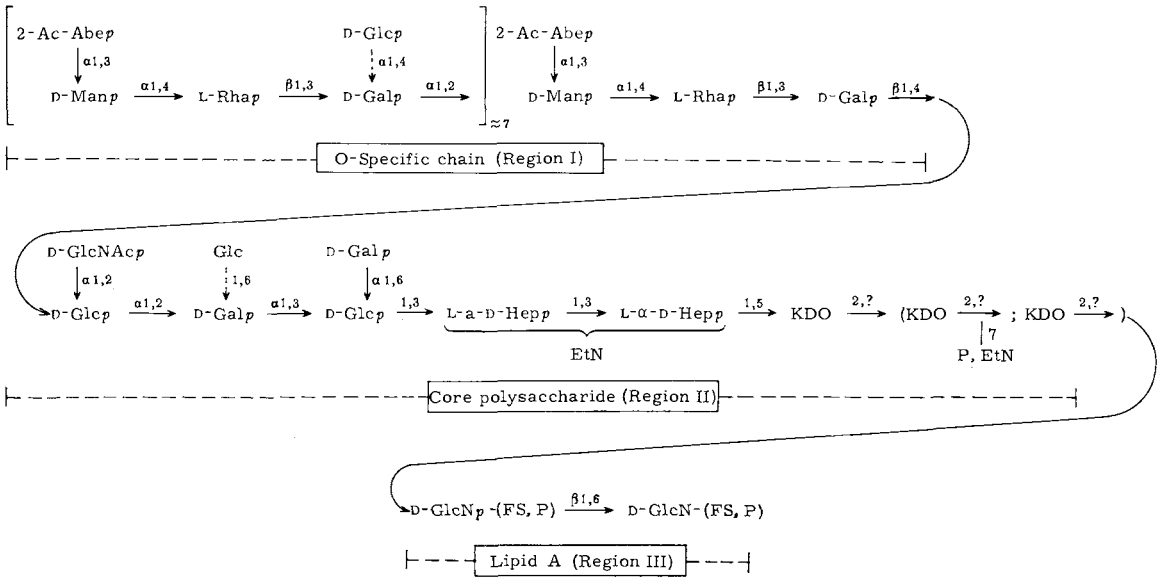


Fig. 16. Structure of the lipopolysaccharide of *S. typhimurium* according to our present knowledge [18, 23, 49a, 49b, 54, 56]. *p* = pyranoside linkage; L-α-D-Hep is equivalent to β-Hep of the preceding figures. EtN = ethanolamine; FS = long-chain (hydroxy) fatty acids.

hand, and lipid A on the other. This combination of hydrophilic and hydrophobic regions leads, in aqueous solutions, to the formation of micellar structures with a high degree of aggregation (see Fig. 3), thus making direct determination of the true molecular weight of lipopolysaccharides impossible. Also the formula of Fig. 16 provides no information about the molecular magnitude, since we do not know whether the phosphate groups bound to heptose or those present in lipid A act as bridges to neighboring chains to form a three-dimensional network. The inner region of the core polysaccharide, the heptose/KDO oligosaccharide, contains a bundle of polar groups (carbonyl groups of KDO, phosphate groups, amino groups of ethanolamine) whose physiological significance is not yet known. It is conceivable that they participate in the binding of other components in the bacterial cell wall. Another function of the ionic groups in the core polysaccharide could be, in analogy to the teichoic acids [56a], that they regulate the flow of ions to the cell membrane, thus maintaining an optimal concentration of bivalent ions necessary for many enzymes.

Biochemical and genetic investigations of recent years have shown that O-specific chains, on the one hand, and core polysaccharide-lipid A, on the other, are synthesized independently by different mechanisms. Their synthesis is determined primarily by the (species-specific) O locus and by the R locus (common to all *Salmonella*), respectively, which are situated far away from each other on the ring-shaped *Salmonella* chromosome.

In general, each defect in the synthesis of the O-specific chains leads to the complete absence of the O-specific chains in the lipopolysaccharide, no matter which biosynthetic step is concerned. O Locus-defective mutants therefore form a phenotypically uniform class, the Ra mutants, whose lipopolysaccharides contain the complete core polysaccharide.

On the other hand, core-defective (R locus-defective) mutants belonging to different genotypes are often phenotypically different. They synthesize the core polysaccharide up to the defective biosynthetic step and belong to the classes Rb to Re. As expected, these mutants also synthesize O-specific chains, which are, however, not transferred onto the incomplete core polysaccharide, but may remain linked to the antigen carrier lipid. After phenol/water extraction they are obtained as a soluble polysaccharide ("specific hapten"). It is obvious that the sequence of the sugar residues in lipopolysaccharides is not determined by a template mechanism but by the substrate specificity of many enzymes which participate in the polysaccharide synthesis. The sequence of the biosynthetic steps is thereby laid down and so also is the polysaccharide structure. There is evidence that in some lipopolysacharides the O-specific chains are not built up of repeating units [25, 40].

Present results indicate that in *Salmonella* species the core polysaccharide and the lipid A component are of identical structure. In other groups of bacteria, however, the core structure may be different [18, 20, 50, 50a–c]. It has been shown that occasionally different core structures carry identical O-specific chains [50b]. Similarly, structural differences exist in the lipid A component of other genera with respect to the glucosamine disaccharide [58] as well as to the fatty acids [59–62].

So far, no mutants have been described with a defect in the synthesis of KDO or lipid A. It is possible that

[56a] *S. Heptinstall, A. R. Archibald,* and *J. Baddiley,* Nature (London) *225*, 519 (1970).

[57] *W. R. Rank,* Dissertation, Universität München 1969.

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[59] *G. A. Adams, M. Kates, D. H. Shaw,* and *M. Yaguchi,* Canad. J. Biochem. *46*, 1175 (1968).

[60] *G. B. Michaelis* and *R. G. Eagon,* Proc. Soc. exp. Biol. Med. *131*, 1346 (1969).

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the usual methods of selection are not suitable for the isolation of such mutants, or that they are not able to grow under the usual cultivation conditions. The identification of substances which would inhibit early stages of lipopolysaccharide biosynthesis in the cell (as do some antibiotics in the synthesis of murein) would be of great theoretical and practical value. Such substances would convert the pathogenic wild types into non-pathogenic R forms which are known to be readily eliminated in the organism by macrophages.

Although the biosynthetic pathway of lipopolysaccharides has been extensively elucidated, very little is known about their degradation in nature. It is surprising that no enzymes have so far been described which degrade lipopolysaccharides specifically, since this would be of extreme value for structural analyses or for the identification of biologically active regions in the molecule. We have recently found that amoebae of *Dictyostelium discoideum* contain an enzyme system which degrades specifically the lipid A component of lipopolysaccharides [55]. After phagocytosis, lysis, and digestion of the fed bacteria, these amoebae egest degraded lipopolysaccharide into the culture medium. This lipopolysaccharide contains intact O-specific chains and core polysaccharide. The lipid A component, however, is quantitatively deacylated. Ester- as well as amide-bound fatty acids are cleaved off and the degraded lipopolysaccharide contains nonacylated glucosamine disaccharide. Amoebae-degraded lipopolysaccharide is *non-toxic*. It is possible that the inactivation (detoxification) of lipopolysaccharides, which is observed after incubation with serum, is based on an analogous reaction with acylases.

Immunochemical and serological studies on lipopolysaccharides have shown that O specificity is determined by defined structures in the O-specific chains; determinant groups, di- to hexasaccharides, determine the individual factors of the Kauffmann-White scheme. In each determinant group one sugar plays the role of the immunodominant sugar. In R mutants, which lack specific chains, the terminal sugars of the various incomplete core polysaccharides function as the immunodominant sugars. R mutants exhibit R specificities. Very recent studies by *Rank* [57] indicate that under certain conditions antibodies against lipid A are detectable which, as expected, can cross-react with nonrelated lipopolysaccharides.

All lipopolysaccharides are highly active endotoxins, irrespective of whether they are derived from S or R forms. The region responsible for this activity is located in the (KDO)-lipid A part of the molecule. The polysaccharide part is non-essential.

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Methods of Virus Formation

By Gerhard Sauer[*]

Viruses occur in a great variety of shapes and sizes, but for all their diversity in appearance they possess certain characteristics in common: all viruses contain a single nucleic acid molecule – deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) – surrounded by a protective protein coat. Among other things, the protein coat enables the genetic information stored in the nucleic acid to enter a host cell in a usable state, where it can initiate the reproduction of identical virus particles. After penetration of the cell the foreign genetic material of the virus particle first induces the synthesis of macromolecules not normally present in the cell: the viral nucleic acid undergoes replication and very many copies are produced, the protein of the virus coat is synthesized, and then these components are assembled to form a new generation of infectious virus particles. Most viruses also exhibit certain common structural features: their protein coat is built up from subunits arranged in helical or icosahedral fashion around the genetic material.

1. Conversion of the Virus Genome into a Functional State

As most viruses consist of nothing but nucleic acid and a protein coat, they lack the prerequisites to carry out elementary life processes, *i.e.* to make constant use of their genetic information. Outside a cell, the virus particle is only a complex but biologically inert structure. For their multiplication the viruses require auxiliary agents that are only available in living cells, consisting of various enzymes, ribosomes, and transfer-RNA molecules. The viral nucleic acid only becomes functional when it penetrates the cell and is freed from its protein coat.

The cycle of infection, *i.e.* the period between the time when a virus particle comes into contact with a

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cell and the time when its new infectious progeny are complete, can be divided into several phases. Adsorption of the virus particles onto the cell is followed by their penetration of the cell wall and liberation of the genetic information. When the protective protein coat is lost from the viral nucleic acid, the virus particle loses its morphological identity. It is now in the "eclipse" phase. During this phase occur the transcription and translation stages, which lead to the accumulation of virus components within the cell. This is followed by maturation of the virus and the release of a new generation of infectious virus particles.

If cells are infected with a definite amount of virus, and the infectivity of the nutrient medium surrounding the cells is determined, the characteristic virus growth curves are obtained as shown in Figure 1.

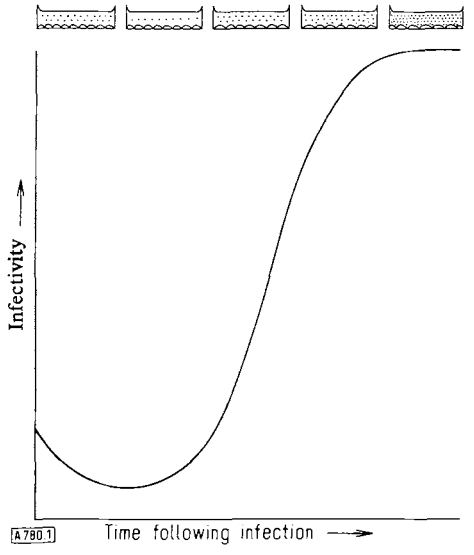


Fig. 1. Virus growth curve. The upper part of the figure shows cross-sections of vessels containing tissue culture cells covered with virus-containing nutrient medium. The amount of infectious virus is indicated by dots. The graph shows the amount of infectious virus during the course of a virus growth cycle.

Shortly after the addition of the virus suspension to the cells, the infectivity of the medium gradually decreases and rises again until finally a plateau is reached, when the synthesizing ability of the cells is exhausted. This is frequently associated with death of the host cells. The initial decrease in the infectivity of the supernatant is caused by adsorption of the viruses onto the cells, whereas the subsequent increase is attributed to the liberation of newly synthesized virus progeny. We shall first consider the initial part of the curve, *i.e.* the phase of adsorption of the virus particles onto the cell and their penetration of the cell interior.

The first cell-virus contact occurs as a result of molecular brownian motion. The number of irreversibly adsorbed virus particles per cell is considerably smaller than that expected from theoretical estimations, since not every collision between a virus and a cell leads to a stable contact. The forces binding the virus particles to the cell membrane are apparently electrostatic in nature. It is natural to ask whether there are any specific receptors on the cell membrane responsible for binding the virus particles, and this conjecture gains some support when it is considered how exacting many kinds of viruses are in their choice of host and even in their choice of the tissue in which they multiply.

One could assume that this selectivity is based on special processes at the site of contact. Here, however, the first complications arise: the members of the large poxvirus group are adsorbed at the same rate by the very many different cells, even by those in which they cannot multiply [1]. In this case the adsorption is obviously not based on any specificity. A very different situation is encountered in the classical example of the myxovirus group, which includes the influenza virus, where specific adsorption processes can be observed. Following its addition to a suspension of erythrocytes, the influenza virus is adsorbed on the erythrocyte surface. Binding of the myxoviruses to the periphery of the erythrocytes gives rise to bridging, as a result of which the erythrocytes form conglomerations, a process that is visible macroscopically and has been termed hemagglutination. By raising the temperature the virus can be displaced from the erythrocytes. An interesting point is that erythrocytes agglutinated once in this way cannot be agglutinated again by the addition of new virus; this obviously means that their surface has been changed by contact with the virus. Fragments possessing hemagglutinating activity – called hemagglutinins – can be isolated from the virus surface [2]. In addition, the myxoviruses contain in their coat an enzyme known as neuraminidase [3,4]. The substrate on which this enzyme acts occurs on the surface of erythrocytes, as well as in many biological fluids and on the surface of the natural host cells of influenza viruses. All these observations indicate that the contact between myxoviruses and host cells is brought about as a result of a special enzyme-substrate relationship. The above remarks show that the processes responsible for the adsorption of viruses onto cells can vary from one virus group to another [4].

The next step in the cell-virus encounter is penetration. Certain bacteriophages (bacterial viruses) infect their hosts by transferring their nucleic acid into the bacterium through an "injection apparatus". The protein coat of the bacteriophage does not in this case penetrate the bacterium but is left behind outside the membrane [5]. Such bacteriophages have been studied very thoroughly and have become a classical example of how a foreign nucleic acid can be transferred into a cell.

Electron microscopy has shown that the viruses of animals behave in quite a different way. They lack such injection apparatus and, in addition, empty virus coats have never been observed on cell surfaces. Everything indicates that animal viruses enter the cells

[1] *A. C. Allison* and *R. C. Valentine*, Biochim. biophysica Acta *40*, 393 (1960).

[2] *W. Schäfer*, Bacteriological Reviews *27*, 1 (1963).

[3] *G. K. Hirst*, J. exp. Medicine *76*, 195 (1942).

[4] *C. Scholtissek*, *R. Drzeniek*, and *R. Rott* in *H. B. Levy*: The Biochemistry of Viruses. Marcel Dekker, New York and London 1969.

[5] *A. D. Hershey* and *M. Chase*, J. gen. Physiol. *36*, 39 (1952).

in a morphologically intact condition. The cell membrane surrounds the adsorbed virus particle, a vacuole is formed which moves to the interior of the cell, and the outer membrane of the cell closes again. In biology this process is termed phagocytosis. Basically, there is nothing specific about it, since cells absorb a wide range of particulate substances, for example metal salts and latex droplets, in the same way. When the walls of the vacuole containing the virus particles break down, these enclosed particles also begin to disintegrate.

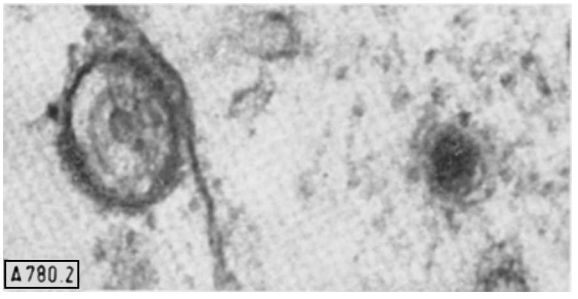


Fig. 2. Penetration of viruses into the cell. This electron micrograph shows the cross-section of a cell infected with herpesviruses. Outside the cell membrane (left) there is an infectious herpes virus particle characterized by an outer membrane, a virus coat, and a core. The identity of the virus particle that has entered the cell (right) is only revealed by the presence of its core. (This photograph was kindly made available by Prof. *K. Munk* and Frau *C. Waldeck*; magnification: 200 000 ×.)

Figure 2 shows the morphological changes a herpesvirus particle undergoes after penetration into a cell. The electron micrograph shows a herpesvirus particle on the outside of the cell and one within the cell. The intact herpesvirus particle adsorbed onto the cell surface consists of an outer membrane-like coat shown in section in the photograph; this coat can be partly of cellular origin. In the interior of the cell is the true virus coat, which surrounds the central structure of the virus particle. The latter consists of a particular protein and the viral nucleic acid closely associated with it; in herpesviruses this is DNA. This inner complex is called the core. Such a core, which has lost its outer membrane and its coat, is found in the interior of a cell. This is the first step in the breakdown of the virus particle leading to liberation of the viral nucleic acid. The virological term for this process is "uncoating". It includes two phases, each of which has been very carefully investigated using DNA-containing poxviruses [6]. The poxviruses consist of a double-stranded DNA, the virus coat protein, and phospholipids. The fate of these three components in uncoating can be traced precisely in radioactively labeled virus preparations. The first part of the uncoating process occurs very rapidly and immediately after adsorption of the virus onto the cell. The phospholipid of the outer virus coat is broken down into acid-soluble degeneration products, which results in particles that are about half the size of the true virus particles and consist only of DNA and protein. These are the cores of the virus particles.

The first stage in the uncoating process is carried out by the cells. As has been shown by the use of inhibitors (substances inhibiting protein or RNA synthesis), this does not require new synthesis of particular proteins or even of RNA. Apparently the cells are equipped with enzymes capable of breaking down the virus particles to reveal the core, *i.e.* of removing the outer virus coat. It is only in the second stage that the viral DNA is liberated from the core and can then be broken down by deoxyribonuclease (DNase) into acid-soluble fragments. This sensitization of the viral DNA to the action of DNase can be used experimentally to determine the degree and the rate of uncoating [6]. The principle of such experiments is relatively simple. Purified virus preparations whose DNA is radioactively labeled for this purpose are used. In order to analyze the rate and extent of the uncoating process the cells are disintegrated by ultrasound treatment at various times after infection and the cell lyzate is treated with DNase. Provided the viral nucleic acid is within the core it cannot be attacked by deoxyribonuclease, as it is still protected by its protein coat. Thus the radioactive components that are degraded by DNase and broken down into acid-soluble fragments must consist of viral DNA released from its inner protein coat (Fig. 3).

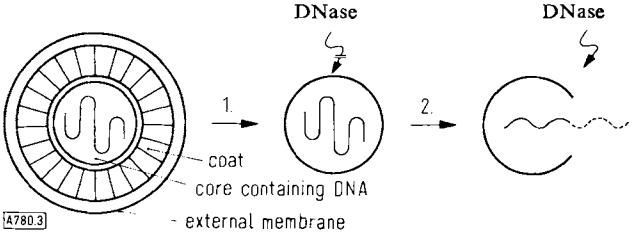


Fig. 3. Intracellular liberation of viral DNA from the enclosing protein coat (uncoating). The figure shows the process in diagrammatic form. The outer membrane, which can be missing in many kinds of viruses, is first removed, followed by the true virus coat. The core is left as a result of this step. The arrangement of viral DNA within the core is here represented very schematically. At this stage the DNA is still protected against DNase. It is only in the second stage, that of the true uncoating, that the DNA is freed from the core and exposed to the action of DNase.

When the process of uncoating is studied with the aid of radioactively labeled simian virus (SV 40) [7], it is found that in the course of a day only about 20 % of the viruses entering the cells liberate their DNA (the virus reproduction cycle does not last longer than two days). This observation shows the inefficiency of virus infection. It is absolutely untrue that every virus particle penetrating a cell can initiate an infectious cycle. Only some of the viruses give rise to infectious progeny.

2. The Phase of Information Transfer

When does the viral genome start to function, and how can this be determined? In discussing this question we have to distinguish between DNA and RNA viruses. In the former the commencement of function

[6] *W. K. Joklik*, J. molecular Biol. *8*, 263 (1964).

[7] *G. Sauer* and *E. C. Hahn*, Z. Krebsforsch. *74*, 40 (1970).

is synonymous with synthesis of messenger RNA on the DNA molecule. The genetic information contained in the DNA is transcribed onto the messenger RNA, and it is only after this that the virus-specific proteins can be synthesized in the cell ribosomes in accordance with the information contained in the messenger RNA. Thus, in DNA viruses the transfer of information initially occurs at the transcription stage (synthesis of messenger RNA on the virus DNA) and then at the translation stage (production of virus-specific proteins in the messenger RNA-ribosome complex). The RNA-containing viruses behave quite differently: there is no need for a transcription stage as their RNA acts directly as messenger RNA. In this case the commencement of function of the virus genome is identical with the production of virus-specific proteins.

The question on the commencement of virus genome function can be answered most easily by experiments using DNA viruses, as in this case one only has to demonstrate the appearance of virus-specific messenger RNA within the cell. With RNA viruses this can only be achieved by demonstrating the appearance of virus-specific protein in the cell, and this presents certain difficulties. Use of the DNA-RNA hybridization technique can demonstrate the presence of even a very small amount of virus-specific messenger RNA in an infected cell. As the sequence of bases in the viral messenger RNA is an exact mirror image of, and complementary to, the viral DNA, under suitable conditions the latter can be bound selectively to the messenger RNA among all the many other kinds of RNA present in a cell.

The synthesis of virus-specific messenger RNA requires the presence of an enzyme, a DNA-dependent RNA-polymerase. This enzyme catalyzes the synthesis of the messenger RNA molecule. It has recently been found that many DNA poxviruses carry this enzyme [8]. They are thus able to actuate their own transcription. It is not yet known, however, whether this enzyme occurs in other DNA viruses.

When does the transcription of the viral DNA begin? For a long time it was believed that this occurred when the viral DNA was completely freed from its protein coat by the uncoating process, but here too some surprising facts emerged from studies of members of the poxvirus group. It was shown that messenger RNA is synthesized if just the outer virus coat is removed, and not the inner protein coat around the virus DNA [9].

Is all the information in the virus DNA transcribed at the same time, or does this happen gradually in a certain order? In the viruses in which this has been investigated, the transcription is gradual. Thus, for example, in simian virus 40, only a quarter of the virus genome is copied as messenger RNA in the early phase of the infectious cycle. This transcription of the "early" messenger RNA is made from the viral DNA after the latter's penetration of the cell, but before replication of the DNA [10]. "Late" messenger RNA is only transcribed after the initiation of viral DNA replication (Fig. 4).

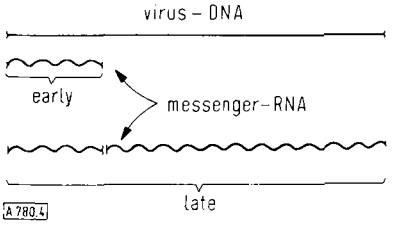


Fig. 4. Synthesis of virus-specific messenger RNA on the viral DNA. The information stored in the virus genome is transcribed in stages. First only one part of the DNA is translated into "early" messenger RNA. The remaining sequences of the DNA can only be transcribed at an advanced stage of the virus infectious cycle when the viral DNA has replicated. Such "late" messenger RNA contains "early" messenger RNA and new base sequences.

Obviously replication of the viral DNA is required before the whole virus genome and not only its early sequences can be transcribed. If one administers inhibitors of DNA replication and thus prevents multiplication of the viral DNA in the infected cell, only early messenger RNA is found and the late virus messenger RNA sequences are missing altogether. In such artificially inhibited cells one can only detect the presence of the "early" gene functions of the virus. For most DNA viruses these early gene functions are expressed by the stimulation of a series of enzymes concerned with DNA metabolism. Thus, in the affected cells the activity of the enzyme thymidine kinase is increased severalfold after infection with most DNA viruses [11]. "Late" virus functions require the presence of "late" virus-specific messenger RNA in the cells, which, as already mentioned, is dependent on replication of the viral DNA. Late viral functions are the synthesis of the virus protein coat and finally, as the last decisive step in the infectious cycle, assembly of the virus particle from its components present in the cell, *i.e.* virus maturation.

It follows from these remarks that the genetic information stored in the viral genome is transcribed sequentially and that this transcription is subordinate to a special control mechanism. It has not yet been explained what factors control the progressive promulgation of the genetic information, and why the viral DNA must undergo replication before being fully transcribed by late virus-specific messenger RNA.

What happens in the promulgation of the genetic information of RNA viruses? The question is somewhat more difficult to answer experimentally than in the case of DNA viruses. As regards the enteroviruses, in which this has been investigated, another set of rules seems to apply. In this case the viral RNA which also serves here as messenger RNA is translated not gradually but all at once, in its entirety, into a single very large protein. This protein is subsequently

[8] *J. R. Kates* and *B. R. McAuslan*, Proc. nat. Acad. Sci. USA *58*, 134 (1967).

[9] *J. R. Kates* and *B. R. McAuslan*, Proc. nat. Acad. Sci. USA *57*, 314 (1966).

[10] *G. Sauer* and *J. R. Kidwai*, Proc. nat. Acad. Sci. USA *61*, 1256 (1968).

[11] *S. Kit* and *D. R. Dubbs*: Monographs in Virology. Vol. 2. S. Karger, Basel and New York 1969.

broken down into several small proteins with different functions [12, 13]. Whether this principle is valid for all RNA viruses requires further demonstration.

Accumulation of the viral gene products in the infected cell is a function of the virus genome and is not dependent on whether it is a DNA or an RNA molecule. The amount of these products only increases strikingly after the initiation of the virus DNA or RNA replication, as shown by Figure 5. As already mentioned, it is not only the quantity but also the quality of the virus-specific proteins present in the cell that changes.

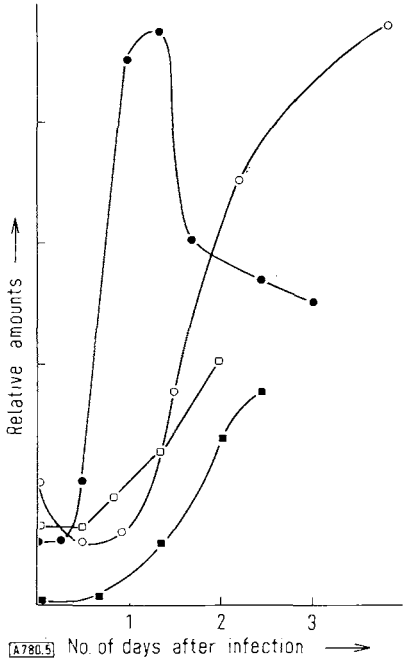


Fig. 5. Synthesis of specific virus products during a virus growth cycle, taking simian virus 40 as an example. In monkey kidney cell culture the replication cycle takes a little less than two days. The initiation of the replication of the viral DNA can be divided into two phases. In the early phase of the infection, even before the start of DNA replication (□), there is an increase in the activity of the enzyme thymidine kinase (●)[*]. The activity of this enzyme is subject to regulation, as may be seen from the fall in the curve toward the end of the infectious cycle. In the late phase of infection at the start of viral DNA synthesis (□), the amount of the virus-specific messenger RNA (■) in the cell increases strikingly. Mature virus particles are formed a few hours later (○).

Large numbers of copies of the virus nucleic acid are produced in the infected cells, and a great quantity of structural protein for the virus coat is synthesized. These are the precursors, the components of the newly maturing generation of virus particles, and their assembly to form infectious virus particles constitutes the end of the virus replication cycle.

3. The Architecture of Viruses

Are there any general principles underlying the structure of virus particles? The possible shape that most virus particles can assume is limited by the fact that only a limited space is available to contain the requisite genetic information. Thus, viruses must be satisfied with a fairly simple structure, since if this were complicated it would require many different kinds of structural proteins; the small amount of genetic information carried by viruses would certainly not be sufficient for this purpose.

Just how few opportunities there are for variation in the shape of virus particles was made clear more than 10 years ago in a review by *Crick* and *Watson* at the symposium on the nature of viruses [14]. *Crick* and *Watson* assumed that the nucleic acid of a small virus particle has a molecular weight of about two million, which corresponds closely with reality. Such a nucleic acid is composed of about 6000 nucleotides. As every three nucleotides determine one amino acid, not more than 2000 amino acids can be formed altogether and be united in one protein. Such a protein, however, is much too small to form a coat around the nucleic acid of the virus particle. To fulfill this purpose, it can be calculated that a protein must be at least 15 times as large. All the genetic information of the virus particle would then have to be used just for the formation of the protein coat. We know, however, that the virus nucleic acid has other functions to fulfil as well.

For this reason *Crick* and *Watson* concluded that the coat of a virus particle cannot consist of a single large protein molecule, but must be formed from many identical but small protein molecules, as only a minor section of the nucleic acid is required for the encoding of small protein molecules. In this way the limited genetic information is used economically. For the same reasons *Crick* and *Watson* concluded even at that time that it seemed unlikely that many small protein molecules of different kinds could participate in the construction of the virus coat: each different protein would require a section of the nucleic acid for its specification, and we would end up with the same difficulty. These possibilities are shown schematically in Figure 6.

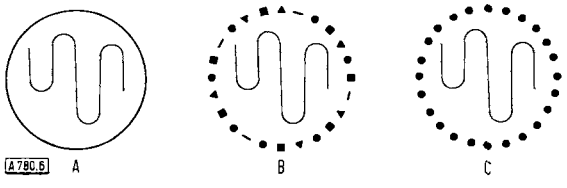


Fig. 6. Possible ways of assembling a virus coat. The diagram shows possible ways in which protein molecules can coat the viral nucleic acid, shown here by wavy lines. Case A, in which a single large protein molecule surrounds the nucleic acid, is not found. Case C is frequently found to occur in small viruses. Here many small, identical, protein molecules form a coat around the nucleic acid. The coat is only constructed of several different proteins in the larger viruses whose nucleic acid has a higher information content (case B).

According to our present knowledge the above views of *Crick* and *Watson* have proved to be thoroughly sound. They do, however, need some modification. It is clear that the structural complexity of the virus coat

[12] *D. F. Summers* and *J. V. Maizel*, Proc. nat. Acad. Sci. USA *59*, 966 (1968).

[13] *E. D. Kiehn* and *J. J. Holland*, J. Virology *5*, 358 (1970).

[*] After *S. Kit* in *J. S. Colter* and *W. Paranchych*: The Molecular Biology of Viruses. Academic Press, New York 1967.

[14] *F. H. C. Crick* and *J. D. Watson* in *G. E. W. Wolstenholme* and *E. C. P. Millar*: Ciba Foundation Symposium on the Nature of Viruses. Churchill, London 1957.

is directly related to the information present in the nucleic acid. There are, for example, small viruses, such as the F2 phages, whose RNA has a molecular weight of only 1×10^6. This phage cannot encode more than three proteins, one of which is that of the protein coat of the virus particle [15]. In contrast, poxvirus, for example, has a more complicated structure. Its DNA has a molecular weight of 1.5×10^7, and so it is not surprising that the poxviruses have a very complex architecture, whose subunits are composed not of one but of several different proteins [16].

These proteins encoded by the virus genome are not joined in simple fashion to give a membrane-like envelope, but form small aggregates, as it were the bricks of the virus coat. After appropriate staining these bricks or subunits of the coat appear in the electron microscope as small cylinders or tubes, pentagonal or hexagonal in cross-section. These are termed capsomeres [17]. The structure formed by all the capsomeres is called the capsid, which surrounds the nucleic acid in the form of a protective coat. Thus, the virus coat consists of large numbers of radially arranged capsomeres or tube-like structures. Some viruses are in addition surrounded by a membrane-like structure, as already described in the previous section. The mature infectious virus particle is formed when all these different morphological structures are assembled together.

The question now arises as to the configuration in which the morphological subunits and thus the capsomeres are arranged, and we can further inquire as to whether there are certain basic forms of particle symmetry that are followed by the most dissimilar viruses. X-ray crystallography and electron microscopy have shown that most viruses are in fact constructed in one of two ways. They either form helical tubes or rods or are spherical capsules with cubic symmetry (Fig. 7).

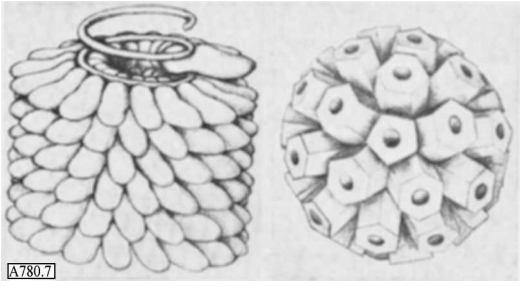


Fig. 7. Models of viruses possessing helical and cubic symmetry. The figure on the left shows a tobacco mosaic virus with a helical arrangement of its monomer proteins; the latter are also the morphological subunits of its coat. These proteins have been removed from the upper part to show the spiral configuration of the RNA. The internal axis of the rod-like particle is hollow [*]. The figure on the right is a model of a cubic (icosahedral) virus particle. The coat is formed of radially arranged morphological subunits, the capsomeres. The viral nucleic acid is in the center of the particle [**].

We shall first consider the group containing the smaller number of viruses, *i.e.* the rod-shaped or helical viruses. The most studied and most prominent member of this group is the tobacco mosaic virus (TMV). This is an elongated rod whose distinctly demarcated subunits have a coil-like configuration. The structure of this virus has been extensively analyzed in work extending over many years [18]. TMV is composed of 2650 chemically identical morphological subunits. Not only is the total number of these subunits known, but also their molecular weight – about 17500. The amino acid sequence of the monomer proteins and thus of these subunits has been analyzed exactly: they are composed of 158 amino acid residues. The ribonucleic acid, with a molecular weight of 2×10^6, has a coil-like configuration and lies between coils formed by the subunits. This arrangement implies that the inner axis of the particle is hollow. Such a virus rod is remarkably stable, and its RNA is very well protected against the action of destructive enzymes such as RNase. The stability of the virus particle is based primarily on the specific binding forces between the protein molecules. Although the nature of these binding forces is still not precisely known, it is suspected that they are essentially hydrogen bonds. In addition to the tobacco mosaic virus there are other plant viruses characterized by helical symmetry. Among the animal viruses a helical structure is shown in particular by the myxoviruses; as already mentioned, this group includes the influenza viruses.

Most kinds of viruses have coats with cubic symmetry. Several regularly constructed bodies with cubic symmetry are distinguished; incidentally, these regular solids were already described by *Pythagoras*. The simplest body is the tetrahedron with four sides, and the next more complicated body is the hexahedron or cube. In order of increasing complexity, then come the octahedron, the dodecahedron, and finally the complicated icosahedron. Of all these bodies the icosahedron is favored by most viruses as the basis of their construction [19]. It is natural to ask why the virus particles are not constructed according to a more simple pattern. In the evolution of organisms it is generally the most economical principle that is preferred, and this in fact is true for the complicated icosahedron, a regular polyhedron with 20 surfaces and 12 vertices. With its many sides the icosahedron approaches the shape of a sphere, and it is precisely because of its many sides that it can be composed of many bricks or subunits. Consequently, these subunits and thus the proteins of the virus coat are also very small. This is a very economical principle, which brings us back to the idea put forward at the beginning, for such protein molecules also only require a small part of the genetic information of the virus particle for

[15] *H. F. Lodish*, Nature (London) *220*, 345 (1968).

[16] *J. A. Holowczak* and *W. K. Joklik*, Virology *33*, 717 (1967).

[17] *D. L. D. Caspar, R. Dulbecco, A. Klug, A. Lwoff, M. G. P. Stoker, P. Tournier*, and *P. Wildy*, Cold Spring Harbor Symposium on Quant. Biol. *27*, 49 (1962).

[*] After *A. Klug* and *D. L. D. Caspar*, Advances Virus Res. *7*, 225 (1960).

[**] After *W. Bernhard*, Umschau *67*, 658 (1967).

[18] *M. A. Lauffer* and *C. L. Stevens*, Advances Virus Res. *13*, 1 (1968).

[19] *D. L. D. Caspar* and *A. Klug*, Cold Spring Harbor Symposium on Quant. Biol. *27*, 1 (1962).

their encoding. As we have already seen, the genetic information in viruses is generally strictly limited.

It is not altogether easy to furnish proof that a virus particle is constructed according to the rules of icosahedral symmetry. An icosahedron is composed of a definite number of structural elements. Thus, in the analysis of viruses by electron microscopy one attempts to determine whether the total number of capsomeres corresponds to this rule [20]. It is not only the total number of capsomeres that must conform to certain crystallographic rules, but the arrangement of the capsomeres must also be in agreement with such principles. An icosahedron has several axes of symmetry. Figure 8 shows schematically an icosahedron from the aspect of a twofold, a threefold, and finally a fivefold symmetry axis. If one rotates the icosahedron body around these axes through 180, 120, or 72° it will assume the same orientation as at the beginning. The same must apply to the configuration of the capsomeres in the virus coat for icosahedral symmetry to be allotted to a virus. As an example of an icosahedron Figure 8 gives in diagrammatic form the capsomere arrangement of bacteriophage φX174. This phage is a very small virus particle; it consists of a total of 12 capsomeres [21].

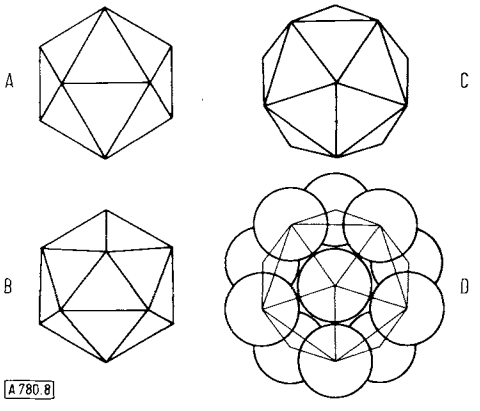


Fig. 8. Symmetry properties of an icosahedron. Most cubic viruses are constructed on the principle of an icosahedron, a polyhedron with 12 vertices and 20 surfaces, *i.e.* the arrangement and the number of its capsomeres (cf. Fig. 7) follow the rules of icosahedral symmetry. A, B, and C show two-, three-, and fivefold symmetry axes, respectively. D shows the capsomere arrangement of a small virus with 12 capsomeres, indicated simply by circles, and superimposed on this is the fivefold symmetry axis of the icosahedron.

Not all kinds of viruses have a helical or icosahedral shape. There are also viruses which cannot be allotted to any definite symmetry class. Thus, there is the complicated T4 phage with its hexagonal head containing the nucleic acid. Attached to this head is an elaborate apparatus whose purpose is to inject the nucleic acid into the host cell. Here we have a highly differentiated morphological structure.

Finally, mention should be made of a problem which has special relevance to general biology. This is the question whether the assembly of a virus particle from its constituent subunits is a self-organizing process, which occurs automatically and does not depend on anything other than the binding forces between the protein subunits. Or does it require a special protein, which controls the temporal and spatial pattern of the formative processes – in somewhat the same way as the organizer protein, which is known from the differentiation processes of higher organisms?

For some years now it has been possible to break down the tobacco mosaic virus into its monomer protein subunits and ribonucleic acid, and then to reassemble these components purely by mixing them in a test-tube, *i.e. in vitro* [22, 23]. The virus particles produced in this way do not differ in any way from those developed normally in a cell, and they prove to be fully infectious. Even in the absence of the ribonucleic acid the monomer protein subunits are united by their binding forces to produce a helical structure, which is very similar to the mature virus particle. No external influence is necessary for the assembly of a tobacco mosaic virus particle, and for this reason the process is said to be one of "self-assembly".

Recently, however, papers have been published which indicate that certain RNA phages require another kind of protein, in addition to their coating protein and their RNA, in order to be able to assemble an infectious particle. This protein has been called maturation protein, as it seems to exert a regulating function on the assembly of the virus coat. During the *in vitro* reconstruction of such phages from their components the presence of this protein seems to be necessary to ensure combination of the RNA and the coat protein to form infectious phages. It has been shown that only a few molecules of this maturation protein are necessary for one phage particle [24]. This observation throws an interesting light on the morphogenesis of such simply formed structures as viruses.

It is just because of the narrow limitations of their genetic information that viruses offer such excellent models for the analysis of many processes which are very difficult to study in higher organisms.

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[22] *G. Schramm*, Z. Naturforsch. *2b*, 249 (1947).

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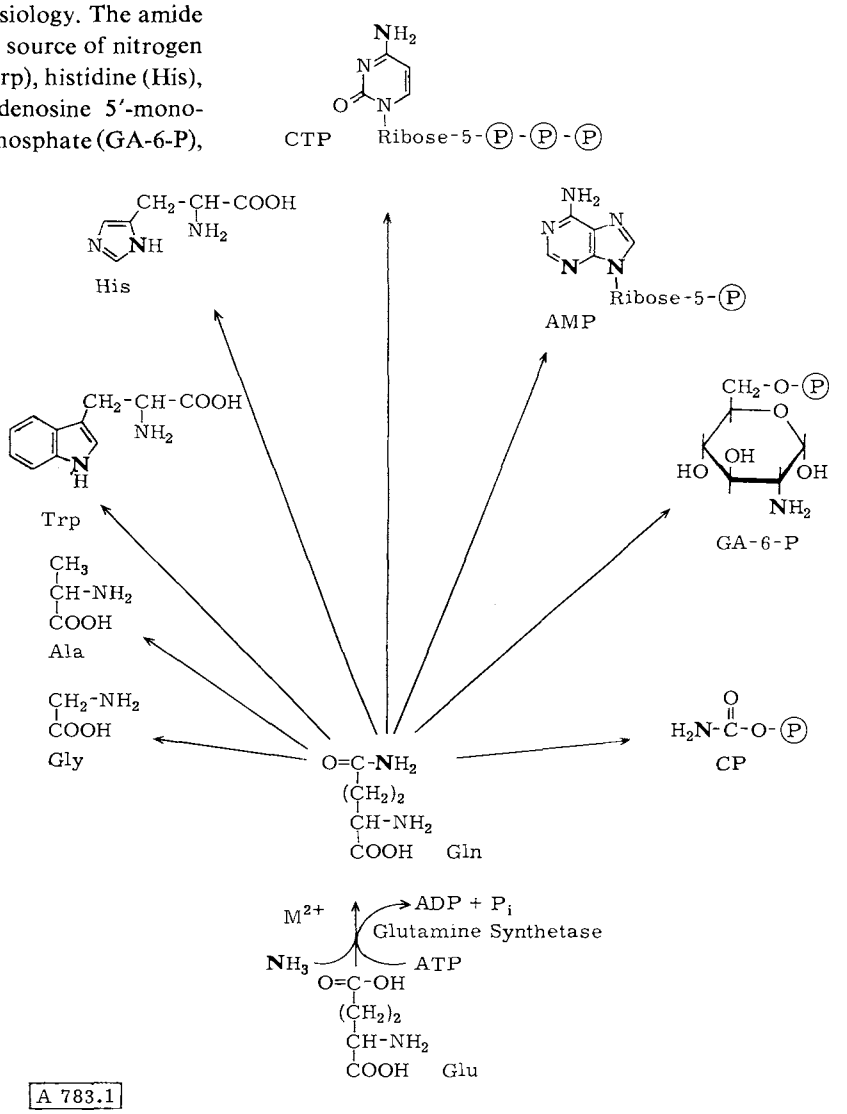
Regulation of Glutamine Synthetase by Enzyme Catalyzed Structural Modification[**]

By Bennett M. Shapiro[*]

A highly sophisticated mechanism for the regulation of glutamine metabolism in Escherichia coli involves the modification of the enzyme glutamine synthetase by the covalent attachment and release of adenylyl residues. Separate enzymes catalyze the adenylylation and deadenylylation reactions, and these enzymes are reciprocally controlled by the state of nitrogen nutrition of the cell. The resultant structural alterations in glutamine synthetase enable it to change its catalytic potential greatly in response to varying cellular demands, in order to maintain nitrogen homeostasis.

1. Introduction

Glutamine serves as the nitrogen donor for a great many metabolites in microorganisms, and thus occupies a central role in cellular physiology. The amide group of glutamine is the preferred source of nitrogen in the biosynthesis of tryptophan (Trp), histidine (His), cytidine 5'-triphosphate (CTP), adenosine 5'-monophosphate (AMP), glucosamine 6-phosphate (GA-6-P), and carbamyl phosphate (CP) (Figure 1). The α-amino group of glutamine may be used in the syntheses of other amino acids by glutamine-specific transaminative reactions (for review see [1]).



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Fig. 1. Biosynthesis and metabolic fates of glutamine (Gln). P_i = inorganic phosphate.

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[**] Presented at the Annual Meeting of the German Biochemical Society, Freiburg im Breisgau, January 1969.

[1] *E. R. Stadtman, B. M. Shapiro, H. S. Kingdon, C. A. Woolfolk,* and *J. S. Hubbard,* Advan. Enzyme Regulation *6*, 257 (1968).

Glutamine synthetase, the enzyme which catalyzes the synthesis of glutamine (Gln) from glutamate (Glu), ammonia, and ATP (Fig. 1) is at the head of a highly branched metabolic pathway, and as such should be a strategic center of cellular regulation. A study of the regulation of the glutamine synthetase from *Escherichia coli* has led to the discovery that the bacterial enzyme is subject to control by at least four different mechanisms. Firstly, there is repression and derepression of enzyme biosynthesis in response to the nature and quantity of the nitrogen source given to *E. coli* for its growth. Secondly, glutamine synthetase is subject to cumulative feedback inhibition by the multiple end products of glutamine metabolism shown in Fig. 1.

Thirdly, the activity of glutamine synthetase is modulated by the relative concentrations of ATP, divalent cation, and other nucleotide tri- and diphosphates. These three mechanisms of regulation have been discussed in an earlier review [1] and will not be dealt with here.

The present article concerns a novel control mechanism effective on glutamine biosynthesis: regulation of the catalytic potential of glutamine synthetase by the covalent attachment and release of adenylyl residues.

2. Multiple Forms of Glutamine Synthetase

A comparison of the properties of glutamine synthetase preparations which had been highly purified from different batches of cells showed that the apparently homogeneous preparations differed markedly in their susceptibility to feedback inhibition by the compounds shown in Fig. 1, as shown in Fig. 2. The

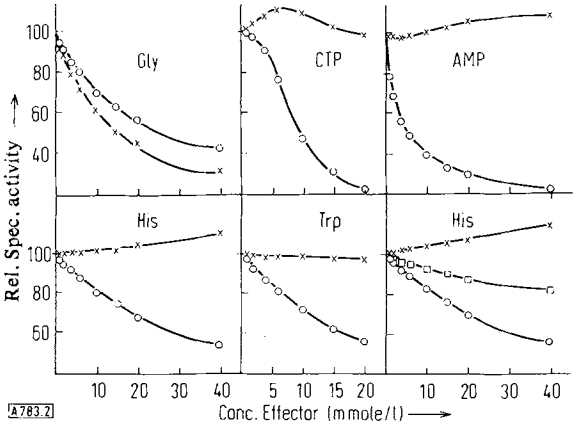


Fig. 2. Effect of products of glutamine metabolism on the activity of two purified preparations of glutamine synthetase. Preparation I (×—×) was purified from cells grown on limiting quantities of NH_4^+; Preparation II (o—o) was purified from cells grown on relatively high amounts of glutamate. Enzyme activity was measured by the γ-glutamyl transfer reaction catalyzed by glutamine synthetase (for details, see [3]).

different behavior of the preparations could not be attributed to structural modifications during the purification procedure, nor to differences in storage or handling of the enzyme preparations. In addition, all attempts to convert one form of the enzyme into another by treatments known to modify the tertiary and quaternary structure were unsuccessful.

The two preparations were made from cells grown under different conditions, and a detailed examination of the relationship between the conditions of growth of *E. coli* and the properties of the glutamine synthetase purified from it led to the discovery that different molecular forms of glutamine synthetase are produced depending upon the state of nitrogen nutrition of *E. coli* during growth [2, 3]. As shown in Table 1,

Table 1. Effect of nitrogen source (limiting NH_4^+ or glutamate) and age of culture on the response of γ-glutamyl transferase activity to various effectors (from [3]).

Effector (mmole/l)	Relative activity [a]			
	Log phase cells		Stationary phase cells	
	Limiting NH_4^+	Glutamate	Limiting NH_4^+	Glutamate
None	100	100	100	100
AMP, 40	131	131	115	20
L-tryptophan, 20	101	102	92	50
L-histidine, 40	115	113	107	53
CTP, 8	83	105	97	51
Glycine, 40	36	32	34	47

[a] Relative specific activities in the transferase reaction, catalyzed by glutamine synthetase, compared to activity without effector = 100. *E. coli* W was grown in medium containing 11 mmole/l glucose and either 6 mmole/l NH_4Cl or 19 mmole/l glutamate, as indicated. Cells were harvested 24 h after inoculating (stationary phase cells) or in late log phase (with NH_4^+, 5.5 h after inoculation; with glutamate 11 h after inoculation).

when *E. coli* was in the logarithmic growth phase, the quantity or nature of the nitrogen source for growth made little difference in the nature of the glutamine synthetase obtained. However, when the organism reached the stationary phase there was a significant difference in the enzyme activity of cell extracts, depending upon whether the nitrogen source was NH_4Cl in growth-limiting quantities or glutamate [3].

The enzyme from glutamate-grown, cells was very sensitive to inhibition by AMP, CTP, L-tryptophan and L-histidine, whereas the enzyme from NH_4-grown cells was insensitive to inhibition by these compounds, but was more susceptible to inhibition by glycine and alanine. Neither the carbon source used (glycerol or glucose) nor the extent of aeration of the culture made any difference in the type of glutamine synthetase obtained.

The results showed that the growth conditions were important in determining the character of the glutamine synthetase found in the cells, but a precise nutritional basis for the observed effects is still not apparent since the onset of the stationary phase in the two types of growth media might be due to different metabolic events. In the NH_4^+ medium the cessation of growth is clearly due to depletion of the available nitrogen source; in the glutamate medium, however, the stationary phase might be initiated by

[2] *B. M. Shapiro, H. S. Kingdon,* and *E. R. Stadtman,* Proc. Natl. Acad. Sci. U.S. *58,* 642 (1967).

[3] *H. S. Kingdon* and *E. R. Stadtman,* Biochem. Biophys. Res. Commun. *27,* 470 (1967); *H. S. Kingdon* and *E. R. Stadtman,* J. Bacteriol. *94,* 949 (1967).

either depletion of the energy supply or other unknown factors. It has been recently shown [5] that in the stationary phase attained after growth on NH_4^+ there is no free ammonia in the medium, but after growth on glutamate there is a fairly high ammonia concentration during the stationary growth phase. Thus, the availability of nitrogen for growth appears to be the decisive factor in determining the nature of the glutamine synthetase produced by *E. coli*.

To determine the structural basis for the different catalytic properties seen in enzyme preparations elaborated by cells grown under different conditions, a comparison was made between glutamine synthetase from cells grown on limiting quantities of NH_4^+ (Preparation I) and from those grown on glutamate (Preparation II).

The differences between the enzyme forms are preserved upon purification. Thus preparation I is more active in glutamine biosynthesis when Mg^{2+} is the activator used (Table 2) whereas Preparation II is

Table 2. Some properties of preparations I and II (from [7]).

Enzyme preparation	Specific activity		Effect of AMP on transferase activity [b]
	Mg^{++}	Mn^{++}	
I	60.1	2.0	10 % activation
II	12.8	8.1	74 % inhibition

[a] Specific activity in biosynthetic assay = μmoles P_i min^{-1} mg^{-1}, which is equivalent to the number of μmoles of glutamine synthesized (Fig. 1).

[b] AMP = 40 mmoles/l.

more active with Mn^{2+}. Moreover, the total biosynthetic activity seen with Preparation I (+ Mg^{2+}) is greater than that seen with Preparation II (+ Mn^{2+}). Thirdly, as shown in Table 2 and Fig. 2, Preparation II is more sensitive to feedback inhibition by the products of glutamine metabolism than is Preparation I.

3. Structural Basis for the Enzyme Multiplicity

Preparations I and II were purified by the same method [2], had the same molecular weight [4], and each migrated as a single molecular species when examined either in the ultracentrifuge or by disk gel electrophoresis [2,4,5]. Additionally, there were no remarkable differences in the amino acid compositions of the two enzyme preparations [2] and each was found to have the same characteristic double hexagon structure when examined by electron microscopy [6] (Fig. 3). However, a distinct difference between the two forms was seen when the ultraviolet spectra of the enzymes were compared (Fig. 4). Preparation II absorbs more ultraviolet light in the region below 280 nm than does Preparation I, and the difference

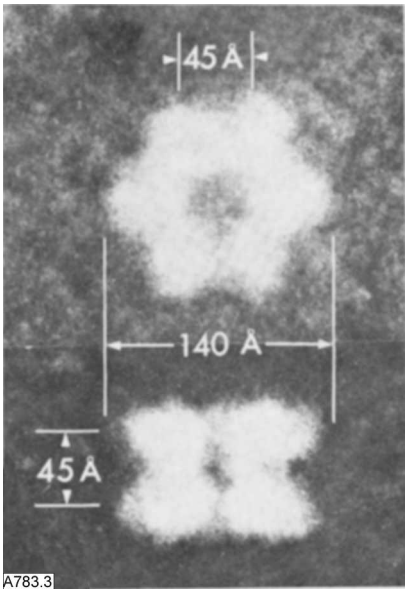


Fig. 3. Electron micrograph of the *E. coli* glutamine synthetase (by *R. Valentine*) showing full (above) and side views (below) of the enzyme molecule. The 12 subunits of the enzyme are arranged in two superimposed hexagons; from this micrograph we were able to calculate the molecular weight of the subunit (48 500) which was found to be in good agreement with that from hydrodynamic measurements. (Data of *Valentine et al.* [6]).

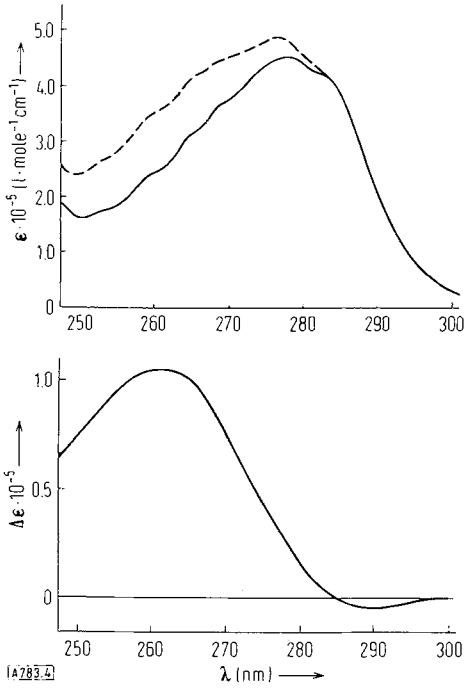


Fig. 4. Above: Ultraviolet spectra of Preparations I (—) and II (— — —). Below: Difference spectrum between the two forms (from [2]).

spectrum is characteristic of nucleotide derivatives. By isolation and chemical analysis of the nucleotide bound to preparation II, it was established that the two preparations differed in their content of AMP.

As is shown in Table 3, Preparation I contained about 1.2 equivalents of bound AMP, whereas Preparation II contained about 9.0 equivalents [2]. The covalent nature of the binding was indicated by the fact that the AMP could not be removed by treatment with charcoal, with acid ammonium sulfate, or by digestion with dilute acid or alkali [2]. On the other hand,

[4] *B. M. Shapiro* and *A. Ginsburg*, Biochemistry 7, 2153 (1968).

[5] *K. Liess, F. Varricchio, D. Mecke*, and *H. Holzer*, Europ. J. Biochem. 4, 193 (1968).

[6] *R. C. Valentine, B. M. Shapiro*, and *E. R. Stadtman*, Biochemistry 7, 2143 (1968).

Table 3. Chemical characteristics of two preparations of glutamine synthetase differing in their state of adenylylation (from [2]).

	Prep. I	Prep. II
	moles/mole enzyme	
Total organic phosphate	1.2	9.0
Total pentose	1.0	6.0
Total adenine nucleotide [a]	1.2	8.6
Adenine nucleotide release by phosphodiesterase digestion [b]	0.6	9.0

[a] Calculated from absorbancy at 260 nm and 280 nm [7].

[b] Calculated from absorbancy at 260 nm for the solution after precipitation of protein with perchloric acid [2]. The product was also characterized by reaction with the specific enzymes, 5'-adenylic acid deaminase and adenosine deaminase.

the nucleotide is readily removed by digestion with snake venom phosphodiesterase, indicating that the linkage is a phosphodiester bond, and the product of this digestion is AMP, as determined by enzymic analysis [2].

4. Adenylylation of Glutamine Synthetase *in vitro*

The existence of preparations of glutamine synthetase which differ in their catalytic properties according to the number of adenylyl groups bound to them could constitute a powerful mechanism for regulating glutamine metabolism *in vivo*. That this type of regulation exists is indicated by the fact that during exponential growth on glutamine as a nitrogen source a relatively unadenylylated enzyme preparation is formed (Preparation I), whereas during the stationary phase the enzyme becomes adenylylated (Preparation II). This observation suggests that *E. coli* can elaborate an enzyme which will catalyze the adenylylation of glutamine synthetase. Such an enzyme has been found in extracts of *E. coli*; it catalyzes the transfer of the adenylyl moiety of ATP to glutamine synthetase [eq. (1)]:

$$\text{glutamine synthetase} + \text{ATP} \xrightarrow[\text{adenylyltransferase}]{M^{2+}} \text{adenylyl glutamine synthetase} + PP_i \quad (1)$$

The reaction is stimulated by glutamine and inhibited by glutamate and α-ketoglutarate [7]. The enzyme activity can be detected either by measuring the incorporation of radioactivity from ^{14}C-labeled ATP into glutamine synthetase, or by re-isolating the glutamine synthetase after adenylylation and determining the number of equivalents of AMP bound by measuring the absorbancy of the enzyme at 260 nm compared to that at 290 nm [7,8]. Both methods yield the same result: glutamine synthetase may be adenylylated to the extent of twelve equivalents of AMP per mole of enzyme (MW = 600000), or one equivalent of AMP per subunit (MW = 50000) [9]. The enzyme that catalyzes this covalent attachment of adenylate to glutamine synthetase has been named ATP: glutamine synthetase adenylyltransferase [7].

If the number of adenylyl groups present on glutamine synthetase were the only structural alteration responsible for the catalytic differences between Preparations I and II, then adenylylation of Preparation I should be accompanied by the following changes in its catalytic properties:

1) a decrease in biosynthetic activity when Mg^{2+} is the activating cation;

2) an increase in the biosynthetic activity with Mn^{2+} as the activating cation;

3) an increase in the sensitivity to feedback inhibition by any one of several products of glutamine metabolism.

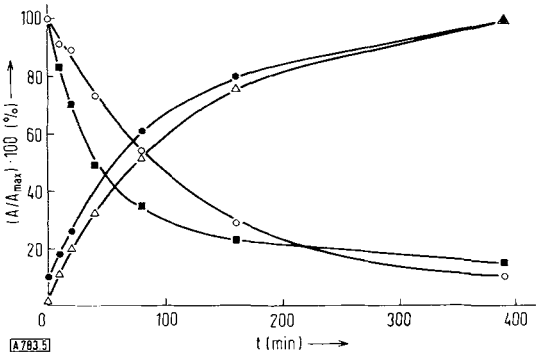


Fig. 5. Changes in several catalytic parameters of glutamine synthetase during adenylylation. Values are expressed as percentages of the maximal change seen as a function of the duration of the adenylylation reaction. △—△ covalent linkage of adenylyl residues; ○—○ Mg^{2+}-specific biosynthetic activity; ●—● Mn^{2+}-specific biosynthetic activity; ■—■ specific activity in the presence of 40 mmoles/l AMP (indicating change in the ability of the enzyme to be inhibited by AMP) (from [7]).

Figure 5 shows the changes seen in these parameters as a result of increasing numbers of adenylyl residues being attached to glutamine synthetase during the adenylylation reaction. The expected changes in the divalent cation specificity are seen to occur, as is the increased sensitivity to inhibition by AMP, as reflected by a decrease in enzyme activity in the presence of high concentrations of AMP. It has similarly been shown [7] that removal of the adenylyl residues, catalyzed by snake venom phosphodiesterase, leads to a conversion of glutamine synthetase from an enzyme with the properties of Preparation II into one with the properties of Preparation I. Thus, it seems that the different amounts of covalently bound AMP present on Preparations I and II of glutamine synthetase is the factor responsible for their different catalytic properties.

Holzer, Mecke, and their co-workers had previously described the presence of an enzyme in cell extracts of *E. coli* which catalyzed the ATP-dependent, glutamine-stimulated inactivation of glutamine synthetase [10]. They had studied the inactivation of glutamine synthetase by observing that the biosynthetic activity of the enzyme decreased when activity was measured in the presence of Mg^{2+} as divalent cation. Since this change in activity is one of several

[7] *H. S. Kingdon, B. M. Shapiro*, and *E. R. Stadtman*, Proc. Natl. Acad. Sci. U.S. *58*, 1703 (1967).

[8] *E. R. Stadtman, B. M. Shapiro, A. Ginsburg, H. S. Kingdon*, and *M. D. Denton*, Brookhaven Symp. in Biology *21*, 378(1968).

[9] *C. A. Woolfolk, B. M. Shapiro*, and *E. R. Stadtman*, Arch. Biochem. Biophys. *118*, 736 (1966).

[10] *D. Mecke, K. Wulff, K. Liess*, and *H. Holzer*, Biochem. Biophys. Res. Commun. *24*, 452 (1966).

associated with the adenylylation of glutamine synthetase, it occurred to us that this inactivation phenomenon might be the same as the adenylylation reaction [7]; the identity of the two phenomena was almost simultaneously demonstrated by *Wulff et al.* [11] when they showed that their "inactivating enzyme" catalyzed a concurrent attachment of the adenylyl moiety of ATP to glutamine synthetase. We prefer the name "ATP:glutamine synthetase adenylyltransferase" to "glutamine synthetase inactivating enzyme", because the loss of Mg^{2+}-dependent catalytic activity is only one of several changes affected by the covalent attachment of adenylyl residues.

5. Properties of the ATP:Glutamine Synthetase Adenylyltransferase

The adenylyltransferase has been purified some 200-fold by a combination of ammonium sulfate precipitation and chromatography on DEAE cellulose and on hydroxylapatite [12]. The enzyme as purified in this fashion is only partly pure, as shown by agar gel electrophoresis [12]. The adenylylating enzyme is stabilized by thiols, glutamate, glutamine, and phosphate [13]. Sucrose density gradient centrifugation showed it to have a molecular weight of 120000 [12].

ATP is the only nucleotide which can serve as a nucleotidyl donor in the modification reaction [eq. (1)] [7,14]. Other nucleoside triphosphates are inhibitory: CTP is a competitive inhibitor [14] and UTP is noncompetitive with ATP [13]. The adenylylation reaction requires divalent cation, Mg^{2+} being most effective; Mn^{2+} has only 30% of the activity of Mg^{2+} [14].

The adenylyltransferase catalyzes an exchange reaction as shown in eq. (2); that is, in the presence of glutamate and Mg^{2+}, the enzyme catalyzes the exchange of ^{32}P between pyrophosphate and ATP [15].

$$ATP^* + \text{enzyme} \xrightarrow{\text{glutamate, } Mg^{2+}} \text{enzyme (AMP)} + {}^*PP_i \quad (2)$$

In fact, the adenylyltransferase is able to complex with ATP (at 25 °C in the presence of Mg^{2+}) and this complex may be isolated from free ATP by rapid gel filtration at 4 °C [13]. By comparing the nature of the complex formed with either ^{14}C-ATP or with γ-^{32}P-ATP, it was found that 50–70% of the nucleotide in the complex exists as intact ATP [13]. The pyrophosphoryl moiety of ATP is then discharged from the complex by subsequent incubation with either unadenylylated glutamine synthetase or with L-glutamate; when glutamine synthetase is used to discharge the pyrophosphate, a concomitant adenylylation of the glutamine synthetase occurs [13]. The nature of the adenylyltransferase-nucleotide bond is still unknown.

The adenylyltransferase exhibits specificity with regard to its enzymic substrate, glutamine synthetase, as well as to its nucleotide substrate, ATP. Thus, although the glutamine synthetase from *Bacillus subtilis* is structurally very similar to that from *E. coli* it cannot act as substrate for the *E. coli* adenylyltransferase, nor does it inhibit the adenylylation of *E. Coli* glutamine synthetase [16].

6. The Nature of the Adenylyl-Glutamine Synthetase Bond

The adenylyl-glutamine synthetase linkage is very stable, resisting cleavage by either 0.3 M HCl or 0.3 M NaOH at 37 °C for several hours [2]. This stability to both acidic and basic cleavage is unusual for the well known serine or threonine linkages which occur in glycoproteins or phosphoproteins. To determine which amino acid residue is responsible for the stable bond, we subjected ^{14}C-adenylyl-labeled glutamine synthetase to proteolytic digestion and isolated the peptide derivative which contained the adenylyl group. A decapeptide was isolated in high yield after exhaustive digestion with pepsin and pronase [17]. Of particular interest in the composition of this peptide is the absence of serine, threonine, or basic amino acids. In fact, tyrosine is the only amino acid present in the peptide that would be expected to form a phosphodiester bond of the required stability. The peptide-adenylyl bond resisted cleavage in 1 N NH_4OH for 5 hours at 105 °C; 50% of the peptide was recovered intact after this treatment [17]. Acid hydrolysis was complicated by the fact that the adenine-ribose linkage was cleaved before the peptide-phosphoribose bond. Tyrosine phosphate esters have been shown to have the required stability to acid and base [18]; *O*-phosphotyrosine releases negligible amounts of inorganic phosphate when heated at 37 °C for 48 hours in either 1 N HCl or 1 N NaOH.

Tyrosine, when present free or in peptide linkage, exhibits a characteristic ultraviolet absorption spectrum at alkaline pH that is due to ionization of the phenolic group; this is absent when the phenolic group is blocked and unable to ionize. To examine whether the adenylyl moiety is indeed linked to the peptide by a phosphodiester bond with tyrosine, we compared the absorption spectra of the peptide in alkaline solution before and after removal of AMP with snake venom phosphodiesterase. Fig. 6 shows the difference spectrum obtained when the deadenylylated peptide

[11] *K. Wulff, D. Mecke*, and *H. Holzer*, Biochem. Biophys. Res. Commun. *28*, 740 (1967).

[12] *E. Ebner*, Thesis, Universität Freiburg 1967; *H. Holzer*, Advan. in Enzymology (1969), in press.

[13] *S. B. Hennig, A. Ginsburg*, and *M. D. Denton*, unpublished.

[14] *C. Gancedo, E. Ebner, F. Schutt*, and *D. Mecke*, Meeting Europ. Biochem. Soc. Praha, 1968; FEBS Abstr., 5th. Meeting, 199 (1968).

[15] *M. D. Denton* and *A. Ginsburg*, Federation Proc. *27*, 783 (1968).

[16] *T. Deuel, S. B. Hennig*, and *A. Ginsburg*, unpublished.

[17] *B. M. Shapiro* and *E. R. Stadtman*, J. Biol. Chem. *243*, 3769 (1968).

[18] *R. H. A. Plimmer*, Biochem. J. *35*, 461 (1941).

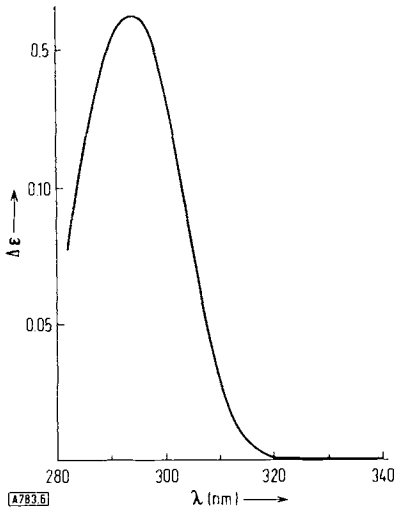


Fig. 6. Difference spectrum between adenylylated and unadenylylated peptide preparations. An adenylylpeptide was isolated after pepsin and pronase digestion of glutamine synthetase [17]. One portion of the peptide was treated with snake venom phosphodiesterase to release the adenylyl residue from covalent linkage; the other portion of peptide served as a spectral control. Both samples were adjusted to pH 13 and their spectra were compared. The phosphodiesterase cleavage resulted in the freeing of a tyrosyl hydroxyl group, which ionized in alkaline solution and gave the spectrum shown above (from [17]).

absorbancy is compared with that of the adenylylated peptide at pH 13. The peak at 292 nm is characteristic of an ionized phenolic hydroxyl group. One can calculate that it is present in equivalent amounts to that of the adenylyl moiety removed by the phosphodiesterase [17]. Thus, from the stability and spectral characteristics of the AMP binding peptide, it appears that the tyrosine residue present is responsible for this novel type of protein-effector covalent bond.

The decapeptide has a rather high proline content (2–3 residues per decapeptide). This may account for the difficulties encountered when we tried to digest the peptide to a smaller unit with other proteolytic enzymes [17]. One might additionally surmise that the high proline content provides a region of the glutamine synthetase molecule of minimal secondary structure. Such a region would be suitable for positioning the reactive tyrosyl residue such that the adenylyl group could be readily bound or removed.

7. Effect of Adenylylation on Subunit Interactions

As mentioned above, completely adenylylated glutamine synthetase contains twelve equivalents of AMP bound per mole of enzyme, or one equivalent per subunit. Therefore, species containing zero to twelve adenylyl residues per mole of enzyme are possible; with two or more adenylyl groups present per mole there exists the possibility of having multiple forms, each being unique with respect to the mutual arrangement of adenylyl residues. In fact, one can calculate [19] that 384 unique forms of glutamine synthetase are possible.

[19] *M. S. Raff*, personal communication.

Do hybrid forms containing a mixture of adenylylated and unadenylylated subunits in any one molecule of enzyme really exist? If they do, the question also arises whether subunit interactions in the hybrid molecules influence the stability and catalytic behavior of the enzyme. Toward this end, enzymes of different states of adenylylation (from 0–12 adenylyl residues per mole) were prepared and studied.

Enzymes exhibiting different states of adenylylation were prepared in one of the following three fashions:

1) Isolation from cells grown under different conditions of nitrogen nutrition;

2) incubation of unadenylylated enzyme preparations with the ATP:glutamine synthetase adenylyltransferase and ATP, to achieve progressive adenylylation of glutamine synthetase;

3) incubation of adenylylated glutamine synthetase with snake venom phosphodiesterase, to achieve progressive deadenylylation.

The partially adenylylated enzyme forms thus prepared were compared with mixtures of fully adenylylated and fully deadenylylated glutamine synthetase preparations which were mixed to have the same average content of adenylyl residues per mole of enzyme.

Two independent pieces of evidence have led to the conclusion that subunit interactions do indeed exist and that they may be of significance in the regulation of glutamine synthetase. The first of these [20] was a careful analysis of the Mg^{2+} and Mn^{2+} biosynthetic activities of hybrid glutamine synthetase forms under saturating substrate conditions. With optimal assay conditions, unadenylylated subunits were specifically activated by Mg^{2+} (pH optimum = 7.5–7.6) while the adenylylated subunits had an absolute requirement for Mn^{2+} (pH optimum = 6.5–6.6). This divalent ion specificity is that found by *Kingdon et al.* [7]. However, under optimal assay conditions, the relationship of divalent ion specificity to state of adenylylation is not a linear one but follows a sigmoidal distribution. Thus, the addition or removal of adenylyl residues at either extreme of adenylylation produces a relatively profound change in the Mg^{2+} or Mn^{2+} dependent catalytic activities, but at intermediate states of adenylylation (between three and eight moles AMP per mole glutamine synthetase) a change in the number of AMP residues covalently bound leads to a less marked alteration of catalytic properties. This non-linear behavior of the enzyme leads to the conclusion [20] that heterologous subunit interactions (between adenylylated and unadenylylated units) must have an effect on the catalytic activity of the enzyme.

The second set of experimental data leading to the conclusion that hybrid forms do exist concerns differential inactivation of adenylylated and unadenylylated enzyme forms in the presence of urea, under carefully defined conditions of temperature and pH [21]. *Ciardi* and *Stadtman* [21] found conditions in which only the adenylylated enzyme preparation was

[20] *A. Ginsburg, J. Yeh, S. B. Hennig*, and *M. D. Denton*, Biochemistry *9*, 633 (1970).

[21] *J. Ciardi* and *E. R. Stadtman*, personal communication.

inactivated, while the unadenylylated preparation was stable. Mixtures of adenylylated and unadenylylated enzyme preparations behaved as one might predict: all of the adenylylated enzyme was inactivated, leaving only unadenylylated enzyme still in the catalytically active form. Naturally occurring potential hybrid forms, on the other hand, are inactivated to a different extent than mixtures with the same average content of adenylyl groups, lending further support to the idea of interaction between subunits in hybrid molecules causing an alteration in the physical properties of the glutamine synthetase molecule. The extent and significance of the hybrid enzyme problem is presently under study [21].

8. The Glutamine Synthetase Deadenylylating Enzyme

In the growth studies cited above (Section 2) it was found that during the course of growth of *E. coli* with glutamate as the nitrogen source, the glutamine synthetase becomes adenylylated as the organism goes into the stationary phase of growth. Similarly, it was found [3,22] that when *E. coli* is changed from a medium containing glutamate to one containing low concentrations of NH_4^+, the glutamine synthetase changes the adenylylated to the unadenylylated enzyme. This led us to suspect the existence of a deadenylylating enzyme in *E. coli* which could remove adenylyl groups from glutamine synthetase in response to changes in growth conditions. To detect this enzyme, we used as substrate ^{14}C-AMP-labeled adenylylated glutamine synthetase, made with the adenylyltransferase as mentioned above (Section 4), and monitored the release of radioactivity [23], as shown in eq. (3):

$$^{14}\text{C-adenylylglutamine synthetase} \xrightarrow{\text{deadenylylating enzyme}} \text{glutamine synthetase} + {}^{14}\text{C-AMP} \quad (3)$$

We found such an enzyme activity in *E. coli* cell extracts and it had the quite interesting feature, from the point of view of cellular regulation (Section 9), that it was stimulated some twenty-fold by α-ketoglutarate and inhibited by glutamine. During the course of removal of adenylyl residues from glutamine synthetase, the enzyme changes from a form with characteristics of Preparation II (Section 2) to one with characteristics of Preparation I [23]. Thus, the removal of adenylyl residues by an *E. coli* glutamine synthetase deadenylylating enzyme leads to the changes in catalytic activity of glutamine synthetase which would be expected from what has been previously discussed. The presence of this enzyme has subsequently been confirmed by *Battig et al.* [24].

The glutamine synthetase deadenylylating enzyme has been purified twenty-fold by a combination of protamine sulfate fractionation, ammonium sulfate fractionation, and adsorption onto and elution from alumina C-γ gel [25]. When this partially purified preparation was chromatographed on a resin which separates macromolecules according to their size, it was resolved into two components, both of which are needed for enzyme activity [25]. *Anderson* [26] has found that component P_I has an approximate molecular weight of 150000 and P_{II} has a molecular weight of about 50000. The smaller component, P_{II}, is fairly stable; P_I is quite unstable and has resisted efforts at further purification [26].

There is a rather complex set of effectors which is required for stimulation of the deadenylylation of glutamine synthetase [25]. Thus, as shown in Table 4, omission of α-ketoglutarate from the reaction mixture decreases the reaction rate fifteen-fold. There is also a requirement for nucleotides; the synergistic effects of ATP and UTP lead to a fifty-fold stimulation of the reaction. Divalent cation is also required for deadenylylation. The most effective cation is Mn^{2+}; Mg^{2+} is needed at ten times as high a concentration to be as effective, and Ca^{2+}, Cd^{2+}, Zn^{2+}, and Ba^{2+} were without effect. Stimulation of the reaction by divalent anions is also observed; hydrogen phosphate and -arsenate were equally effective, and activated the reaction two-fold.

Table 4. Requirements for *E. coli* deadenylylation reaction. Enzyme used was 40-fold purified mixture of components P_I and P_{II}. (See ref. [25] for precise conditions of experiment.)

Reaction mixture	Activity (units)
Complete system	4.6
Complete system without α-ketoglutarate	0.3
Complete system without UTP	0.7
Complete system without ATP	3.5
Complete system without UTP and ATP	0.1
Complete system without $MnCl_2$	0.0
Complete system without phosphate	2.0
Complete system without dithiothreitol	4.1

The stimulation by α-ketoglutarate occurred at relatively low concentrations (K_m = 2.0 mM). Neither glutamate nor other α-keto acids could replace α-ketoglutarate in its stimulatory role. Conversely, 50 % inhibition occurs with glutamine [25] at 0.35 mM.

Thus, the deadenylylating enzyme is stimulated by α-ketoglutarate and inhibited by glutamine, whereas the ATP:glutamine synthetase adenylyltransferase was stimulated by glutamine and inhibited by α-ketoglutarate. The possible significance of these reciprocal effector responses is discussed in Section 9.

One of the most interesting features of the deadenylylation reaction is that it is specifically activated by nucleotide fractions [25], the most active of which are a combination of UTP and ATP (Table 4). This requirement was discovered during purification of the enzyme, when removal of nucleic acids from the

[22] *L. Heilmeyer, D. Mecke,* and *H. Holzer,* Europ. J. Biochem. *2*, 399 (1967).

[23] *B. M. Shapiro* and *E. R. Stadtman,* Biochem. Biophys. Res. Commun. *30*, 32 (1968).

[24] *F. Battig, L. Heilmeyer,* and *H. Holzer,* Meeting Europ. Biochem. Soc., Praha, 1968; FEBS-Abstr., 5th Meeting 194 (1968).

[25] *B. M. Shapiro,* Biochemistry *8*, 659 (1969).

[26] *W. Anderson,* personal communication.

enzyme preparation led to a loss of deadenylylating activity. Subsequently it was shown that several polynucleotide fractions could stimulate the twenty-fold purified deadenylylating enzyme preparation, with ribosomal RNA preparations being the most effective, and these only when employed synergistically with UTP[24]. When RNA is added to the maximally stimulated UTP-ATP activated deadenylylating reaction, it leads to inhibition of the reaction[25]. In all cases the stimulatory effects of RNA preparations was removed by treatment with ribonuclease. Of the mononucleotides tested, ATP and UTP were certainly the most effective, and behaved synergistically, as shown in Figure 7. Thus, UTP activates the deadenylylating reaction by itself in a sigmoidal fashion. In the presence of a saturating concentration of ATP, however, the shape of the saturation curve for UTP changes considerably, and UTP is now effective at much lower concentrations[24]. It is the ATP effect on the UTP-stimulated deadenylylating reaction that can be replaced by polynucleotide preparations, as mentioned above. Nucleoside di- and mono-phosphates had little effect either alone or in concert with ATP or UTP. Stimulation of deadenylylating enzyme activity in crude cell extracts by nucleoside triphosphates has also been noted by *Heilmeyer et al.*[27].

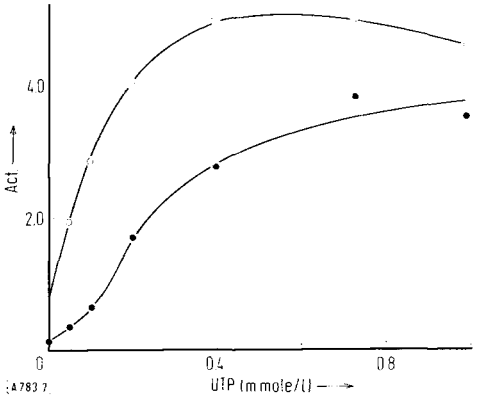


Fig. 7. Stimulation of deadenylylation by UTP alone (●—●) and by UTP in the presence of ATP (o—o) (from [25]).

The complexity of the requirements for deadenylylating enzyme activity in *E. coli* is rather puzzling. This complexity does not appear to reflect the necessity of exposing the adenylyl moiety prior to cleavage, a process which might be thought of as requiring energy (in the form of UTP and ATP) as well as structural effectors of the glutamine synthetase molecule (divalent cations and possibly α-ketoglutarate and phosphate), since the hydrolysis of the adenylylglutamine synthetase bond may be effected by a snake venom phosphodiesterase preparation which requires only divalent cation for activity. Thus the complex *E. coli* deadenylylation system, involving two macromolecular components and several other cofactors, most likely reflects a powerful means of control of the deadenylylation of glutamine synthetase in response to demands imposed by the need to maintain rigorous regulation of the synthesis of glutamine, and thus of other nitrogenous metabolites, during the growth and development of the organism. Although the physiological role of several of these effectors, notably the nucleotides, remains obscure, one can readily imagine the utility of having controls imposed by α-ketoglutarate and glutamine.

[27] *L. Heilmeyer, F. Battig,* and *H. Holzer,* Europ. J. Biochem. *9,* 259 (1969).

9. The Physiological Regulation of Nitrogen Metabolism by Adenylylation

The demand for intermediary metabolites of nitrogen probably fluctuates with the life cycle of the cell depending upon the need for specific biopolymer synthesis (*e.g.*, protein, nucleic acid, cell wall, membrane, *etc.*). In addition a variation in supply of nitrogen may occur with environmental change. To achieve maximal growth under all conditions, the cell would need to adapt itself efficiently to such alterations in the supply of and demand for nitrogen.

For an analysis of the possibilities for control of nitrogen metabolism, it is probably most graphic to consider the extremes of nitrogen nutrition, nitrogen starvation and nitrogen excess. In nitrogen starvation, there would be a relative decrease in nitrogen-containing metabolites in the cell. Among the most important of these are glutamine and its metabolic products (Fig. 1) because these are critical intermediates in nitrogen utilization. Along with this, there should be a reciprocal increase in the relative concentration of α-ketoglutarate, the carbohydrate skeleton of glutamine. Thus, it is postulated that the nitrogen saturation ratio, defined as (glutamine + glutamine products)/α-ketoglutarate, would be low.

On the other hand, with nitrogen excess, there should be a plethora of nitrogenous metabolites. If present in excess, these intermediates would decrease their own production, by means of the many feedback controls operative in biosynthetic reactions (for review, see [28]), leading to an increase in the relative concentration of glutamine. The increase in the concentration of glutamine and its metabolic products would lead to a relative increase in the nitrogen saturation ratio defined above. Although it is difficult to assess the absolute change expected in any one intermediate as a result of a simple perturbation in the multiply branched pathways of metabolism, a consideration of the nitrogen saturation ratio is helpful, since it stresses the importance of relative concentrations of several metabolic intermediates in reflecting alterations in nitrogen supply and demand.

In fact, *E. coli* has evolved a system for the regulation of its nitrogen metabolism that is very sensitive to alterations in the nitrogen saturation ratio. This system is composed of three enzymes which regulate the biosynthesis of glutamine: 1) glutamine synthetase; 2) the ATP:glutamine synthetase adenylyltransferase;

[28] *E. R. Stadtman,* Advan. Enzymology *28,* 41 (1966).

and, 3) the glutamine synthetase deadenylylating enzyme. Equation 4 shows the adenylylated and unadenylylated forms of glutamine synthetase, with their respective properties, as well as the enzymes which interconvert the two forms, and their effectors.

Activated by glutamine. Inhibited by α-ketoglutarate and UTP

Unadenylylated glutamine synthetase $\underset{\text{Deadenylylating enzyme}}{\overset{\text{Adenylyltransferase}}{\rightleftharpoons}}$ Adenylylated glutamine synthetase (4)

Activated by α-ketoglutarate and UTP. Inhibited by glutamine and glutamate

More active form
Resistant to feedback inhibition
Mg^{2+} specific

Less active form
More sensitive to feedback inhibition
Mn^{2+} specific

It is clear from this scheme that conditions of nitrogen starvation, with a correspondingly low nitrogen saturation ratio, lead to activation of the deadenylylating enzyme as well as to an inhibition of the adenylyltransferase, owing to the alterations in the relative levels of glutamine and α-ketoglutarate. This results in the formation of relatively unadenylylated glutamine synthetase, the form of the enzyme which is intrinsically more active and less sensitive to feedback inhibition. In this condition, ammonia will be converted into nitrogenous metabolites with high efficiency.

On the other hand, with high levels of the nitrogen saturation ratio, as might be expected with a surfeit of nitrogen-containing compounds, the deadenylylating enzyme would be inhibited and the adenylyltransferase activated. The result of this reciprocal enzyme control would be to convert the glutamine synthetase to the adenylylated form, which is less active and additionally more susceptible to inhibition by several of the products of glutamine metabolism. In this form glutamine synthetase activity is thus further diminished by the accumulated nitrogenous metabolites, which has as its result the lowering of the level of glutamine in the cell.

The three-enzyme nitrogen regulatory system has as its most obvious role the preservation of homeostasis in cellular nitrogen metabolism; any shift away from the "normal" nitrogen saturation ratio is accompanied by adjustments in the three enzymes which tend to restore the ratio toward the preexisting level. These intricate controls have as an ancillary effect the preservation of cellular ATP, since both glutamine synthesis and adenylylation of glutamine synthetase consume ATP; in fact, the adenylylation-deadenylylation system without reciprocal control would be a wasteful ATPase activity. The reason for the nucleotide controls in the adenylylation and deadenylylation phenomena is as yet obscure; a possible link between glutamine synthesis and polynucleotide metabolism is suggested by the effects of ribonucleic acid species on the deadenylylating system.

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Nucleosides and Nucleotides as Potential Therapeutic Agents

By T. Y. Shen[*]

The present article summarizes recent progress in the study of nucleoside derivatives as antiviral and immunosuppressive agents. A number of 5'-substituted 5'-deoxy nucleosides have been found to be permeable and nonincorporable antimetabolites of 5'-nucleotides. N^6-isopentenyladenosine and analogs show certain promising immunosuppressive activities. Encouraged by the antibody-stimulating effect of oligonucleotides, we have developed a convenient synthesis of oligonucleotides using fully protected phosphorylated intermediates. A group of tetradeoxyribonucleotides, dApdApdApdX, was prepared for biological and physical evaluations. Nucleotide derivatives may prove valuable in the treatment of several immunological disorders.

1. Introduction

A brief review of some recent studies of nucleosides and nucleotides in the field of chemotherapy and immunology is presented below. The purpose of this discussion is to highlight several biomedical targets of interest to medicinal chemists and to indicate the therapeutic potentials of nucleosides and nucleotides [1].

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[1] Adapted from presentations at the Symposium on Recent Advances in Nucleoside Chemistry. 156th American Chemical Society Meeting, Atlantic City, New Jersey, Sept. 11, 1968, and at the Gordon Conference on Carbohydrate Chemistry, New Hampshire, June 1969.

During the past fifteen years, extensive chemical and biological studies of nucleosides and some nucleotide analogs have been stimulated mainly by their antitumor and antibiotic properties. The cytotoxic or bactericidal activities of these antimetabolites are often attributable to the inhibition of enzyme systems involved in the biosynthesis of nucleic acids, such as nucleotide reductases, kinases, and polymerases, or to the formation of fraudulent nucleic acids through incorporation [2]. Several nucleoside antibiotics such as puromycin, blasticidins, and gugerotin inhibit protein synthesis, either by chain termination or by interference with the normal function of peptide synthetase or ribosomes [3]. However, since these components are also essential in the biosynthesis of protein and nucleic acids in normal cells, the therapeutic value of nucleoside antimetabolites are frequently diminished by their potential toxicity.

The need for a better therapeutic index is particularly important in the application of nucleoside analogs to viral chemotherapy [4] or metabolic diseases. Lack of incorporation into normal cells (*i.e.*, lack of mutagenic effect) and a high degree of selectivity toxicity are almost mandatory for any useful agent.

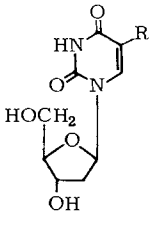
2. Inhibitors of DNA Viruses

2.1. 2′-Deoxyribo- and Arabinonucleoside Analogs

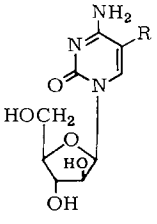
The first clinical application of a nucleoside as antiviral agent with an adequate therapeutic index was demonstrated by a well-known thymidine analog, 5-iodo-2′-deoxyuridine *(1)* (idoxuridine), in the treatment of an eye infection, herpes keratitis [5]. The apparent safety in this case was accomplished by a unique physiological phenomenon, namely, ophthalmic infections are topical and not unlike an *in vitro* system. Since then several more potent DNA-synthesis inhibitors or thymidine antimetabolites, such as trifluorothymidine *(2)* [6], cytosine arabinoside (cytarabine) *(3)* [7], and its 5-fluoro analog *(4)* [8], have also shown similar efficacy. A homolog of thymidine, 5-ethyl-2′-deoxyuridine *(5a)*, was also reported to have antiherpes activity [8a].

In our laboratory another analog, 5-methylamino-2′-deoxyuridine (MADU) *(5)*, was investigated [9]. As found by *Visser* and his co-workers, MADU is only poorly active as a thymidine antagonist in the bacterial system [10]. Surprisingly, in tissue culture and rabbit-eye systems MADU is as effective as idoxuridine against herpes simplex [11]. The high degree of selective toxicity against herpes virus was further dramatized by its lack of inhibition against other DNA and RNA viruses. It was suggested that the phosphorylated derivatives of MADU block the utilization of thymidine 5′-triphosphate for DNA synthesis. The selectivity of MADU is thus the consequence of an enhanced phosphorylating capacity of infected cells [12]. Unfortunately the activity of MADU against systemic herpes infections proved to be a disappointment.

The *in vivo* activity of nucleosides is often limited by their unfavorable distribution or metabolic characteristics [13]. It was observed recently that the *in vivo* immunosuppressive activity of 5′-adamantoyl cytarabine *(6)* is more potent and longer lasting than that of the parent nucleoside *(3)* [14]. Selective localization, sustained hydrolysis, and resistance to enzymatic degradation were suggested as possible explanations. It would seem that similar derivatization of active nucleosides with an *in vivo* cleavable group, a technique well studied in the production of other drugs, may well expand the potential application of other nucleoside analogs.



R = I (Idoxuridine) *(1)*
CF_3 *(2)*
$NHCH_3$ *(5)*
CH_2CH_3 *(5a)*



R = H (Cytarabine) *(3)*
F *(4)*

More recently a purine nucleoside, adenine arabinoside *(7)* [15], was described as a broad-spectrum anti-DNA viral agent *in vitro* and *in vivo* [16]. It is probably superior to idoxuridine in the treatment of herpes keratitis but its utility in systemic viral infections remains to be established. In view of the recent impli-

[2] *J. A. Montgomery*, Progr. Drug Res. *8*, 431 (1965).

[3] *R. E. Monro* and *K. A. Marcker*, J. Molecular Biol. *25*, 347 (1967); *M. Yukioka* and *S. Morisawa*, J. Biochemistry (Japan) *66*, 241 (1969).

[4] For summary see: Antiviral Substances. Ann. New York Acad. Sci. *130* (1965); *W. H. Prusoff*, Pharmacol. Rev. *19*, 209 (1967).

[5] *H. E. Kaufman*, *E. L. Martola*, and *C. Dohlman*, Arch. Ophthalmol. *68*, 235 (1962).

[6] *H. E. Kaufman* and *C. Heidelberger*, Science (Washington) *145*, 585 (1964); *R. A. Hyndiuk* and *H. E. Kaufman*, Invest. Ophthalmol. *5*, 424 (1966).

[7] *D. A. Buthala*, Proc. Soc. exp. Med. *69*, 115 (1964).

[8] *R. Duschinsky*, *T. Gabriel*, *M. Hoffner*, *J. Berger*, *E. Titsworth*, *E. Grunberg*, *J. H. Burchenal*, and *J. J. Fox*, J. med. Chem. *9*, 566 (1966); *T. Y. Shen* and *W. V. Ruyle*, US-Pat. 3328388 and unpublished results.

[8a] *K. K. Gauri*, *G. Malorny*, and *W. Schiff*, Chemotherapy *14*, 129 (1969), and literature cited there.

[9] *T. Y. Shen*, *J. F. McPherson*, and *B. O. Linn*, J. med. Chem. *9*, 366 (1966).

[10] *D. W. Visser*, *S. Kabat*, and *M. Lieb*, Biochim. biophysica Acta *76*, 463 (1963); *S. Kabat* and *D. W. Visser*, *ibid. 80*, 680 (1964).

[11] *M. M. Nemes* and *M. R. Hilleman*, Proc. Soc. exp. Biol. Med. *119*, 515 (1965).

[12] *R. W. Burg* and *M. M. Nemes*, Federat. Meetings Abstract (1970).

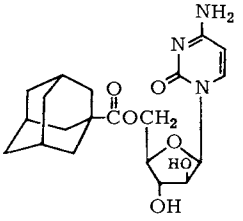
[13] *K. Gerzon* and *D. Kau*, J. med. Chem. *10*, 189 (1967).

[14] *G. D. Gray*, *M. M. Mickelson*, and *J. A. Crim*, Biochem. Pharmacol. *18*, 2163 (1969).

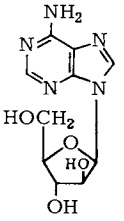
[15] *W. W. Lee*, *A. Benitez*, *L. Goodman*, and *B. R. Baker*, J. Amer. chem. Soc. *82*, 2648 (1960).

[16] *F. M. Schabel*, Chemotherapy *13*, 321 (1968).

cation of herpes virus in infectious mononucleosis, Burkitt's lymphoma [17], and cervical carcinoma [18] a safe and more effective compound is obviously very desirable.



(6)

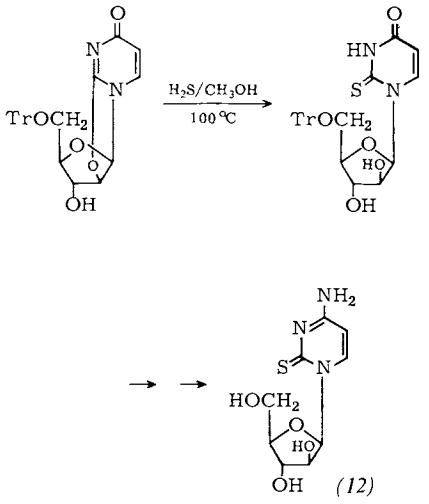


(7)

2.2. Search for Novel Structures

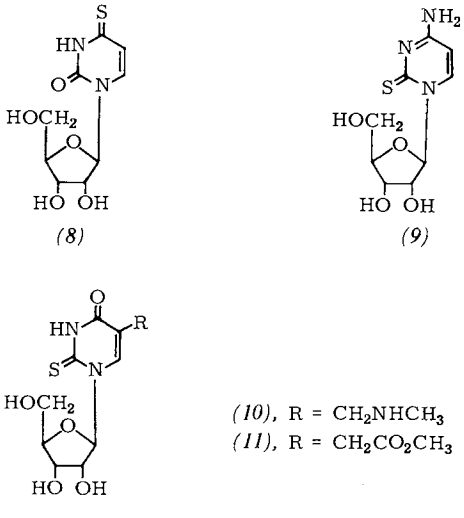
The potential role of soluble RNAs as regulators of nucleic acid metabolism has often been discussed [19]. The significance of various minor or abnormal nucleotides present is particularly intriguing. In our study of pyrimidine nucleosides as novel antimetabolites it was noted that several thiopyrimidine nucleosides, such as 4-thiouridine *(8)* [20], 2-thiocytidine *(9)*, and the 5-substituted derivatives *(10)* [21] and *(11)* [22], have been detected in t-RNA. Alteration of ^{35}S incorporation into t-RNA has also been observed after a phage infection [23].

2-Thiocytosine arabinoside *(12)* was synthesized in our laboratory by the ring-opening of a cyclonucleoside [24], but to our disappointment it does not possess any significant antiviral properties.

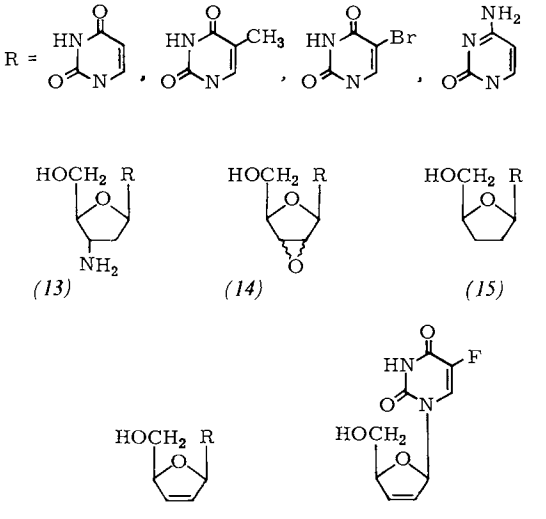


(12)

So far, anti-DNA viral activity seems to be mostly associated with pyrimidine analogs with 2′-deoxy-D-ribose and D-arabinose moieties. A group of compounds with pyrimidine bases such as uracil, thymine, 5-bromouracil, and cytosine attached to modified pentofuranoses such as 3-amino-2-3-dideoxyribose *(13)*, 2,3-anhydroribose *(14)*, 2,3-dideoxyribose *(15)*, or its 2,3-didehydro analog *(16)*, and several hexopyranoses are all inactive [25]. Recently, the 2′,3′-didehydro analog of 5-fluorouridine was found to be an anti-tumor agent [26], but its antiviral activity has not been described.



(10), R = CH_2NHCH_3
(11), R = $CH_2CO_2CH_3$



(13) (14) (15)

(16) (17)

A group of branched chain nucleosides, *e.g.*, 2′-*C*-methyl and 3′-*C*-methyl homologs of adenosine and cytidine, was synthesized recently [27,28]. Compared

[17] *G. Henle, W. Henle,* and *V. Diehl,* Proc. nat. Acad. Sci. USA *59*, 94 (1968); *L. N. Chessim, P. R. Glade, J. A. Kasel, H. L. Moses, R. B. Heberman,* and *Y. Hirschaut,* Ann. intern. Med. *69*, 333 (1968).

[18] *W. E. Rawls, W. A. F. Tompkins, M. E. Fiqueroa,* and *J. L. Melnick,* Science (Washington) *161*, 1256 (1968).

[19] *M. J. Robins, R. H. Hall,* and *R. Thedford,* Biochemistry *6*, 1837 (1967).

[20] *M. N. Lipsett,* J. biol. Chemistry *240*, 3975 (1965).

[21] *J. Carbon, H. David,* and *M. H. Studier,* Science (Washington) *161*, 1146 (1968).

[22] *L. Baczynsky, K. Biemann,* and *R. H. Hall,* Science (Washington) *159*, 1481 (1968); *L. Baczynsky, K. Biemann, M. H. Fleysher,* and *R. H. Hall,* Canad. J. Biochem. *47*, 1202 (1969).

[23] *S. B. Weiss, Wen Tah Shu, J. W. Foft,* and *N. H. Scherberg* Proc. nat. Acad. Sci. USA *61*, 114 (1968).

[24] *W. V. Ruyle* and *T. Y. Shen,* J. med. Chem. *10*, 331 (1967).

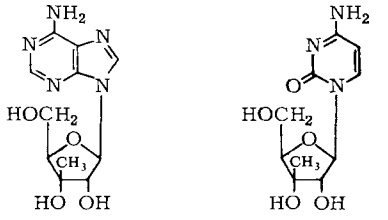
[25] Unpublished results from our laboratories.

[26] *T. A. Khwaja* and *C. Heidelberger,* J. med. Chem. *10*, 1066 (1967).

[27] *E. Walton, S. R. Jenkins, R. F. Nutt, M. Zimmermann,* and *F. W. Holly,* J. Amer. chem. Soc. *88*, 4524 (1966).

[28] *E. Walton, F. W. Holly, S. R. Jenkins, R. F. Nutt,* and *M. M. Nemes,* J. med. Chem. *12*, 306 (1969).

with 3′-deoxyadenosine (cordycepin), both 3′-*C*-methyladenosine *(18)* and 3′-*C*-methylcytidine *(19)* are much less toxic to cell cultures [29]. However, both showed interesting activity against vaccinia infection in mice when administered at doses of 1–2 mg and are superior to the standard drug, Marboran. The corresponding 2′-*C*-methyl analogs are much less active [28].

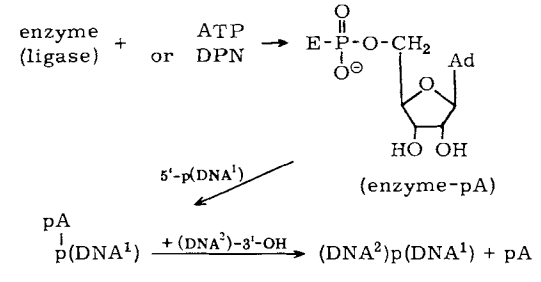


(18) *(19)*

3. Search for Inhibitors of RNA Viruses

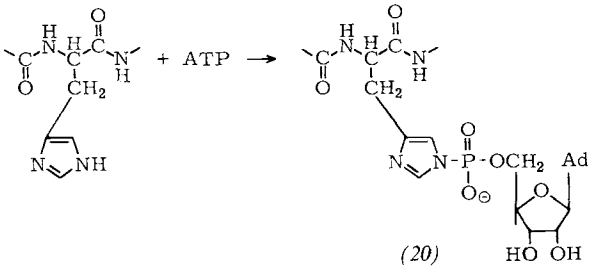
3.1. Structure Information of RNA Polymerase

In the search for anti-RNA viral agents, our attention was directed to the unique synthesis of viral RNA, which involves a single-stranded RNA template, a double-stranded replicative intermediate, and a viral specific polymerase. The complexity of viral replication has generated much speculation and many hypotheses [30]. It would seem that novel reversible or irreversible inhibitors derived from nucleosides, in addition to their therapeutic value, might also be useful as molecular probes of the active site in polymerase and help to elucidate its mechanism. Current studies of RNA polymerases indicate that the incoming nucleoside triphosphate may interact first with the active site to form a reactive nucleoside-5′-phosphoryl-enzyme intermediate which then participates in coupling with the 3′-hydroxy group of the growing polymer. The sequence of reaction is similar to that in polynucleotide ligase [31] (an enzyme whose activity is changed significantly after viral infection and which may turn out to be a chemotherapeutic target also) [32].



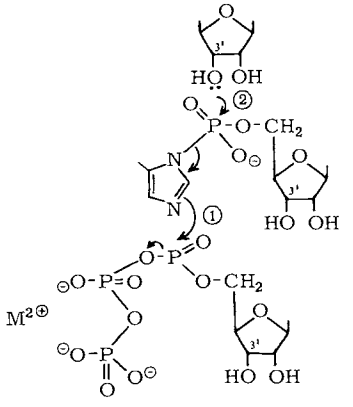
(DNA-adenylate)

The active site of RNA polymerase contains a histidyl residue [33] which is essential for chain elongation. Analogous to the active site in nucleoside diphosphokinases [34], the histidyl group may form a phosphoryl-imidazole intermediate *(20)*, with the nucleoside triphosphate.



(20)

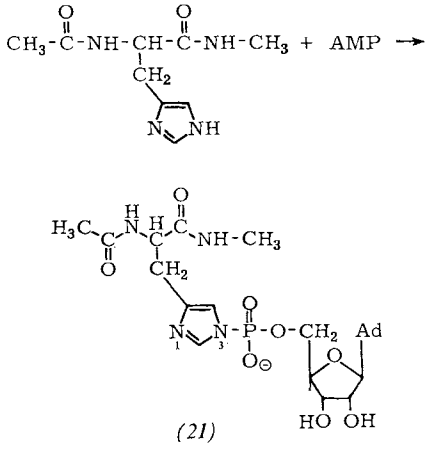
Speculatively, a concerted activation (step 1) and transfer (step 2) sequence may be visualized as shown in Scheme 1.



Scheme 1.

3.2. Models of the Enzyme Intermediate

As a model of this active intermediate we have synthesized the crystalline compound *(21)* [35]. The site of phosphorylation is tentatively assigned as N-3, based on the observation that the N-3-phosphoryl derivatives



(21)

[29] *H. T. Shigeura*, unpublished observations.

[30] Nature (London) *219*, 675 (1968).

[31] *Z. W. Hall* and *I. R. Lehman*, J. biol. Chemistry *244*, 43 (1969).

[32] *J. Sambrook* and *A. J. Shatkin*, J. Virology *4*, 719 (1969).

[33] *A. Ishihama* and *J. Hurwitz*, J. biol. Chemistry *244*, 6680 (1969).

[34] *P. L. Pedersen*, J. biol. Chemistry *243*, 4305 (1968).

[35] *K. H. Boswell* and *T. Y. Shen*, unpublished.

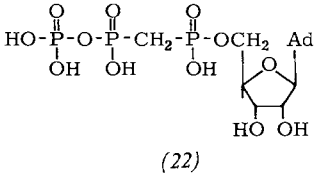
of histidine are generally more stable than those phosphorylated at N-1 [36].

Unlike many adenylic acid derivatives, which have ORD spectra similar to that of 5′-AMP with a negative Cotton effect at 277 nm, compound *(21)* gave an anomalous ORD spectrum with a positive Cotton effect near 270 nm. Whether the reversal of Cotton effect is indicative of a conformational change due to the intramolecular interaction of the imidazole moiety and adenine chromophore remains speculative, but any correlation of the physicochemical properties with those of the active intermediate of polymerase would certainly be worth investigating. A similar reversal of the Cotton effect is found for the 5′-adenylyl derivative of imidazole, pyrazole, and 2-hydroxypyridine [35].

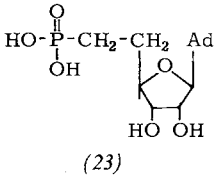
The possibility of using these analogs of an active intermediate to interfere with the enzyme action are still being investigated. It is assumed that in the normal course of polymerization the formation of the active intermediate (imidazole-p-A) is followed by transfer of p-A to the growing chain of the polynucleotide. This would require either a conformational change of the active site, *e.g.*, prompted by the elimination of the charged pyrophosphate group, or a translocation of the active intermediate itself. One could imagine that these analogs may well interfere with the transfer step. Classical antimetabolites of the substrate ATP, with their charged triphosphate-like side chain, will probably interfere only with the activation step and the formation of the active intermediate.

3.3. 5′-Substituted Nucleoside Analogs as Nucleotide Equivalents

The best known classical antimetabolites of nucleotides are their methylene phosphonate isosteres, *e.g.*, compounds *(22)* [37] and *(23)* [38]. In both cases an oxygen linkage is replaced by a methylene group that is noncleavable under physiological conditions.

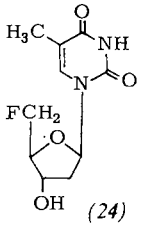


(22)

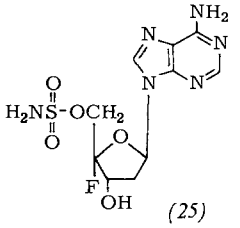


(23)

Depending on which oxygen atom is replaced by the methylene group, these analogs are either substrates or inhibitors [37]. However, their practical applications are obviously restricted by their poor permeability properties. To circumvent this barrier, we decided to investigate a group of nucleoside derivatives bearing a polar organic moiety at the 5′-position which might mimic the triphosphate-Mg^{2+} side chain of the polymerase substrate [39]. These 5′-substituted nucleosides probably permeate easily into cells. In addition, they are attractive for several important reasons. Firstly, with their 5′-hydroxyl group replaced by a substituent they are totally nonincorporable, thus fulfilling our safety requirement mentioned above. Secondly, unlike most nucleoside antimetabolites, any inhibitory action of a 5′-substituted nucleoside should not depend upon its prior enzymatic conversion into a nucleotide, and resistance development is therefore less likely [40]. Furthermore, as recently shown by 5′-deoxy-5′-methylthioadenosine [41], 5′-substituted adenosine derivatives might be more resistant to catabolic enzymes such as adenosine deaminase and purine nucleoside phosphorylase. Although unknown at the beginning of our study, the feasibility of using a 5′-substituted nucleoside as kinase or polymerase inhibitors was strongly indicated by the recent disclosure of 5′-deoxy-5′-fluorothymidine *(24)* as a competitive inhibitor, not of thymidine to its kinase, but of thymidylic acid to thymidylate kinase [42]. Another example of a 5′-substituted nucleoside analog is the naturally occurring antibiotic nucleocidin *(25)* [43] whose structure was elucidated recently.

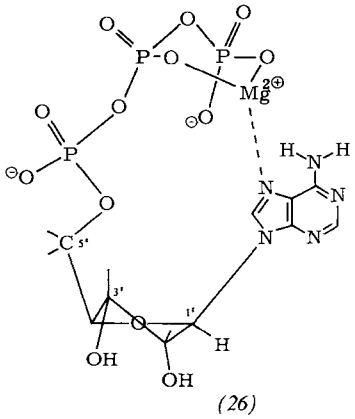


(24)



(25)

Our endeavor to construct an organic equivalent of the 5′-triphosphate-Mg^{2+} complex was much hampered by the uncertainty on the configuration of nucleotides such as the ATP-Mg^{2+} complex. In general, a cyclic chelating structure formed by the β and γ phosphates and Mg^{2+} is favored, but the possible



(26)

[36] *D. E. Hultquist*, Biochim. biophysica Acta *153*, 329 (1968).

[37] *T. C. Meyers, K. Nakamura*, and *A. B. Danielsaheh*, J. org. Chemistry *30*, 1517 (1965).

[38] *G. H. Jones* and *J. G. Moffat*, J. Amer. chem. Soc. *90*, 5337 (1968).

[39] *T. Y. Shen*, Abstracts of Papers, 154th Amer. Chem. Soc. Meeting, Sept. 1967, Chicago, Ill., p. 29.

[40] *B. R. Baker* and *P. M. Tanna*, J. pharmac. Sci. *54*, 1774 (1965).

[41] *A. E. Pegg* and *H. G. Williams-Ashman*, Biochem. J. *115*, 241 (1969).

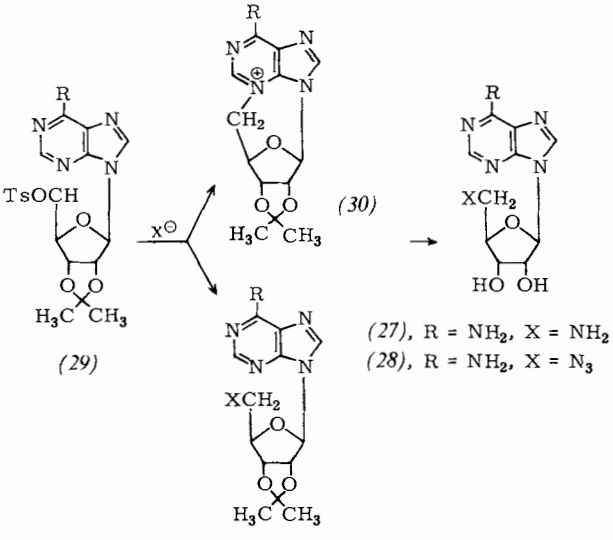
[42] *P. Langen* u. *G. Kowollik*, Europ. J. Biochem. *6*, 344 (1968).

[43] *G. O. Morton, J. E. Lancaster, G. E. Van Lear, W. Fulmor*, and *W. E. Meyer*, J. Amer. chem. Soc. *91*, 1535 (1969).

involvement of a ring nitrogen in the coordination remains to be established. Very recently structures *(26)* involving the participation of N^7, instead of the 6-amino group, have been suggested on the basis of relevant X-ray data [44]. The three-dimensional structure of ATP in the hydrated disodium salt, with the phosphate chain folded back towards the purine base, was reported by another group [45].

3.4. Derivatives of 5'-Amino-5'-deoxy Nucleosides

Our initial plan was to explore various nucleoside derivatives which have a cyclic or chelating structure at the 5'-position to mimic the triphosphate side chain, and the 5'-amino-5'-deoxy and 5'azido-5'-deoxy derivatives of adenosine *(27)* and *(28)*, respectively [46], were chosen as key intermediates for their synthesis. These selections turned out to be particularly fortuitous since both compounds exhibited antiviral activity *per se*; inhibition of parainfluenza III was demonstrated [47] at 8–30 μg/ml in tissue cultures with therapeutic indices ranging from 16 to 128, depending upon the severity of the infection. Encouraged by these findings, we synthesized a number of simple derivatives from the versatile 5'-tosylate *(29)* by similar nucleophilic displacement reactions. To minimize formation of the cyclonucleoside *(30)*, the N^6-formyl and 6-methylthio derivatives were employed in some cases.

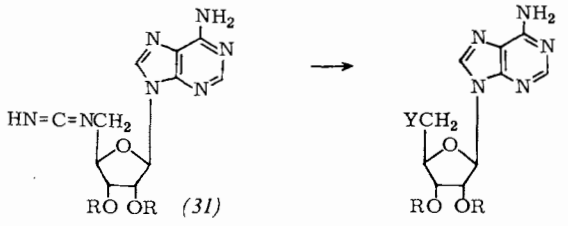


(29) *(30)* *(27)*, R = NH_2, X = NH_2; *(28)*, R = NH_2, X = N_3

R = CH_3S, HCNH, (Cl, NH_2, SH)

$X^- = N_3$, NH_2, CH_3NH, $(CH_3)_2N$, CH_3–C(O)S, –N=C=NH, –SC≡N

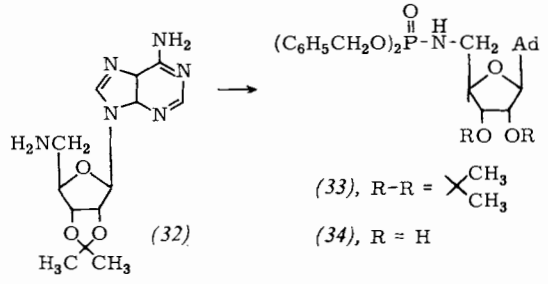
Several guanidine and urea derivatives were readily prepared from the cyanamide precursor *(31)*.



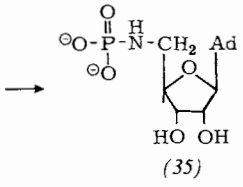
(31)

R = H or Y = NH–CO–NH_2, NH–C(NH)–NH_2,
R–R = isopropylidene NH–CS–NH_2, NH–C(NH)–NHC_4H_9

The protected 5'-amino-5'-deoxyadenosine *(32)* was phosphorylated with dibenzyl phosphite and *N*-chlorosuccinimide in methylene chloride to the phosphoramidate *(33)*. The isopropylidene group was first removed by dilute formic acid to give *(34)*, which, on

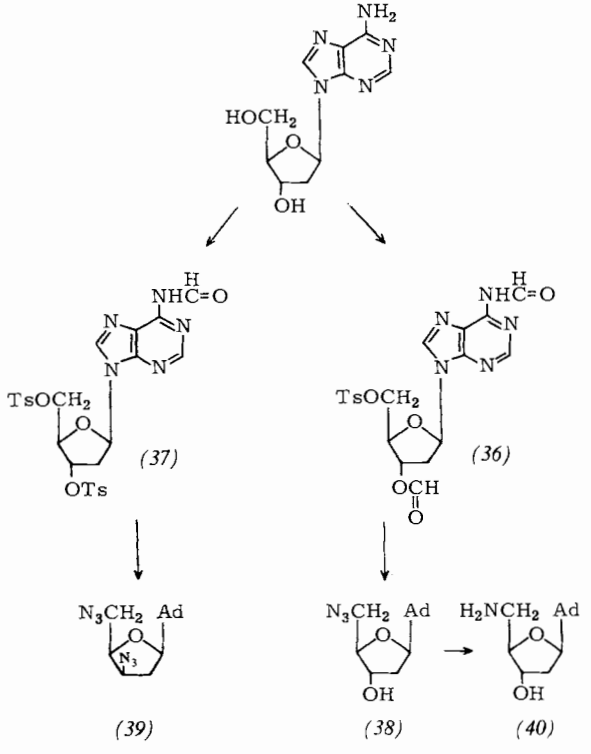


(32) *(33)*, R–R = *(34)*, R = H



(35)

hydrogenolysis in the presence of sodium hydroxide afforded a product, believed to be the desired 5'-aza AMP, that was too unstable for cyclization to the



(37) *(36)* *(39)* *(38)* *(40)*

[44] *M. Sundaralingam*, Biopolymers *7*, 821 (1969).

[45] *O. Kennard, N. W. Isaacs, J. C. Coppola, A. J. Kirby, S. Warren, W. D. S. Motherwell, D. G. Watson, D. L. Wampler, D. H. Chenery, A. C. Larson, K. A. Kerr*, and *L. R. DiSanseverino*, Nature (London) *225*, 333 (1970).

[46] *W. Jahn*, Chem. Ber. *98*, 1705 (1965).

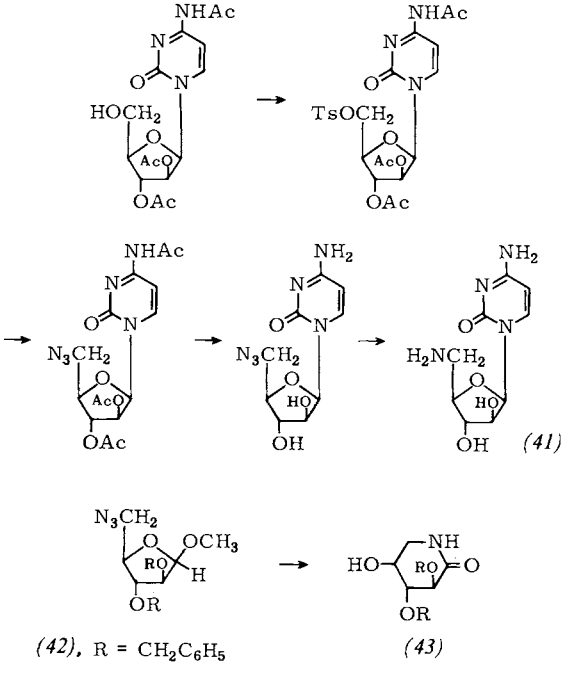
[47] *M. M. Nemes*, unpublished observations.

desired 5′-aza-3′,5′-cyclic AMP. A similar observation regarding the stability of *(35)* was reported recently [48].

In the 2′-deoxyribonucleoside series, 2′-deoxyadenosine, a known antimetabolite, was sulfonated to give a mixture of mono- and di-tosylates. Treatment of their formyl derivatives *(36)* and *(37)*, respectively, with sodium azide gave the corresponding azido derivatives *(38)* and *(39)*. The former was reduced to 5′-amino-2′-5′-dideoxyadenosine *(40)* [49].

3.5. 5′-Substituted Arabinosyl Nucleosides

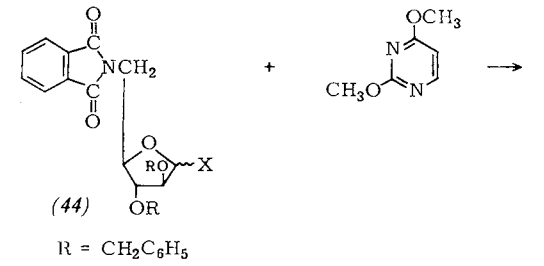
The importance of arabinosyl nucleosides in the therapeutic field has been amply demonstrated by cytosine-, adenine- and 6-methylthiopurine arabinosides. Cytosine arabinoside was readily transformed to its 5′-amino analog *(41)*.



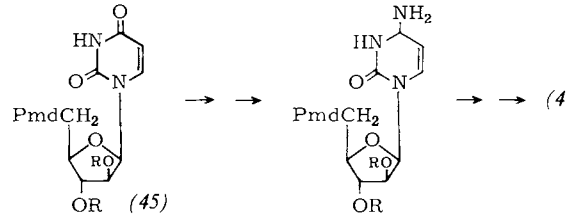
(42), R = $CH_2C_6H_5$ *(43)*

In order to develop a versatile route to study 5′-substituted arabinosyl nucleosides, we first synthesized methyl 5′-azidoarabinofuranoside *(42)* as a potential intermediate. Unexpectedly, attempted mild acid hydrolysis yielded a new crystalline compound which was found to be the piperidone *(43)* [50].

On the other hand, when a phthalimido group was placed at the 5′-position, the protected arabinosyl halide *(44)* could be prepared readily from the corresponding arabinosyl *p*-nitrobenzoate and used in the standard Hilbert-Johnson reaction. The β-nucleoside *(45)* was formed as the predominant product from the α-chloride. The stereospecificity is reminiscent of our earlier experience with 2,3,5-tri-*O*-benzylarabinosyl halide in the synthesis of cytosine arabinoside

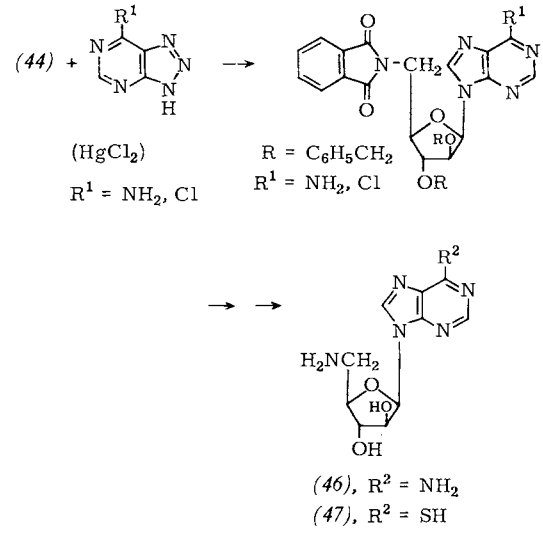


(44) R = $CH_2C_6H_5$



itself [51]. The 4-keto group in *(45)* was converted to the 4-amino *via* the methylthio intermediate, and the protecting groups were removed to give *(41)*.

The arabinosyl halide *(44)* was condensed with adenine and then deblocked to give 5′-amino-5′-deoxyadenine arabinoside *(46)*. The 6-mercaptopurine analog *(47)* was obtained in a small yield from the protected 6-chloropurine precursor by treatment with thiourea. In this case the removal of protecting groups was complicated by the formation of disulfide and other decomposition products.



(46), $R^2 = NH_2$
(47), $R^2 = SH$

The β-configuration of these purine arabinosides was corroborated by the similarity of their ORD spectra with that of adenosine. Previous workers have shown that the configuration of the 2′-hydroxyl group has no significant effect on the ORD of these nucleosides.

3.6. Biological Properties of 5′-Substituted Nucleosides

The new analogs exhibited moderate to good cytotoxicity *vs.* HeLa cells at concentrations of 1 millimole/l [29]. The 5′-azido-5′-deoxy derivatives of both

[48] *B. Jastorff* and *H. Hettler*, Tetrahedron Letters *1969*, 2543.

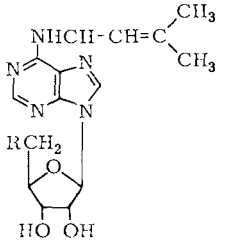
[49] An independent synthesis of this compound was recently reported: *M. G. Stout*, *M. J. Robins*, *R. K. Olsen*, and *R. K. Robins*, J. med. Chem. *12*, 658 (1969).

[50] *W. V. Ruyle*, unpublished observations.

[51] *T. Y. Shen*, *H. M. Lewis*, and *W. V. Ruyle*, J. org. Chemistry *30*, 835 (1965).

adenosine and 6-methylthiopurine riboside are highly toxic at this level. Several analogs, *e.g.*, the 5′-amino, 5′-azido, 5′-ureido, and 5′-ethoxycarbamyl derivatives of adenosine, were shown to inhibit the conversion of adenosine to its phosphorylated derivatives in ascites cells to *ca.* 60 % at concentrations of 0.9 mmole/l [29]; however, no significant antiviral activity was uncovered. The inhibition of adenosine utilization by these compounds is reminiscent of the inhibition of thymidine utilization by 5′-deoxy-5′-fluorothymidine *(24)* mentioned earlier.

As part of our systematic structure modifications, the 5′-azido derivative *(49)* of 6-isopentenyladenosine *(48)* (6-IPA) [52] was also synthesized. This derivative is again a nonincorporable antimetabolite. Yet, like 6-IPA, it inhibited HeLa cells to almost 100 % at a concentration of 1 mmole/l, although its potency was somewhat less at lower concentrations.



(48), R = OH (6-IPA)
(49), R = N_3

4. Immunological Effects of Nucleosides and Nucleotides

4.1. Immunosuppressive Nucleosides

Our interest in 6-IPA analogs was further stimulated by their potential application as immunosuppressive agents. Nucleoside antimetabolites such as 6-mercaptopurine, imuran, and cytarabine *(3)* have been used in clinical treatment of various immunological disorders. 6-Mercaptopurine arabinoside *(50)* and 6-methylthiopurine riboside *(51)* and its periodate oxidation product have also been studied in the laboratory [53]. Using the hemagglutinin response to sheep erythrocytes as a model for humoral antibody production and graft *versus* host reactions as representative cell-mediated immune reactions, the mechanism of action of these immunosuppressants is gradually being elucidated [53]. It is instructive to realize that these DNA synthesis inhibitors are very effective in suppressing the proliferation of sensitized lymphocytes and cell-mediated immunity, but the biochemical blockades imposed are easily overcome. Humoral antibody response is generally not inhibited by these compounds [54].

[52] *K. Biemann, S. Tsunakawa, K. Sonnenbichler, H. Feldmann, D. Dütting*, and *H. G. Zachau*, Angew. Chem. *78*, 600 (1966); Angew. Chem. internat. Edit. *5*, 590 (1966).

[53] *J. P. Bell, M. L. Faures, G. A. LePage*, and *A. P. Kimball*, Cancer Res. *28*, 782 (1968).

[54] *R. H. Gisler* and *J. P. Bell*, Biochem. Pharmacol. *18*, 2115, 2123 (1969).

4.2. Properties of Cytokinin Derivatives

Kinetin riboside *(52)*, 6-IPA, and other cytokinin derivatives represent a new group of immunosuppressants. The primary effect of 6-IPA was suggested as interference with RNA and protein synthesis [55]. It has recently been observed that, depending on the concentration and on the particular stage of the cell cycle, 6-IPA has a biphasic effect on the transformation and mitosis of human lymphocytes treated with phytohemagglutinin. This biphasic response is reminiscent of the antibody stimulating or inhibitory effect of another RNA synthesis inbibitor, 6-MP, in several *in vivo* systems [56].

6-IPA and cytokinins also exert an indirect influence on certain humoral immune responses mediated by nucleic acids. The participation of two or more cell types, macrophages and lymphocytes, in the primary response has been demonstrated [57, 58]. In the case of certain soluble antigens, a 4 S RNA or a RNA-protein complex is released by macrophage after phagocytosis of the antigen. This RNA-containing material, the nature of which is still being elucidated, is possibly involved in the sensitization of lymphocytes [59].

Coincidentally, nucleic acid digests or oligonucleotides have been shown to have an adjuvant effect in enhancing the phagocytosis of antigen by macrophage and in stimulating the production of antibodies by sensitized lymphocytes (Fig. 1) [60]. For reasons not yet understood, the antibody stimulating effect is inhibited by 6-IPA, kinetin riboside *(52)*, and other analogs [61].

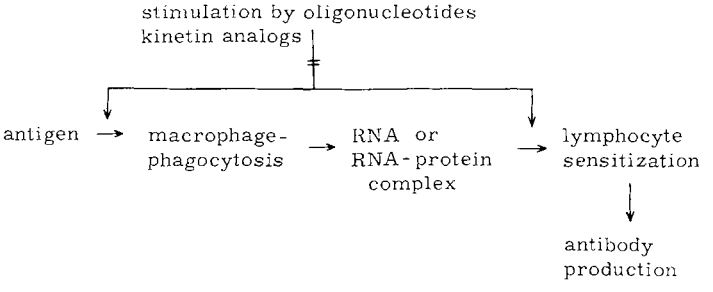


Fig. 1. Effect of cytokinin on antibody production.

Cytokinins are usually alkylated purine derivatives [62], but a pyrimidine cytokinin, 6-methyluracil (pseudothymine) *(53)*, was described recently [63]. It would be of interest to compare the immunosuppressive activity of pseudothymine nucleosides [64].

[55] *R. C. Gallo, J. Whang-Peng*, and *S. Perry*, Science (Washington) *165*, 400 (1969).

[56] *E. Gabrielson* and *R. A. Good*, Adv. Immunology *6*, 148 (1967).

[57] *M. Fishman* and *F. L. Adler*, J. exp. Med. *117*, 595 (1963).

[58] *M. Fishman*, Annu. Rev. Microbiol. *23*, 199 (1969).

[59] *A. A. Gottlieb, V. R. Glisin*, and *P. Doty*, Proc. nat. Acad. Sci. USA *57*, 1849 (1967); *A. A. Gottlieb* and *D. S. Straus*, J. biol. Chemistry *244*, 3324 (1969).

[60] *W. Braun* and *W. Firshein*, Bacteriol. Rev. *31*, 83 (1967).

[61] *O. J. Plescia* and *W. Braun*: Nucleic Acids in Immunology. Springer-Verlag, Wien-New York 1968, p. 347.

[62] *J. P. Helgeson*, Science (Washington) *161*, 974 (1968).

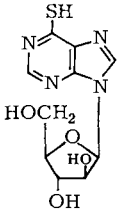
[63] *B. I. Pozsar* and *Gy. Matolcsy*, Life Sciences *7*, 699 (1968).

[64] *M. W. Winkley* and *R. K. Robins*, J. org. Chemistry *33*, 2822 (1968).

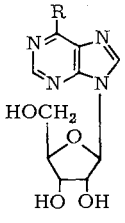
Another alkylated purine, 1-methyladenine *(54)*, is a potent meiosis inducer which stimulates ovulation in star fish at a concentration of 0.02 μg/ml [65]. The corresponding 1-ethyl homolog is much less active. We have noted that 1-isopentenyl adenine *(55)*, an intermediate in the synthesis of N^6-isopentenyladenine, inhibits thymidine incorporation in the HeLa cells at 1 mmole/l but increases thymidine and uridine incorporation in phytohemagglutinin-stimulated rat spleen cells at 10 μg/ml [66].

Both 6-IPA *(48)* and its 2-methylthio derivative have been found to occupy positions adjacent to certain anticodon regions in t-RNA [67,68]. The special location of these bases and the effectiveness of hydrophobic N^6 side chains have led to the suggestion that the cytokinin in t-RNA functions in the codon-anticodon interaction, possibly with an increasing ribosomal binding by the N^6-substituents. Whether the regulatory effect of exogenous cytokinins is achieved by the incorporation into t-RNA *per se* or by an indirect influence on the "pool" of cytokinin-containing t-RNA species remains to be elucidated. The asymmetric N^6-alkyl side chains in several cytokinins preferentially adopt the (*S*)-configuration [69].

The effects of these nucleoside analogs on mammalian cells have received much attention recently. Differential toxicity to certain leukemic cells and normal lymphocytes has been observed with a group of N^6-alkylated adenosines [70–72]. Obviously an extension of this kind of inhibitory action to immunological disorders would be of considerable interest.

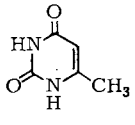


(50)

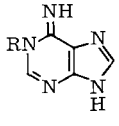


(51), R = SCH_3

(52), R = $NHCH_2$ 



(53)



(54), R = CH_3

(55), R = $-CH_2-CH=C(CH_3)_2$

[65] *H. Kanatani, H. Sirai, K. Nakanishi*, and *T. Kurokowa*, Nature (London) *221*, 273 (1969).

[66] *H. T. Shigeura* and *T. L. Feldbush*, unpublished observations.

[67] *W. J. Burrows, D. J. Armstrong, F. Skoog, J. M. Hecht, J.T. A. Boyle, N.J. Leonard*, and *J. Occolowitz*, Science (Washington) *161*, 691 (1968).

[68] *D. J. Armstrong, W. J. Borrows, F. Skoog, K. L. Roy*, and *D. Söll*, Proc. nat. Acad. Sci. USA *63*, 834 (1969).

[69] *K. Koshimizu, A. Kobayashi, T. Fukita*, and *T. Mitsui*, Phytochemistry *1*, 1989 (1968).

[70] *N. J. Leonard, S. M. Hecht, F. Skoog*, and *R. Y. Schmitz*, Proc. nat. Acad. Sci. USA *59*, 15 (1968).

5. Oligonucleotides

5.1. Adjuvant Effect of Oligonucleotides

In our laboratory we were also intrigued by the enhancement of host resistance to infection by oligonucleotides [60]. In the original immunological experiments an antibody-stimulation effect was observed with a gross mixture of DNA digest and the optimal size of the oligomers from DNA digest was estimated to be tri- to hexanucleotides. Our aim then was to delineate the active structural features of oligomers, and, if possible, to shed further light on the mechanism of this stimulating effect. Base sequence, charge distribution, molecular conformation, nature of backbone, and stability to nuclease cleavage were some of the parameters to be evaluated. The cellular uptake of oligonucleotides and the site of action, whether membrane or cytoplasmic, also required clarification (see Fig. 2).

Fig. 2. Immune stimulating effect of oligonucleotides.

1. Enhancement of phagocytic activity.
2. Reduction of induction period in antibody production.
3. Increase of deoxynucleotide kinase activity (dCMP, dGMP).
4. Protection against bacterial infection *in vivo*.

Active structures: Oligonucleotides (n = 3–6)

Poly C, Poly A (Poly C + Poly I).

5.2. Synthesis of Oligo(2′-deoxynucleotides)

As an initial step, a group of tetradeoxynucleotides of the general type dApdApdApdX *(56)* with dX = dA, dG, dI, T, and dC were synthesized by a modified procedure which incorporates the advantages of several well known techniques [73,74a,74b].

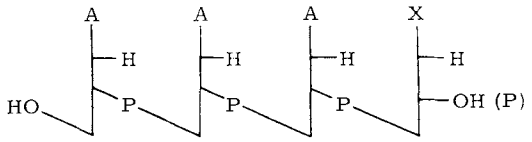
N^6-Benzoyl-5′-*O*-monomethoxytrityl-2′-deoxyadenosine *(57)* was used as starting material. Treatment with trichloroethyl phosphate and mesitylenesulfonyl chloride in pyridine gives the 3′-phosphorylated derivative *(58)*. Condensation with the 5′-hydroxyl of N^6-benzoyl-2′-deoxyadenosine was also carried out in pyridine in the presence of triisopropylbenzenesulfonyl chloride to give the dinucleotide *(59)*. The sequence of 3′-phosphorylation and 5′-condensation was repeated to give the trinucleotide *(60)* and this in turn was condensed with appropriately protected deoxyadenosine, deoxyguanoside, and deoxycytidine. 2′-Deoxyinosine and thymidine were used directly. The use of fully protected intermediates enabled us to employ silica gel column chromatography for their isolation and to obtain 10–20 mg of products without

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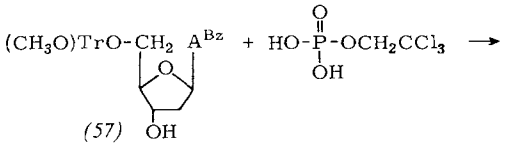
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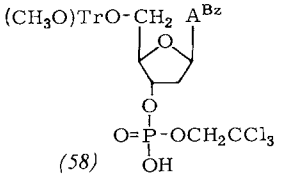
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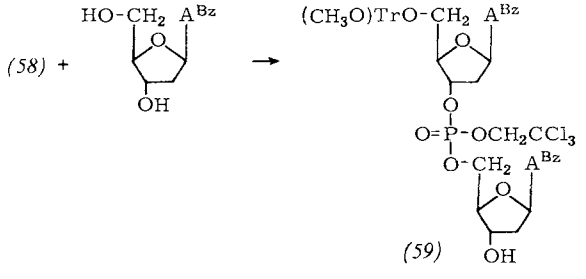
(56), X = A, T, G, C, I



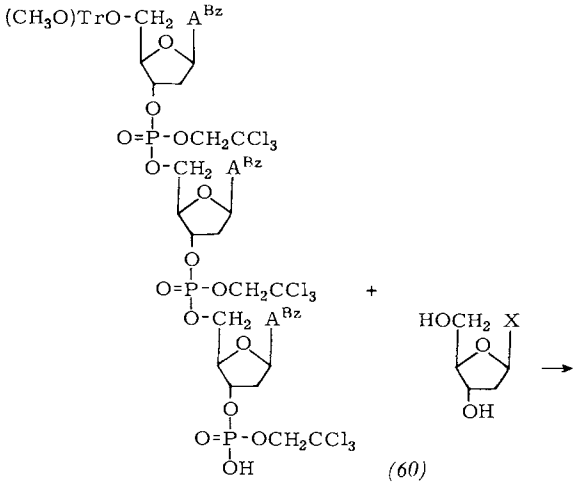
(57)



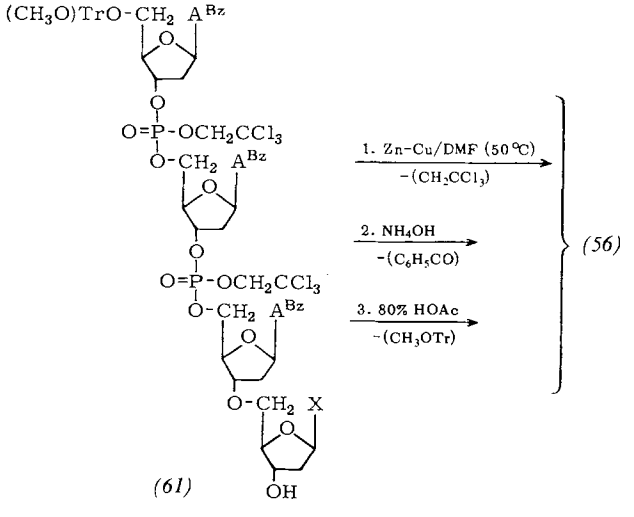
(58)



(59)



(60)



(61)

too much difficulty. The protecting groups in the tetranucleotide *(61)* were removed sequentially by treatment with Zn/Cu couple, dilute ammonia, and aqueous acetic acid. The selection of trichloroethyl as our phosphate-protecting group also conferred versatility to this approach for further structure modifications. The scope of this synthetic sequence was recently extended to the oligoribonucleotide series in which the 2′-tetrahydropyranyl was used as protected intermediate [75]. Conversion of our oligodeoxyribonucleotides to cyclic (circular) analogs in order to increase their resistance to nucleases and to enhance cellular uptake is still under study; we are particularly interested in the physicochemical properties of the products.

5.3. Potential Applications of Oligonucleotides

Another potential application of nucleotide derivatives lies in the area of autoimmune diseases, such as systemic lupus erythmatosus (SLE) and other chronic degenerative disorders, which are characterized by the production of anti-nuclear antibodies directed against nucleic acids and nucleoproteins. A variety of antibodies to native DNA, single-stranded DNA, and even double-stranded RNA are found in patients with SLE [76, 77]. These antibodies react with nucleic acids to form antigen-antibody complexes which cause inflammation along the basement membrane of renal glomerulus leading to the development of glomerular lesions. On considering the formation of pathogenic antigen-antibody complexes one is reminded of the fact that the binding of antigen with antibody is analogous to enzyme-substrate interactions. It is well established that the interaction of polysaccharide and its antibody can be inhibited by chemical analogs of the determinant group, such as oligosaccharides [78]. Similarly, a partial inhibition of SLE sera by tetra- or pentanucleotides was demonstrated several years ago [79]. With more precise information on the nature of binding involved it is conceivable that one may find oligonucleotide derivatives not only with higher affinity but also capable of cross-reacting with a large group of SLE sera. The formation of soluble antigen-antibody complexes between oligonucleotide analogs and anti-DNA antibodies would presumably minimize immunological lesions and possibly facilitate the induction of tolerance (see Fig. 3) [80].

The concept of using derivatives of oligonucleotides or much simplified "structure equivalents" to mimic or to compete with biologically active polynucleotides should be applicable to other important problems of

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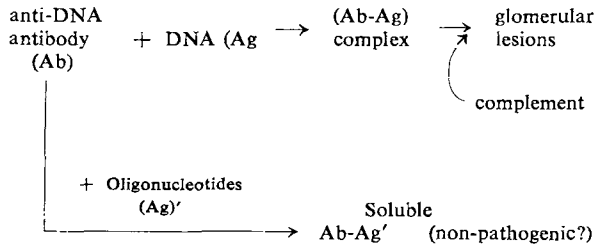


Fig. 3. Pathogenesis in systemic lupus erythmatosus.

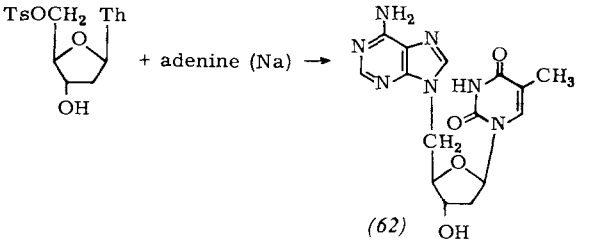
medicinal interest such as interferon induction, viral RNA polymerase inhibition, specific t-RNA inhibition, and episome transfer. In each case one may assume that the interaction of nucleic acid with a protein molecule or a receptor involves only one region or several regions of oligonucleotides and that the specificity is determined by the base sequence and secondary structure of those regions. The feasibility of this kind of approach is clearly indicated by recent sequence determinations of Qβ and R17 phage RNA. The base sequence of Qβ phage was determined from both the 3'-[81,82] and 5'-terminals[83], and no less than 175 nucleotides from the 5'-terminus with a well-defined loop-like secondary structure have been elucidated[83]. The identification of a specific binding region should enable us to design chemical structures either to compete for the protein binding site or to interact with the oligonucleotide region itself by means of intercalation, base pairing, or formation of other hydrogen bonds.

6. Novel Nucleoside Derivatives

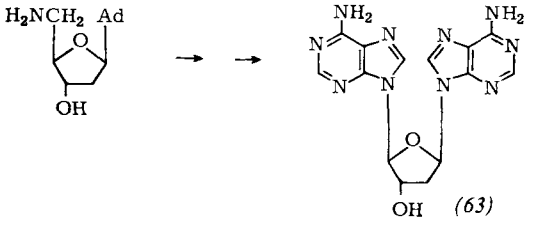
6.1. "Double-Headed" Nucleosides

To explore nucleoside analogs which might show a selectivity for certain base-sequences on interaction with nucleic acid, we have utilized the versatile 5'-*O*-tosyl and 5'-amino-5'-deoxy derivatives of nucleosides described above to synthesize novel ribonucleosides and 2'-deoxyribonucleosides which possess a second purine or pyrimidine moiety at the 5'-carbon[84,85].

It is hoped that with the proper selection and spacing of the two bases, one may utilize one base for Watson-Crick type pairing and the other to intercalate between the next two adjacent nucleotides in a polynucleotide.



(62)



(63)

The specificity of these interactions will be the basis for selective binding of three nucleotides by one double-headed unit. The nucleoside *(63)* gave an unusual CD spectrum[84], presumably due to intramolecular interactions between the two proximate bases. These compounds are useful models for the study of base-base interactions. The pronounced Cotton effect may also serve as a convenient marker in following the intermolecular interactions between these compounds and polynucleotides.

7. Conclusion

The medical applications of nucleotide derivatives have not received much attention in the past partly because of the difficulties in chemical synthesis and partly because of their poor absorption and cellular permeability characteristics. However, recent developments in synthetic methods and isolation techniques have brought oligomers within the sphere of medicinal chemical explorations. New discoveries, such as the use of double-stranded polynucleotides as interferon-inducers in viral chemotherapy[86,87], have broadened the traditional concept of using only monomeric drugs. The growing knowledge of membrane receptor sites and membrane enzymes such as ATPase in the regulation of cellular activities also provides new extracellular targets for drug action. With the structure elucidation of nucleic acids and the understanding of their interaction with protein receptors, further advances in the application of nucleoside and nucleotide derivatives as novel therapeutic agents are certainly to be expected.

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Gel Chromatography

By Walter Heitz[*]

Gel chromatography can be regarded as a network-limited partitioning of substances. The theory of this method and the preparation and properties of various gel systems are reviewed. Optimization of the method is illustrated for the separation of oligomers.

1. Introduction

Gel chromatography, also known as gel permeation chromatography [1] and gel filtration [2] has become a valuable laboratory method for separating mixtures according to the molecular weight of their components.

As in other chromatographic methods, a mobile phase capable of mass exchange is made to migrate through a stationary phase. The mobile phase is a liquid that can readily dissolve the sample mixture to be separated. The stationary phase is a porous material whose pore size is about as large as the molecules to be separated. Such porous structures can be obtained with inorganic polymers (glass [3] and silica gel [4–7]), but cross-linked organic polymers having the required structure at least in the swollen state are mostly used. The present article deals with the main advances made in this field in the past four years (for earlier surveys, see [8–14]).

2. Experimental Arrangement

In the simplest case a column is packed with swollen gel, the sample solution is poured in, the eluate is collected in fractions, and the fractions are investigated.

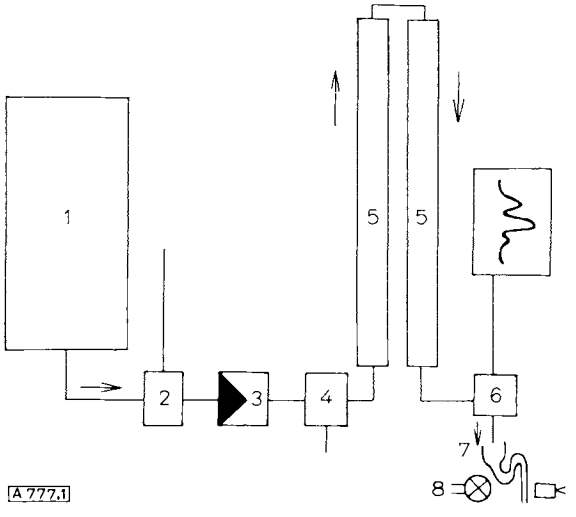


Fig. 1. Experimental arrangement in gel chromatography.
1 = solvent reservoir; 2 = degassing device; 3 = pump; 4 = sample inlet; 5 = column; 6 = recorder; 7 = siphon; 8 = light barrier.

The best experimental arrangement is shown schematically in Fig. 1.

The solvent flows from a reservoir (1) through a sintered glass plate into a degassing device(2); this is an electrically heated metal block with an upright tube or a Liebig condenser heated by a thermostated liquid. When the eluent is water, peristaltic pumps can be used, but piston pumps are preferred in the case of organic eluents. The piston strokes must be damped with the aid of a harmonica joint, particularly when a soft gel is used. As in gas chromatography, the sample in an aqueous system may be injected through an elastomer packing; for samples in organic systems, on the other hand, ball valves are used [15], or a sample loop is inserted in the solvent stream *via* a multiway valve. Having traversed the column, the eluent enters an indicator device (6). Differential refractometers have proved particularly suitable in this capacity, besides UV and IR apparatus [16, 17]. Owing to the high noise level, flame ionization detectors are used only in isolated cases in this field [18]. The volume of eluate is measured by a siphon (7) with a light barrier (8) or by a drop counter, and is recorded directly on the recorder.

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3. Theory of Gel Chromatography

3.1. Principle of Separation

In the elution of a mixture down a column filled with swollen gel particles, the first component of the mixture appears in the eluate when a volume of liquid equal to the volume of solution (V_0) between the gel particles has left the column. This component comprises all the compounds whose molecules are too large to penetrate the gel pores. If interaction with the gel matrix is ignored, one may say that the last component of the sample leaves the column when a further volume of liquid equal to the volume of solution inside the gel particles (V_I) has emerged. The entire separation takes place between the eluent volumes V_0 and (V_0 + V_I) (Fig. 2). This indicates that the separating efficiency is considerably lower here than in other chromatographic methods, *e.g.* in gas chromatography.

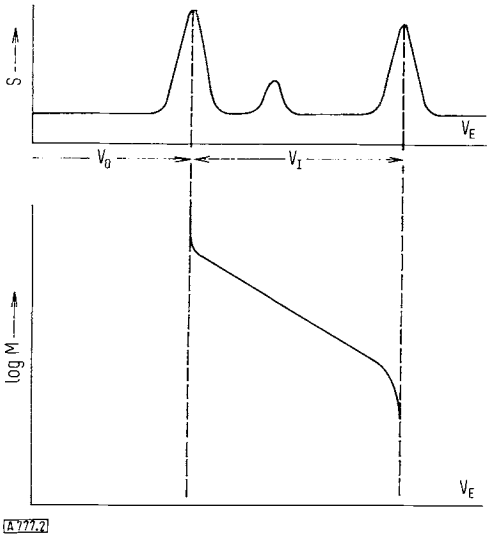


Fig. 2. Schematic gel-chromatographic elution pattern. For explanation see text. S = recorder deflection; V_E = elution volume.

The smaller the molecules the larger the proportion α of the total pore volume that is at their disposal. Molecules of different sizes therefore migrate at different speeds, the largest molecules leaving the column first, and the smallest leaving it last. The interactions between the solute and the gel phase (gel matrix and the trapped solvent) are not necessarily identical with those between the solute and the pure solvent, which leads to a substance-specific distribution between the external volume V_0 and the part α of the pore volume V_I that is available to the molecules on the basis of their size, this distribution being characterized by a partition coefficient K. Migration through the column is determined by a partition index G:

$$G = K \frac{V_0}{\alpha V_I} \qquad (1)$$

The polymeric network of the gel phase restricts the latter to the occupation by molecules of appropriate size, and so gel chromatography can be described as a form of network-limited partitioning.

On the assumption of multistage distribution, the following expression is obtained for the maximum of the elution curve V_{max}, analogously with other chromatographic techniques[19]

$$V_{max} = V_E = \frac{n-1}{n} V_0 \left(1 + \frac{1}{G}\right) \qquad (2)$$

where n is the number of equivalent distribution steps, *i.e.* the number of theoretical plates. Insertion of Eq. (1) into (2) gives

$$V_E = \frac{n-1}{n} \left(V_0 + \frac{\alpha}{K} V_I\right) \qquad (3)$$

For large values of n,

$$V_E = V_0 + \frac{\alpha}{K} V_I \qquad (4)$$

The following expression gives the mean deviation σ, which represents the distance between the point of inflection on the curve and a vertical line drawn from the saddle point of the peak (cf. Fig. 2):

$$\sigma = \frac{\sqrt{n-1}}{n} V_0 \left(1 + \frac{1}{G}\right) \qquad (5)$$

This can be simplified as follows with the aid of Eq. (3):

$$\sigma = \frac{1}{\sqrt{n-1}} V_E \qquad (6)$$

The number of theoretical plates is thus

$$n = (V_E^2/\sigma^2) + 1 \approx (V_E/\sigma)^2 \qquad (7)$$

We have that $b = 4\sigma$, where b is the peak width, *i.e.* the distance b along the base line between the tangents to the two points of inflection. It follows that

$$n = 16 (V_E/b)^2 \qquad (8)$$

This is the general equation for the number of theoretical plates in gel chromatographic columns, and it is usually checked with low-molecular compounds such as benzene, chlorobenzene, ethyl acetate, and octane, the resulting value depending on the substance used (cf. Section 3.3).

Furthermore, $\alpha/K = K_D$, where K_D is the apparent partition coefficient of *Flodin* and *Granath*[20]. Gel-chromatographic separation is essentially a function of the pore size and of the pore-size distribution, but the assumption of substance-specific interactions leads to a better understanding of the separation. The partition can be demonstrated experimentally in the separation of oligomers[21]. The assumption of network-based partitioning also explains why α/K is sometimes greater than unity[22,23], although the elution curves are symmetric.

Determann has pointed out that the gels have a large internal surface[14], and the adsorption isotherms are therefore linear over a fairly wide range. This assumption too could explain the experimental observations, but a number of gels are composed of individual solvated polymer

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chains, crosslinked to form network units, and in such cases it is better to explain the concentration difference between the mobile and the accessible stationary phase by partitioning.

3.2. Calibration Equation

Gel chromatography permits the separation of mixtures of substances having different molecular dimensions, but it is not an absolute method and it requires calibration. *Determann* and *Michel*[24] have surveyed the systematic investigations of the relation between the elution volume and the molecular weight. In practice, use is generally made of the linear relationship between the elution volume and the logarithm of the molecular weight:

$$\log M = A - BV_E \tag{9}$$

where A and B are constants. There is a calibration plot for each homologous polymer series, so the interpretation of the experimental results by this technique is possible only if appropriate authentic samples are available. Whereas in the case of proteins one generally has at one's disposal well-characterized samples that are homogeneous in their molecular weight, synthetic polymers always show a certain molecular-weight distribution. However, the inhomogeneity in this respect ($\overline{M}_w/\overline{M}_n$) is often sufficiently low in the case of polymers made by anionic polymerization. Thus, it is possible to obtain polystyrenes[*] and polypropylene oxides[**] with a narrow molecular-weight distribution. Furthermore, polymers with a wide molecular-weight distribution may also be used for calibration if a correction is effected to eliminate perturbations due to concentration effects (cf. Section 3.3)[25]. However, well-characterized polymers are not available in all cases, and hence the need for a universal calibration equation. The latter also affords a better insight into the method, since it shows which factors determine the separation.

To find a universal calibration equation containing only parameters that are fixed by the compounds to be separated, the specific interactions between these compounds and the gel matrix must be negligible, *i.e.* K must be 1.

The experimental demonstration of specific interactions in the case of oligomers indicates that there is no universal calibration equation in this molecular weight range. However, gels used with oligomers differ greatly in their structure from gels used with polymers (cf. Section 4), and so there is no contradiction in finding a universal calibration equation for polymers that is at least approximately valid.

A calibration plot is obtained by plotting the elution volume against the logarithm of the length of the stretched molecular chains, account being taken of the bond angles and the bond lengths (stretched zigzag chains). This calibration plot should enable one to read off the molecular weight of any polymer after multiplication by the molecular weight per unit length[1,26,27]. However, several authors have shown that this relationship does not have a general validity[28–34]. The viscosity index $[\eta]$ and the diffusion coefficient D similarly cannot be used as calibrating parameters[29,30].

The size of polymer chains, which are coiled up in solutions, certainly has a great influence on the separation, but – as *Meyerhoff*[29,30] has shown – one cannot obtain a universal calibration equation by using the radius of gyration r_G and thus the mean distance between the chain ends. However, the following functions do represent approximately such a correlation.

$$M^{1/2} r_G = f(V_E) \tag{10a}$$

$$M^{1/2} [\eta]^{1/3} = g(V_E) \tag{10b}$$

According to *Benoit et al.*[35], the radius of equivalent hydrodynamic spheres r_{eq} can be used to devise a universal calibration equation. *Einstein*[36] showed that the macroscopic viscosity of a suspension of spheres depends on the volume fraction φ of the suspended spheres. If the polymer molecules in solution are regarded as such suspended spheres, the following relationship holds:

$$\varphi = (Nc/M)V_{eq} \tag{11}$$

where N is Avogadro's number, c is the concentration (in g/ml), and V_{eq} is the equivalent hydrodynamic volume of the polymer molecules. The bracketed ratio gives the number of polymer molecules per unit volume. Insertion of Eq. (11) into Einstein's equation gives

$$M[\eta] = kV_{eq} = k' r_{eq}^3 \tag{12}$$

where k and k' are constants and $[\eta]$ is the Staudinger index

$$[\eta] = \lim_{c \to 0} \frac{\eta - \eta_0}{\eta_0 c}$$

According to Eq. (12), a plot of log $M[\eta]$ against the elution volume V_E gives a universal calibration line within the experimental error (cf. Fig. 3). The validity of this relationship has been checked by several

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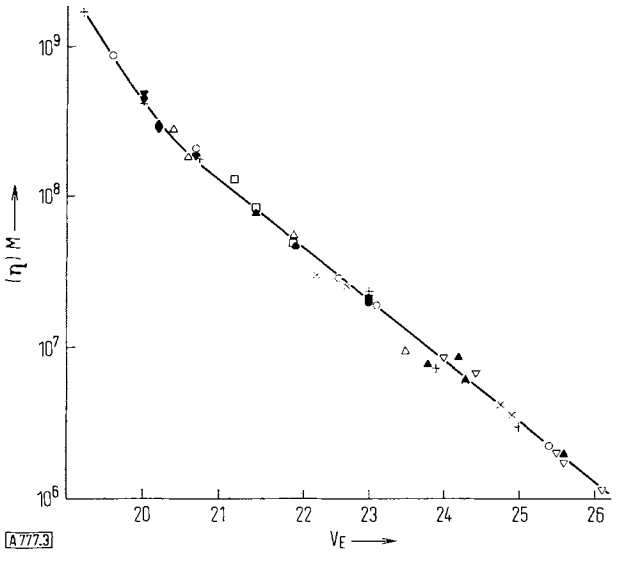


Fig. 3. Relationship between log $[\eta]$ M and V_E according to *Benoit* [42]. $[\eta]$ is given in cm³/g. and V_E in arbitrary units (siphons). ○ linear polystyrene; △ linear polymethyl methacrylate; ▽ linear polyvinyl chloride; □ linear polybutadiene; + comb-shaped polystyrene; × star-shaped polystyrene; ● comb-shaped graft copolymer of polystyrene and polymethyl methacrylate; ▲ graft copolymer of polystyrene and polymethyl methacrylate; ▼ polyphenylsiloxane; ■ linear statistical copolymer of polystyrene and polymethyl methacrylate.

authors [35, 37–42]. In particular, a calibration line obtained for linear polymers can also be used for branched ones, and so it is possible to obtain from the calibration line $M_{branched}$ for a polymer with a known viscosity $[\eta]_{branched}$, and to calculate $[\eta]_{linear}$ for the same M value [43]. The average number of branching points in the polymer molecule can be estimated from the $[\eta]_{branched}/[\eta]_{linear}$ ratio [44–47]. The molecular weight of an unknown sample (I) can be found from the calibration line obtained for polystyrene, provided that the constants appearing in Eq. (13) are known.

$$[\eta] = FM^s \tag{13}$$

According to Eq. (12), we then have that

$$F_I M_I^{s_I+1} = F_{II} M_{II}^{s_{II}+1} \tag{14}$$

or

$$\log M_I = \frac{1}{s_I+1} \log F_{II}/F_I + \frac{s_{II}+1}{s_I+1} \log M_{II} \tag{15}$$

Benoit et al. have shown that the specific interactions between a solute and the gel matrix can be neglected in the gel-chromatographic separation of polymers, but other authors [48–51] have found that log $M[\eta]$ does not always permit normalizing representation.

3.3. Separation Efficiency

Only a limited volume is available for the separation in gel chromatography, and the peak width for each substance determines how many substances can be separated within this limited volume. The following expression gives the resolution R, *i.e.* the extent of separation of two adjacent peaks [52]:

$$R = \Delta V_E/4\,\sigma \tag{16}$$

where ΔV_E is the difference between the two elution volumes, and the two peaks are assumed to have the same mean deviation σ.

Several authors have investigated the influence of experimental factors on the width of gel-chromatographic peaks [15, 50, 53–57], and have concluded that the relationships deduced for other chromatographic methods [58, 59] apply in gel chromatography as well.

The elementary processes i in the column make for a probability distribution of substances about the center of gravity of peaks whose variance σ_i^2 is additive:

$$\sigma^2 = \sigma_1^2 + \sigma_2^2 + \ldots\ldots \tag{17}$$

The height equivalent to a theoretical plate H is given by

$$H = l/n = \sigma^2/l \tag{18}$$

where l is the length of the column. The additivity of the contributions thus holds also for H:

$$H = H_1 + H_2 + \ldots \tag{19}$$

[37] *Z. Grubisic, P. Rempp,* and *H. Benoit,* J. Polymer Sci., Part B *5,* 753 (1967).

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[55] *F. W. Billmeyer jr.* and *R. N. Kelley,* J. Chromatogr. *34,* 322 (1968).

[56] *W. Heitz* and *J. Coupek,* Makromolekulare Chem. *105,* 280 (1967).

[57] *J. Coupek* and *W. Heitz,* Makromolekulare Chem. *112,* 286 (1968).

[58] *J. J. van Deemter, F. J. Zuiderweg,* and *A. Klinkenberg,* Chem. Engng. Sci. *5,* 271 (1956).

[59] *J. C. Giddings* and *K. L. Mallik,* Analytic. Chem. *38,* 997 (1966).

The particle size of the stationary phase is obviously decisive for the efficiency of the separation, but its influence can be eliminated by introducing reduced quantities [15, 58, 59]:

$$h = H/d_p;\ \nu = u\,d_p/D \qquad (20)$$

where h is the reduced plate height, ν the reduced velocity, d_p the diameter of the gel particles in the swollen state, u the linear elution velocity of the mobile phase, and D the diffusion coefficient of the solute in the mobile phase. When these reduced quantities are used, the van Deemter equation becomes

$$h = a + b/\nu + c\nu \qquad (21)$$

The three terms on the right-hand side are due to the irregular solvent flow, the diffusive broadening of the solute zone, and the exchange process. The quantity a describes the regularity of the packing: for good packing, its value is 2–3. The particle size distribution has a strong influence on packing regularity, and for good packing the standard deviation should not exceed 5 % of the mean particle diameter. However, fairly small particles can be separated only with difficulty in such narrow limits. Even when the particle size is uniform, one obtains a statistical packing of spheres ($V_0 \approx 0.37 \times$ total column volume) instead of a close packing of spheres ($V_0 = 0.26 \times$ total column volume) [60].

The quantity b is due to the diffusive broadening of the zones. The greater the elution velocity the less significant is the effect of b, whose value varies between 0.8 and 1.8 [61]. Since in the usual gel-chromatographic experiments ν is greater than 10, and mostly even greater than 100, the effect of the longitudinal diffusion can be neglected.

Only the exchange process is responsible for c. This must be investigated with substances that do not participate in partitioning, since in this case c is zero. For reduced velocities $\nu > 10$, the reduced plate height must then be constant, *i.e.* independent of the elution velocity.

According to *Giddings* [62], the terms contributing to the irregularity of the packing and the irregularity of the zone profile in the mobile phase are not independent quantities, and their variance σ^2 is not additive but coupled.

$$h = B/\nu + C_s\nu + \sum_i \frac{1}{1/A_i + 1/C_{m_i}\nu} \qquad (22)$$

where B, C_S, and A_i correspond respectively to b, c, and a in the van Deemter equation; C_{mi} represents the substance exchange in the mobile phase.

Giddings differentiates between five perturbing effects ($i = 5$), but only four of these are significant for gel chromatography (cf. Fig. 4). The theoretical estimation of the magnitude of these effects is uncertain. The magnitude of the perturbations that are responsible for the sum term in Eq. (22) varies closely with the experimental conditions and mainly with the quality of the packing. The trans-column effect should increase with the column cross-section, but experiments show that it can be kept negligibly small even when the column diameter d is 5 cm ($d/d_p \approx 10^3$) [63, 64].

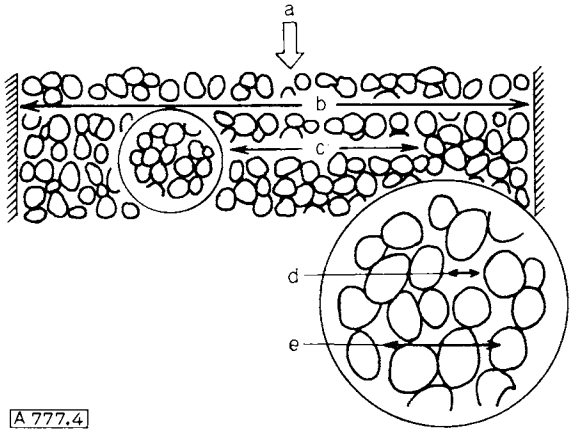


Fig. 4. Magnified cross-section of a chromatographic column. Region of various exchange processes (after *Giddings* [62]).
a = direction of flow; b = trans-column effect; c = long-distance interchannel effect; d = intrachannel effect; e = short-distance interchannel effect.

Fig. 5 shows the variation of the reduced plate height $h = H/d_p$ with the reduced velocity $\nu = ud_p/D$ for two polyvinyl acetate gels having different particle sizes (the same type of graph is obtained for polystyrene gels). The use of reduced quantities leads to a normalized representation of the separating efficiency, this representation being independent of the chemical nature of the gel and the sample, the particle size of the gel, and the flow velocity. Deviations from this state of affairs occur in the case of homogeneously cross-linked gels (cf. Section 4.1) in which the amount of the cross-linking agent exceeds about 5 %: here the graph varies with the substance, though not with the particle size of the gel [56, 57]. In the case of substances that are excluded from the gel and that thus do not participate in the separation the width of the peaks is independent of the elution velocity, as predicted by theory [15, 57].

The gels used always have more than one particle size, and generally the arithmetical mean of these particle sizes is used for Eqs. (21) and (22). Since $H \sim d_p^2$ for fairly large reduced velocities, we have the following approximate equality on the assumption that Eq. (19) can be used:

$$\bar{d}_p \approx \sqrt{\Sigma m_i d_{pi}^2}$$

where m_i is the fraction with a particle diameter i. The approximation is within the limits of error when the particle size distribution is very narrow, but otherwise

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[62] *J. C. Giddings*: Dynamics of Chromatography I. Marcel Dekker, New York 1965.

[63] *W. Heitz* and *H. Ullner*, Makromolekulare Chem. *120*, 58 (1968).

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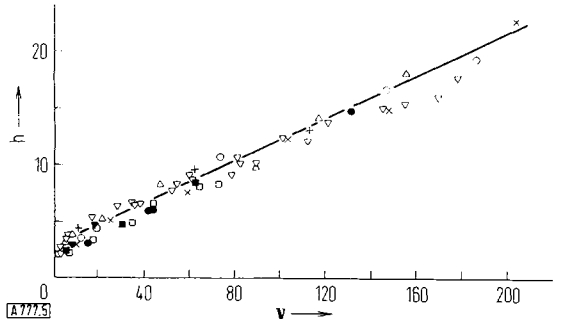
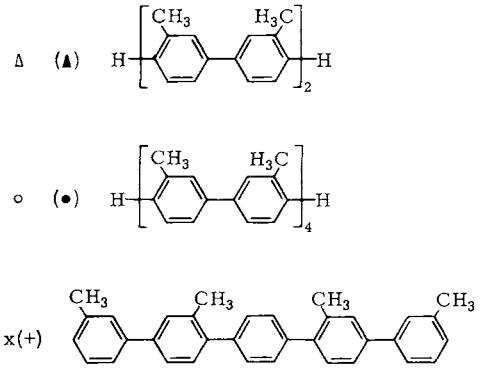


Fig. 5. Reduced separating efficiency of polyvinyl acetate gel cross-linked with 5 mole-% of butanediol divinyl ether; THF; methyl-substituted *p*-oligophenylenes [15]; $\bar{d}_p$ = 0.0191 cm (0.0382 cm). □ (■) benzene; ▽ (▼) *m*-bitolyl.



a considerably greater value is obtained for d_p. In a comparison of gels having the same mean particle size (arithmetical mean) but different particle size distributions, the gel that has a broader particle size distribution is found to give the less efficient separation.

In gel chromatography substances emerge from the column in decreasing order to molecular weight. Since the diffusion coefficient increases with decreasing molecular weight, the reduced velocity decreases as the elution proceeds at a constant linear elution velocity. As a result, the reduced plate height decreases and the efficiency of the separation increases. This explains the well-known observation that assuming a constant number of plates the bands of the last compounds to emerge are too narrow compared to the compounds emerging first from the gel column.

The separation of polymers is accompanied by perturbations that are absent in the elution of low-molecular compounds. When the molecular weight is high, the elution volume varies linearly with the amount of the sample [65, 66], and this effect becomes more conspicuous as the molecular weight increases.

3.4. Evaluation

With substances having a single molecular weight, the latter can be determined from the elution curve maximum and the appropriate calibration plot (cf. Fig. 2). When a differential refractometer is used, the absolute or relative quantities are found by integrating the recorded curve, since the response is proportional to the concentration. At high molecular weights the dependence of the refractive index on the molecular weight can be neglected, provided that there is a sufficient difference between the refractive index of the solute and that of the solvent. When a usual single-beam UV apparatus is used, the error in the determination of the quantities is somewhat greater, owing to the logarithmic concentration dependence and the necessary subtraction. Polymers give a broad band that can be regarded as a close succession of superimposed Gaussian distribution curves. In the simplest case the mean molecular weight is found from the maximum of the peak and the calibration curve. However, this mean is correct only when the molecular weight distribution is narrow, otherwise it is between $\overline{M}_w$ and $\overline{M}_n$ [67]. For polymers with a Schultz-type distribution [68], the peak maximum gives $\overline{M}_w$ [67,69].

The polymer is further characterized by its inhomogeneity U (= $\overline{M}_w/\overline{M}_n$), and *Bly* [70,71] has shown experimentally that the peak width b of a polymer is proportional to the inhomogeneity, *i.e.*

$$U_1/b_1 = U_2/b_2 \qquad (23)$$

This means that the inhomogeneity of an unknown sample can be found from that of a known one. The validity of Eq. (23) has been checked for U = 1.3–3.6, and the maximum error for U/b has been found to be 10 %. A better approximation is obtained by taking into account the ordinate values in a diagram of b against U (cf. Fig. 6). The peak width of polymers is

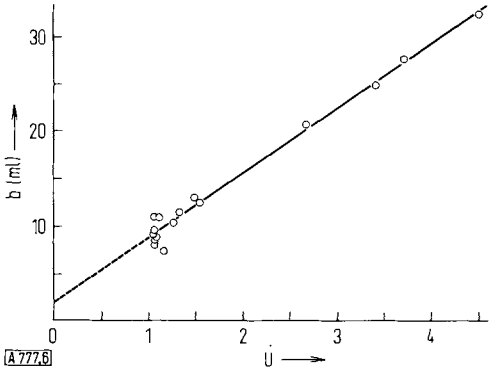


Fig. 6. Variation of the peak width b with the inhomogeneity U of polymers on the basis of *Bly*'s values [71].

determined by two factors: that of a polymer with U = 1 (ordinate value for U = 1) and the molecular weight distribution. Eq. (23) can be used if a) the polymer has a normal distribution; b) the chemical constitution is uniform; c) the peak lies in the linear part of the semilogarithmic calibration curve; and d) the column has a high separating efficiency.

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[69] *G. Meyerhoff,* J. Polymer Sci., Part C *21,* 31 (1968).

[70] *D. Bly,* J. Polymer Sci., Part C *21,* 13 (1968).

[71] *D. Bly,* Analytic. Chem. *41,* 477 (1969).

The inhomogeneity can also be determined if the polymer sample and the reference sample have different calibration curves [70,71].

The molecular weight distribution can be calculated from the recorded curve by stepwise integration [28,30,72] provided that the resolution [Eq. (16)] is very good. As a result of the finite peak widths, however, the recorder deflection is a function not only of a substance with a given molecular weight, but also of the adjacent Gaussian curves. The finite peak width has been taken into account in the methods of *Tung* [73–75], *Hess* and *Kratz* [76], and *Pierce* and *Armonas* [77] with the aid of a computer programme [78,79]. By determining the moments of the corrected chromatogram, the mathematical oscillations in the latter can be eliminated [80].

4. The Stationary Phase

4.1. Preparation

Spherical particles give a good packing. The crosslinked copolymers used as stationary phases are usually prepared by bead polymerization. For this purpose, the monomer is dispersed mechanically in droplet form in water, and the resulting suspension is stabilized with a protective colloid during the polymerization [81]. The effects of the conditions on the particle size of the polymer have been investigated by *Hopff et al.* [82,83].

When a monovinyl compound is polymerized in the presence of a divinyl compound, the amount of the cross-linking agent determines the mesh size of the cross-linked copolymer. In the dry state the latter is not porous, but it can be swollen, as a result of which the molecular chains are solvated and form a loose, statistical network. The porosity is therefore present only in the swollen state (swelling porosity).

The order of magnitude of the mean range in which these gels are used is determined by the mean pore size, which in turn is a function of the amount of the crosslinking agent incorporated. It follows that these gels are in the statistical sense homogeneously crosslinked. The exclusion limit, *i.e.* the excluded molecular weight [*] increases as the amount of the crosslinking agent is decreased. However, such gels are only suitable for the separation of oligomers. As the amount of the crosslinking agent is decreased, the extent of swelling increases, and the mechanical strength of the gel falls off. Similar problems arise in the preparation of ion exchangers for large ions.

This led to polymerization techniques giving polymers with a heterogeneous structure and a high mechanical strength [10,84,85]. In these techniques, a crosslinkable monomer mixture is polymerized in the presence of inert and soluble components that can be removed from the end product. The inert components must not polymerize or be incorporated in the network, but they must be miscible with or soluble in the monomer. In the case of bead polymerization, the inert component is advantageously insoluble or only sparingly soluble in water. These conditions are fulfilled by numerous organic substances. Organic liquids that act as swelling agents or precipitants for the resulting crosslinked polymer are generally used. Polymers can also be used as the inert component [84,86].

When a mixture of a monovinyl compound and a divinyl compound is polymerized and a certain conversion is reached, gelling sets in at the gel point, where the viscosity and the molecular weight ($\overline{M}_w$) tend to infinity. Each molecular chain has here on average one crosslinking site. The resulting crosslinked polymer has a limited ability to absorb solvents. Therefore, when the amount of the inert component exceeds the absorption capacity of the polymer, phase separation should occur (on the assumption that the system is in thermodynamic equilibrium).

The type of phase separation depends essentially on when gelling sets in. When the polymerizing droplets form a loose network and the crosslinking becomes gradually more and more pronounced, the network may contract, expelling all the inert component (syneresis). The phase separation may occur before the gel point is reached. As in precipitation polymerization, the crosslinked copolymers (microgels) separate out and then coalesce into a porous polymer during further polymerization. In bead polymerization this process occurs in each monomer droplet. The inert component can be removed from the crosslinked polymer *e.g.* by steam distillation after the polymerization. The polymer thus obtained is often porous

[72] *J. C. Moore* and *J. G. Hendrickson*, J. Polymer Sci., Part C *8*, 233 (1965).

[73] *L. H. Tung*, J. appl. Polymer Sci. *10*, 375 (1966).

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[77] *P. Pierce* and *J. Armonas*, Amer. chem. Soc. Polymer Preprints (2) *8*, 1319 (1967).

[78] *J. H. Duerksen* and *A. E. Hamielic*, J. Polymer Sci., Part C *21*, 83 (1968).

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[80] *A. Hamielec*, 6. Int. Gel Permeation Chromatography (GPC) Seminar, Seminar Proc. p. 312, Miami Beach, Florida 1968.

[81] *H. Logemann* in *Houben-Weyl-Müller*: Methoden der organischen Chemie. Thieme, Stuttgart 1961, Vol. XIV/1, p. 406.

[82] *H. Hopff*, *H. Lüssi*, and *P. Gerspacher*, Makromolekulare Chem. *78*, 24, 37 (1964).

[83] *H. Hopff*, *H. Lüssi*, and *E. Hammer*, Makromolekulare Chem. *82*, 184 (1965).

[*] The exclusion limit or excluded molecular weight is obtained by extrapolating the linear section of the plot of log M *vs.* V_E to V_0. It is approximately the molecular weight of those molecules which are just unable to penetrate into the pores.

[84] *J. Abrams*, Ind. Engng. Chem. *48*, 1469 (1956).

[85] *H. Corte* and *A. Mayer*, DBP 1045102 (1958).

[86] *J. Seidl* and *J. Malinsky*, Czechoslovakian Pat. 102478 (1960).

even in the unswollen state (permanent porosity), and it possesses in addition swelling porosity. Owing to the heterogeneous constitution of the product, this technique is called heterogeneously crosslinking polymerization. The amount of the crosslinking agent and the nature and amount of the inert component determine mainly the heterogeneity of the product.

However, the particle size distribution of the bead polymerized products obtained by these two methods is too wide for gel-chromatographic purposes. When the particle size exceeds 50 μ, the gel is prepared by wet screening, while smaller particles are separated by sedimentation. According to Stokes' law, the sedimentation velocity v is given by

$$v = \frac{2\,\Delta\rho\, r^2\, g_n}{9\eta} \qquad (24)$$

where $\Delta\rho$ is the difference between the density of the polymer and that of the medium, r is the radius of the polymer beads, g_n is the acceleration due to gravity, and η is the viscosity of the medium.

When a constant liquid stream is produced with a piston pump or a peristaltic pump, the linear flow velocity decreases as the square of the diameter of the vessel. The sedimentation is generally carried out in water. In the case of copolymers having a permanent porosity, the surface tension of water is reduced with the aid of surfactants. Gels with a particle size of 40—80 μ are used for most separations.

4.2. Hydrophilic Gels

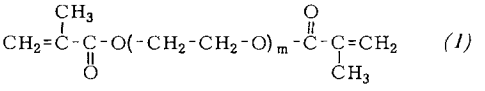
The rapid development of gel chromatography owes much to commercial crosslinked dextrans [86a]. Dextrans dissolved in water are crosslinked with epichlorohydrin in the presence of alkali. The crosslinked structure varies with the amount and the molecular weight of the starting dextran and the amount of the crosslinking agent. The commercial products permit a separation of proteins with molecular weights of up to about 5×10^5.

There are also several commercial types of acrylamide crosslinked with *N,N'*-methylenebis(acrylamide) [86b]. These too permit the separation of samples with molecular weights of up to about 5×10^5.

The porous structure may also be brought about by crosslinking with the aid of secondary valences, and such gels can be made from agarose [86a,86b]. *Determann* has described the preparation of cellulose gels by regenerating viscose [87]. Both gels can be made with exclusion limits of over 10^6.

Except for *Determann*'s cellulose gel, the hydrophilic gels described here have a large gel bed volume and thus a low mechanical strength at high exclusion limits, which hampers separation under pressure.

Hydrophilic gels with a high mechanical strength, obtained by heterogeneously crosslinking polymerization, can be prepared by subjecting polyethylene oxide dimethacrylate *(1)* to bead polymerization in the presence of inert components [88]. Substances capable



(1)

of crosslinking are formed in the reaction between methacryl chloride and the terminal OH groups of polyethylene oxide, which is soluble in water up to a high molecular weight. The exclusion limit can be varied over a wide range by varying the molecular weight of the polyethylene oxide and the nature and the amount of the inert component (cf. Table 1). Crosslinked polyethylene oxides can be used in water and organic solvents. Table 1 also shows for comparison the exclusion limits for polystyrene, as determined in THF.

Fig. 7 shows the superimposed elution curves for dextrans. The shape of curve 4, obtained for dextran

Table 1. Gel-chromatographic data for gels prepared from dimethacrylates of polyethylene glycols and polyethylene oxides [88]. V_{Sch} = bulk volume; V_G = specific gel bed volume; M_{lim} = exclusion limit (molecular weights).

Monomer (weight ratio)	Inert components (Part by volume in the total organic phase)		V_{Sch} (ml/g)	V_G (ml/g)		M_{lim}	
				H_2O	THF	H_2O	THF
Tetraethylene glycol dimethacrylate	*n*-Butyl acetate	(0.66)	2.0	4.05	5.55	10^6 [a]	$5\cdot10^6$ [c]
Tetraethylene glycol dimethacrylate	Isoamyl alcohol	(0.66)	1.65	2.3	2.6	10^4 [a]	$5\cdot10^4$ [c]
Tetraethylene glycol dimethacrylate	Isoamyl alcohol	(0.75)	1.5	2.7	5.0	6500	$1.2\cdot10^3$
Tetraethylene glycol dimethacrylate	Isoamyl alcohol	(0.80)	no swelling in water				
Tetraethylene glycol dimethacrylate	Isooctanol	(0.80)	1.55	3.1	5.4	8500 [a]	$8.5\cdot10^5$ [c]
Tetraethylene glycol dimethacrylate	Amyl alcohol/di-*n*-butyl ether (3/1)	(0.80)	1.65	4.75	6.35	$5\cdot10^8$ [b]	10^9 [c]
Polyethylene glycol-($\overline{M}_n$ = 420)-dimethacrylate	n-Butyl acetate	(0.66)	1.9	4.2	4.8		$5\cdot10^4$ [c]
Polyethylene oxide-($\overline{M}_n$ = 1000)-dimethacrylate/ Ethylene glycol dimethacrylate (10:3)	Toluene	(0.66)	1.65	3.2	3.4	4000 [a]	7000 [c]
Polyethylene oxide-($\overline{M}_n$ = 1000)-dimethacrylate/ Ethylene glycol dimethacrylate (10:1)	Isoamyl alcohol	(0.66)	1.6	5.5	5.5	1500 [a]	1200 [c]

[a] Determined with polyethylene oxides. [b] Determined with dextrans. [c] Determined with polystyrenes.

[86a] Sephadex and Sepharose, Pharmacia, Uppsala (Sweden).

[86b] Biogel P and A, Bio-Rad-Laboratories. 8 München 13.

[87] *H. Determann, H. Rehner,* and *Th. Wieland,* Makromolekulare Chem. *114,* 263 (1968).

[88] *W. Heitz* and *H. Winau,* Makromolekulare Chem. *131,* 75 (1970).

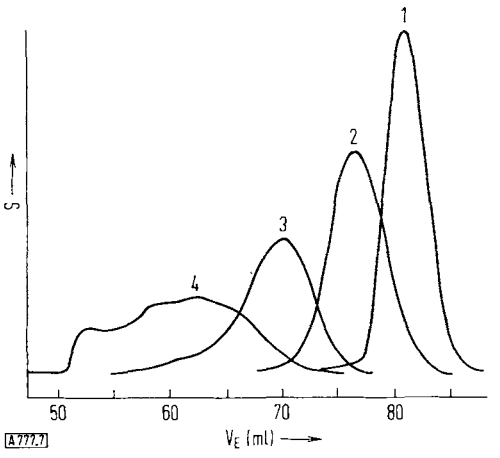


Fig. 7. Superimposed elution diagram of polyethylene oxide with $\overline{M}_w$ = 400 (curve 1) and $\overline{M}_w$ = 10000 (curve 2), and of dextran with $\overline{M}_w$ = 243000 (curve 3) and $\overline{M}_w$ = 2×10^6 (curve 4), separated in water on a polyethylene oxide gel [88]. S = recorder deflection.

with $\overline{M}_w \approx 2\times10^6$, is due to a wide molecular weight distribution. (Hydrophilic gels are summarized in [2,8,14].)

4.3. Organophilic Gels

It was logical to utilize the experience gained with crosslinked dextrans and to convert these hydrophilic gels into gels that swell in organic solvents. This has been done by reacting the OH groups, and the preparation and the use of acetyl [8], methoxy [89], and urethane derivatives [5] have been described. A hydroxypropyloxy derivative is known commercially as Sephadex LH 20® [*]. However, these reactions can be carried out easily only in the case of gels with a low exclusion limit (Sephadex G 25® and Sephadex G 50®).

The homogeneously crosslinking copolymerization of styrene with divinylbenzene [5,90], of methyl methacrylate with glycol dimethacrylate [5,88,91], and of vinyl acetate with divinyl adipate [92] gives gels that are suitable for the separation of oligomers. Fig. 8 shows the elution data obtained with polyvinyl acetate gels of different degrees of crosslinking; the straight lines run almost parallel to one another, which means that the elution-volume difference is roughly the same in all the gels at a given difference in the molecular weights. Therefore, the resolution at low molecular weights cannot be improved considerably by increasing the degree of crosslinking. Owing to the less intense swelling, the amount of the crosslinked copolymer needed for packing the column increases with the concentration of the crosslinking agent. This reduces the volume that is available for the separation.

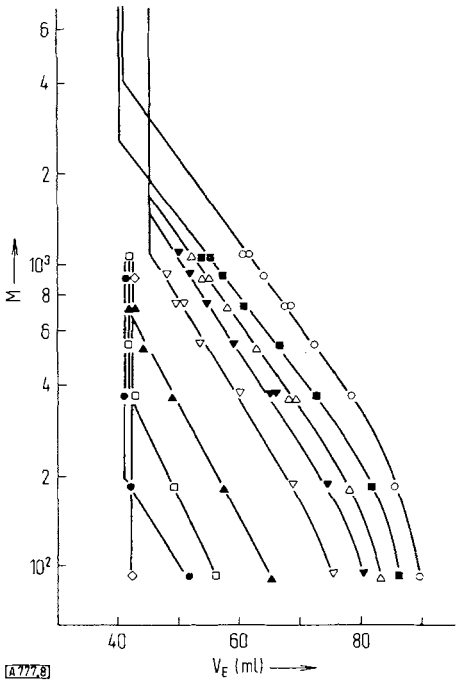


Fig. 8. Elution pattern of homogeneously crosslinked copolymeric vinyl acetates [92] in THF. Amount of divinyl adipate (in wt-%): ○ 0.5; ■ 1; △ 2; ▼ 3; ▽ 5; ▲ 10; □ 20; ● 30; ◇ 63. Samples: methyl-substituted *p*-oligophenylenes.

The exclusion limit is proportional to the specific gel bed volume, irrespective of the chemical nature of the gel. This indicates that the structure of all these gels is similar. The chain segments are pushed apart roughly to the same distance in swelling to a certain degree, so that similar pore size distributions are obtained.

The mechanical strength determines the range of applications of these gels. Gels with a very low degree of crosslinking swell heavily, and the column tends to clog even under a low pressure. However, gels with an exclusion limit of about 4000 can still be used without considerable difficulty.

Moore's use of heterogeneously cross-linked polystyrene gels constituted a great advancement [1], and these gels are now available commercially [*]. Gels suitable for practically any purpose can be obtained by an appropriate choice of the polymerization conditions. Polymethyl methacrylate gels [88,93,94] and polyvinyl acetate gels [92] can be prepared with a similarly wide range of modifications. Polyvinyl acetate gels are also on the market [**].

The copolymerization of styrene with divinylbenzene in the presence of a good solvent such as toluene and diethylbenzene gives gels with exclusion limits of up to about 2×10^3 (cf. Table 2). If the solvent power is reduced by adding a nonpolar precipitant, the exclusion limit first increases and then decreases. This phenomenon has not been observed with polar precipitants; in this case, one obtains very high exclusion limits, which should sometimes be regarded only as a

[89] *E. Nyström* and *J. Sjövall*, Analyt. Biochem. *12*, 235 (1965).

[*] Sephadex LH 20®, Pharmacia, Uppsala, Sweden.

[90] *C. L. Tripton*, *J. W. Paulis*, and *M. D. Pierson*, J. Chromatogr. *14*, 486 (1964).

[91] *H. Determann*, *G. Lüben*, and *Th. Wieland*, Makromolekulare Chem. *73*, 168 (1964).

[92] *W. Heitz* and *K. L. Platt*, Makromolekulare Chem. *127*, 113 (1969).

[*] Styragel, made by Waters Ass., Framingham, Mass., USA.

[93] *G. Heufer* and *D. Braun*, J. Polymer Sci., Part B *3*, 495 (1965).

[94] *H. Determann*, *M. Kriewen*, and *Th. Wieland*, Makromolekulare Chem. *114*, 256 (1968).

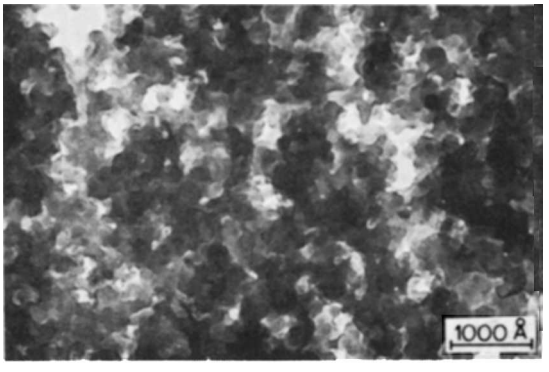
[**] Merckogel OR, made by Merck, Darmstadt, Germany.

Table 2. Exclusion limit M_{lim} of heterogeneously crosslinked styrene-divinylbenzene copolymers (3:1), prepared in the presence of 60 % of inert component in the organic phase by *Moore*'s method [1].

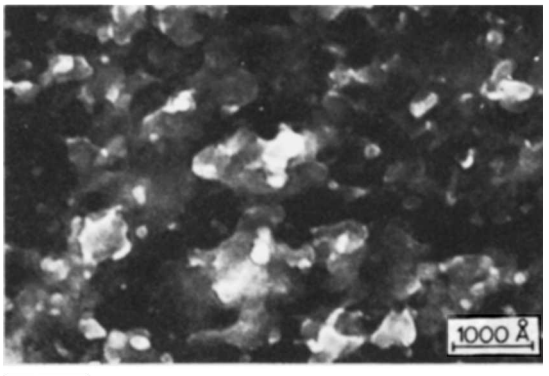
Inert component (parts %)	M_{lim}
60 Toluene	$7 \cdot 10^3$
30 Toluene; 30 diethylbenzene	$1.5 \cdot 10^4$
60 Diethylbenzene	$1.2 \cdot 10^4$
45 Toluene; 15 *n*-dodecane	$1 \cdot 10^5$
30 Toluene; 30 *n*-dodecane	$3 \cdot 10^5$
15 Toluene; 45 *n*-dodecane	$2 \cdot 10^6$
10 Toluene; 50 *n*-docecane	$2 \cdot 10^3$
40 Diethylbenzene; 20 isoamyl alcohol	$3.6 \cdot 10^3$
20 Diethylbenzene; 40 isoamyl alcohol	$8 \cdot 10^6$
13.3 Diethylbenzene; 46.7 isoamyl alcohol	10^{10}
60 Isoamyl alcohol	very high

formal quantity on account of the size of the corresponding molecular coil. The elution volume V_0 can then be determined with a crosslinked polymer obtained by emulsion polymerization [92]. Electron micrographs reveal the heterogeneity of such copolymers; thus, Figs. 9a and 9b show clearly the different structures obtained by the use of a good solvent and a precipitant [95,96].

Polystyrene gels containing 55 % of a crosslinking agent still possess a little swelling porosity. The internal surface area of these gels is sometimes over 500 m^2/g [97].



A777.9a



A777.9b

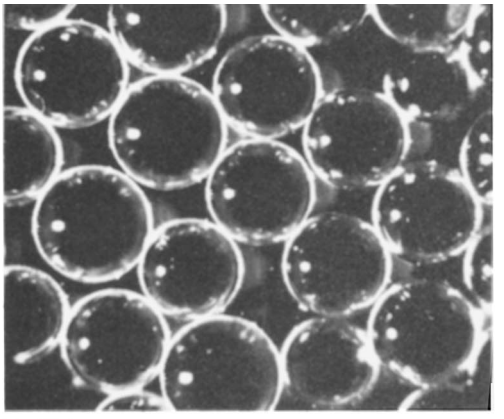
Fig. 9. Electron micrographs of heterogeneously crosslinked styrene-divinylbenzene copolymers, prepared in the presence of toluene (Fig. 9a) and heptane (Fig. 9b), according to *Millar* [95,96]. Magnification *ca.* 80000 ×.

[95] *J. R. Millar, D. G. Smith, W. E. Marr,* and *T. R. E. Kressman,* J. chem. Soc. (London) *1963,* 218.

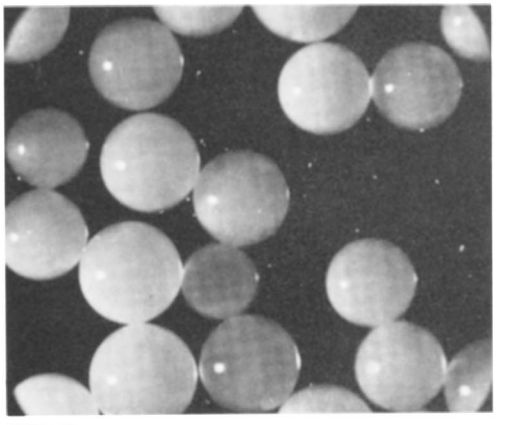
[96] *J. R. Millar, D. G. Smith,* and *T. R. E. Kressman,* J. chem. Soc. (London) *1965,* 304.

[97] *W. Heitz,* Angew. makromolekulare Chem. *10,* 115 (1970).

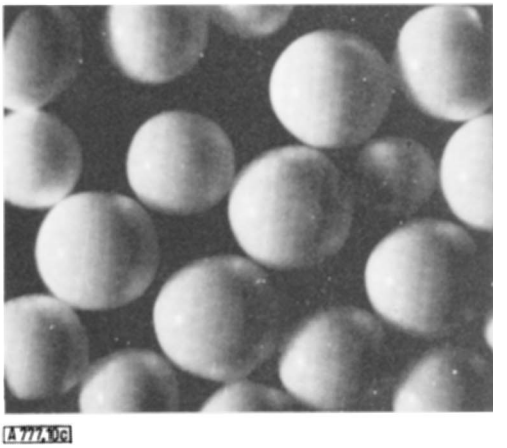
Heterogeneously crosslinking polymerization leads to gels with high exclusion limits in the case of vinyl acetate gels as well, and the heterogeneity of such networks can be seen even under an ordinary microscope (cf. Fig. 10). As the heterogeneity increases, the crosslinked copolymers at first become opaque, though retaining a certain surface gloss, and finally assume a chalky appearance.



A777.10a



A777.10b



A777.10c

Fig. 10. Micrographs of polyvinyl acetate gels with homogeneous cross-linking (Fig. 10a), and polyvinyl acetate gels crosslinked heterogeneously with 20 vol-% (Fig. 10b) and with 30 vol-% (Fig. 10c) of *n*-octane. Magnification 175 ×.

In the case of vinyl acetate gels and a good solvent (*e.g.* butyl acetate) as the inert component, there is no permanent porosity even when 40 % of divinyl adipate crosslinking agent is used. The apparent density ρ_0, which is the density of the polymer matrix and of the air enclosed in the pores,

is not affected by the addition of butyl acetate, *i.e.* no pores are present in the dry state. If *n*-octane is added, however, the apparent density greatly decreases within relatively narrow limits. The fact that the addition of butyl acetate does not alter the apparent density does not mean that the network is not heterogeneous. Between 40 and 50 vol-% of butyl acetate there is a pronounced jump in the exclusion limit, indicating that the gels are heterogeneous. However, this heterogeneity cannot be demonstrated either under the light microscope or through the apparent density.

The permanent porosity of crosslinked copolymers does not mean that the exclusion limit is high (Fig. 11). Although the greatest change in density occurs between 30 and 40 vol-% of added octane, the exclusion limit once more decreases. These gels, which lie to the right of the maximum in Fig. 11, all show a similar behavior. They are very brittle and can be readily made into a powder. Their gel-chromatographic behavior affords an insight into their structure (Fig. 12).

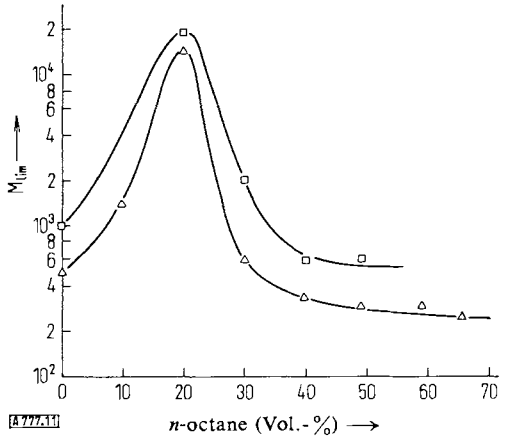


Fig. 11. Exclusion limit M_{lim} of heterogeneously crosslinked copolymers of vinyl acetate and divinyl adipate as a function of the *n*-octane concentration (on the total organic phase). Concentration of crosslinking agent: □ 10 wt-%; △ 20 wt-% (on the monomer mixture).

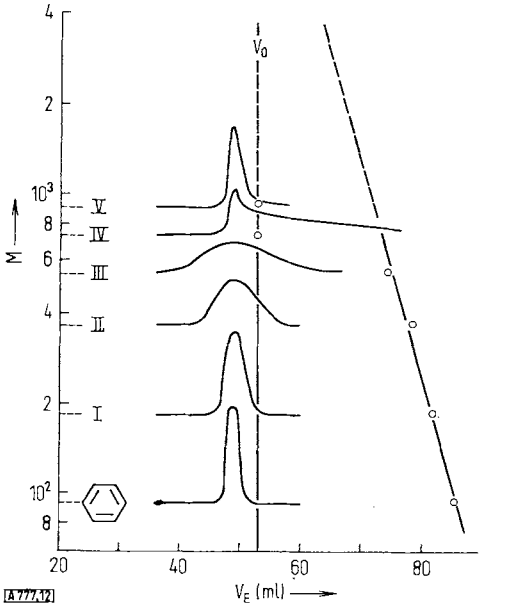


Fig. 12. Elution behavior of a heterogeneously crosslinked copolymeric vinyl acetate prepared with 40 vol-% of *n*-octane (on the total organic phase) and 10 wt-% of divinyl adipate (on the monomer mixture). The shape of the peaks is given in the middle.

While an exclusion limit of 10^4 would be extrapolated from the elution volume of the low-molecular compound, all the compounds beyond a molecular weight of about 800 appear at V_0. The shape of the elution curves is particularly informative: only compounds with very small or very large molecules give symmetric peaks, while compounds with intermediate molecular dimensions have peaks that at first broaden and then become unsymmetric as the molecular weight increases. This phenomenon is to be expected when the establishment of the equilibrium is greatly perturbed [98,99].

To explain these characteristics, one can assume that the gel particles have a heavily crosslinked surface. Such a surface is formed when the microparticles arising in the polymerization have a greater affinity for water than the inert component, and when they consequently accumulate at the phase boundary. These phenomena have not been observed with polar inert components.

5. Optimization of the Method

Chromatographic methods can be optimized with respect to the resolution or the time of the analysis. The resolution R [Eq. (16)] may be adjusted *via* the difference in the elution volumes and the peak width of the substances. According to Eq. (9), the following relationship holds for the linear part of the log M *vs.* V_E function:

$$\frac{d\,V_E}{d\,M} = -\frac{1}{BM} \qquad (25)$$

On the basis of Eq. (16), we obtain

$$\Delta\,M/M = -\,R\,4\,\sigma\,B \qquad (26)$$

When a homologous polymer series is separated into fully resolved peaks ($R = 1$), the limit is given by

$$P = -1/(4\,\sigma\,B)$$

where P is the degree of polymerization. The experimental peak width is approximately constant in the case of a homologous polymer series. The usual experimental arrangements should give a complete separation up to about the octamer. However, a satisfactory quantitative determination is possible even at $R = 1/2$, and the oligomers can still be isolated in the pure state if an appropriate fraction is chosen. For the separation of oligomers, the exclusion limit should be about 2000.

Polymers have small diffusion coefficients; the reduced velocities are therefore high, so that $H \sim d_p^2 u$. When the linear elution velocity is doubled, a certain separating efficiency can be maintained only by

[98] *H. Vink*, J. Chromatogr. *18*, 25 (1965).

[99] *T. C. Laurent* and *E. P. Laurent*, J. Chromatogr. *16*, 89 (1964).

doubling the length of the column. This means that when using a constant total volume of the columns only the total time of analysis – and not the number of columns – is important for the separation of polymers. Optimization with respect to the time of the analysis is possible here by a reduction of the gel particle size. Thus, a twofold reduction in the latter permits a fourfold reduction in the length of the column l at the same linear elution rate and separating efficiency. The working pressure is the same in the two cases, since the pressure drop along the column is given by $\Delta p \sim l/d_p^2$.

6. Examples of Separation

6.1. Oligomers

The separation of oligomers [63,64] is both of scientific and of technical importance. Single molecular-weight oligomer samples are ideal model substances for numerous investigations. As regards technical polymers, it is important to know the oligomer content; some technical products (epoxy resins and surfactants) consist almost entirely of oligomers.

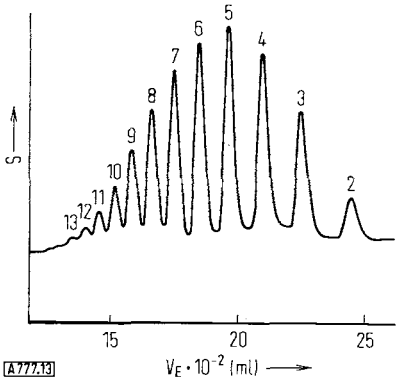
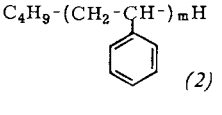


Fig. 13. Gel-chromatographic separation of oligostyrenes $C_4H_9(CH_2CHC_6H_5)_mH$ [64]. The numbers by the peaks give the degree of polymerization m. Column: 200×5 cm; eluent: THF; polystyrene gel (2 % of divinylbenzene), $\bar{d}_p$ = 74 μ; $\overline{M}_n$ = 583; S = recorder deflection.

Fig. 13 shows the separation of a polystyrene with $\overline{M}_n$ = 583 (determined by vapor pressure osmometry). The polymerization was initiated with the aid of butyllithium, and the oligomers had structure *(2)*. The indicated assignment of the peaks was confirmed by isolating the oligomers and



(2)

determining their molecular weights, as well as by the admixture of hexylbenzene (n = 1). When the indicator sensitivity was adjusted to the same value for all the oligomers, integration of the peak areas gave $\overline{M}_n$ = 580. In the case of a polystyrene with $\overline{M}_n$ = 1050, obtained analogously, the higher-molecular fraction was not resolved in the chromatogram, although it was still well below the exclusion limit of the gel.

The separation of technical polyethylene oxides is another interesting example. Monodisperse oligomeric ethylene oxides are available up to a degree of polymerization of 45 [100], and so the peaks can be identified with certainty. Technical polyethylene oxides were separated into their oligomers in the molecular-weight region between 300 and 400 (Fig. 14a). The molecular weight distribution, obtained for the oligomers by taking into account the different indicator sensitivities, was narrower than calculated by *Flory*'s method in the case of a Poisson distribution [101]. This agrees with *Törnquist*'s [102] gas-chromatographic findings and with results obtained by countercurrent

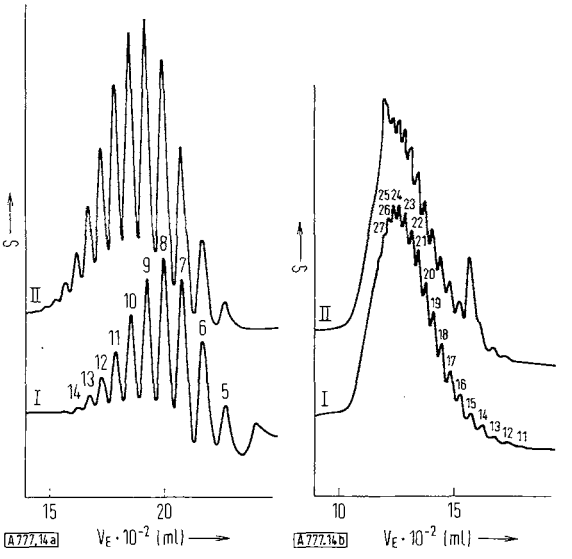


Fig. 14. Gel-chromatographic separation of oligomeric ethylene oxides. For the experimental details, see Fig. 13. Fig. 14a: $\overline{M}_n \approx 300$ (curve I); $\overline{M}_n$ = 430 (curve II). Fig. 14b: $\overline{M}_n \approx 1000$ (curve I); $\overline{M}_n \approx 1000$ admixed: terms with degrees of polymerization 15 and 27 (curve II)

distribution [103]. The condition for the use of *Flory*'s equation, namely that all the end groups should have the same reactivity, is evidently not fulfilled by polyethylene oxides in this range of molecular weights. The molecular weight distribution obtained would be explained by a higher reactivity of the low-molecular oligomers of the homologous series.

The unresolved background increases with the molecular weight (Fig. 14b). The peaks that can be assigned to these oligomers can be increased by mixing these oligomers in the pure state. Polyethylene oxides with $\overline{M}_n \approx 1000$ are no longer resolved into isolated peaks at the high-molecular end.

The gel-chromatographic separation of surfactants permits conclusions to be drawn about the molecular structure. Fig. 15a shows the separation of a technical fatty alcohol polyglycol ether that was prepared by the addition of ethylene oxide to a higher alcohol. This can be easily seen from the sharp termination of the chromatographic curve. The elution of several higher alcohols indicates that this last peak has the same elution volume as dodecyl alcohol. Fig. 15b shows the separation of a technical alkylphenol polyglycol ether, the alkylphenol moiety carrying on average about ten ethylene oxide units. The relatively poor resolution indicates that the starting phenol was not homogeneous.

[100] *B. Bömer*, Dissertation, Universität Mainz 1968.
[101] *P. J. Flory*, J. Amer. chem. Soc. *62*, 1561 (1940).
[102] *J. Törnquist*, Acta chem. scand. *21*, 2095 (1967).
[103] *K. E. Almin*, Acta chem. scand. *13*, 1293 (1959).

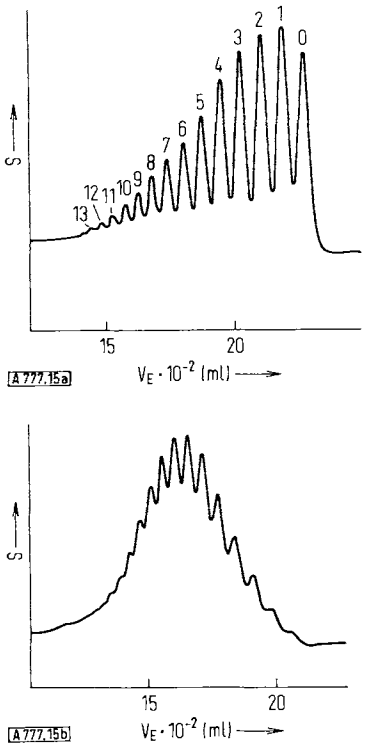


Fig. 15. Gel-chromatographic separation of surfactants. For the experimental details see Fig. 13. Dodecyl polyglycol ether $C_{12}H_{25}O(CH_2CH_2O)_mH$ (Fig. 15a); alkylphenol polyglycol ether (Fig. 15b).

Technical polyepoxides often have a low molecular weight and can be separated into their constituent oligomers. Fig. 16 shows the chromatogram for a polyepoxide pre-

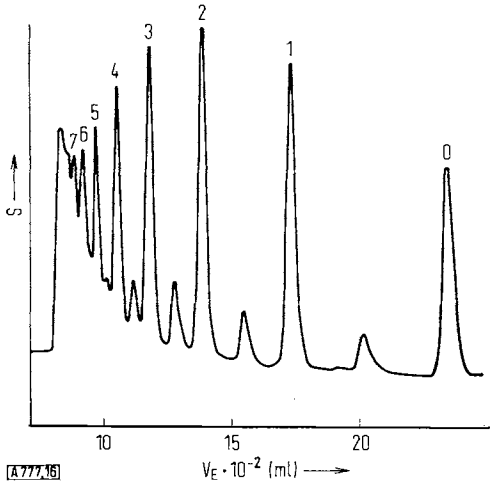
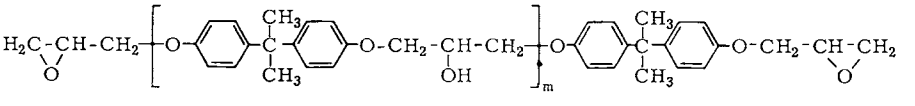


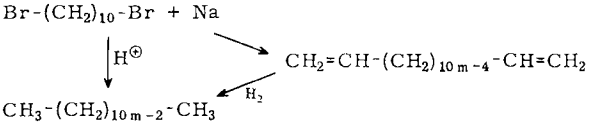
Fig. 16. Gel-chromatographic separation of a polyepoxide made from biphenol A and epichlorohydrin. For the experimental details see Fig. 13. The numbers by the peaks give the value of m in the homologous series of polymers.



pared from bisphenol A and epichlorohydrin[104]. The alternation of small and large peaks indicates the presence of two series of oligomers, the main series corresponding to compounds with two epoxy end groups.

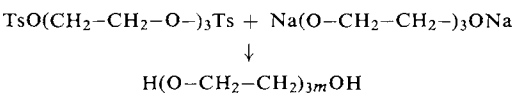
[104] *D. Braun, H. Cherdron*, and *W. Kern*: Praktikum der makromolekularen organischen Chemie. Hüthig, Heidelberg 1966.

The above examples show that it is not possible to isolate gel-chromatographically a compound with a degree of polymerization of *e.g.* 50 from a continuous homologous series of polymers. However, such monodisperse polymers can be obtained by separating a discontinuous homologous series of polymers, *i.e.* a series comprising only terms with certain multiples of the degree of polymerization. Such a molecular weight distribution should be ensured by appropriate synthesis. The first example of this is due to *Carothers*[105], who condensed 1,10-dibromodecane and thus obtained a mixture of alkanes in each of which the number of carbon atoms could be only a multiple of 10. A side reaction led to products with terminal



double bonds, which could be catalytically hydrogenated into alkanes[106]. The alkanes could be separated up to $C_{90}H_{182}$. The use of 1,20-diiodoeicosane gave a mixture of alkanes which could be identified in the chromatogram up to $C_{120}H_{242}$[107].

By *Williamson*'s ether synthesis, triethylene glycol can be converted into a mixture of polyethylene oxides whose degrees of polymerization are all multiples of 3.



The nonaethylene glycol can be separated from this mixture by molecular distillation. A second ether synthesis gives a mixture of components whose degrees of polymerization are all multiples of 9[100]. Preparative gel chromatography of this mixture permits the oligomers to be isolated up to $m = 45$.

6.2. Polymers

Polymers can be separated gel chromatographically when the polymer has a suitable solvent in which the stationary phase swells to a sufficient extent. Gels with a permanent porosity contain pores even in precipitants, but adsorption-induced perturbations are then obtained fairly often. Table 3 shows the working conditions for some polymers.

[105] *W. H. Carothers, J. W. Hill, J. E. Kirby*, and *R. A. Jacobson*, J. Amer. chem. Soc. *52*, 5279 (1930).

[106] *T. Wirth*, Dissertation, Universität Mainz 1968.

[107] *R. Peters*, Diplomarbeit, Universität Mainz 1969.

Table 3. Working conditions for the gel-chromatographic separation of polymers.

Polymer	Molecular weight range × 10^3	Solvent	Stationary phase [a]	Temp. (°C)	Ref.
Polystyrene	13—3500	Toluene	PS	90	[1]
	82—3500	*o*-Dichlorobenzene	PS	25	[28]
	119—267	1,2,4-Trichlorobenzene	PS	130	[24]
	0.9—540	THF	PS	23	[29, 37, 69, 108]
	0.6—1800	THF	PVA	23	[92]
	0.6—1800	THF	PMMA	23	[88]
	0.6—1800	THF	SiO_2	25	[50, 109]
Polymethylmethacrylate	2—12000	THF	PS	23	[29, 30, 37, 110]
Polyethylene	0.1—10000	1,2,4-Trichlorobenzene, *o*-Dichlorobenzene	PS	130, 135	[27, 32, 111, 112, 113]
Polypropylene	230—520	1,2,4-Trichlorobenzene	PS	130	[114]
Polyisobutene	0.1—1000	1,2,4-Trichlorobenzene	PS	35—150	[33]
Poly-1-butene	100—1500	1,2,4-Trichlorobenzene	PS	135	[115]
Polybutadiene	1—2000	THF	PS	—	[27, 28, 37]
Polyisoprene	120—170	$CHCl_3$	PS	—	[116]
Polyvinylchloride	1—2000	THF	PS	25	[27, 37, 117]
	6—250	THF	SiO_2	25	[50, 109]
Cellulose trinitrate	50—4200	THF	PS	25	[34, 118, 119]
Polyethylene oxides	30—200	THF	PS	—	[120]
Polypropylene oxides	0.1—6	THF, Toluene	PS	25	[51]
Epoxide resin	0.2—20	THF	PS	—	[64, 121, 122]
Phenol-Formaldehyde-Condensate	—	THF	PS	25	[123]
Aliphatic polyester	5—20	THF	PS	37	[124]
Polyethylene glycol terephthalate	0.2—30	*m*-Cresol	PS	125	[125]
Polysulfone	40	THF, DMF	PS	—	[126]
Polydimethylsiloxanes	0.8—145	Toluene	PS	20	[127, 128]
Dextrans	11—2000	H_2O	SiO_2	25	[50, 109]
	11—2000	H_2O	PEO	25	[88]
Polyphosphate	—	H_2O	H_2O—PS	25	[129]
Nylon 6	9—27	*m*-Cresol	PS	110	[130]
Nylon 66	—	Trifluoroethanol	PS	43	[131]

[a] PS = polystyrene gel, PVA = polyvinylacetate gel, PMMA = polymethylmethacrylate gel, SiO_2 = sphaerosil (Pechiney-Saint-Gobain), H_2O—PS = modified water-compatible polystyrene gel, PEO = polyethylene oxide gel.

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[108] *H. W. Osterhoudt* and *L. N. Ray*, J. Polymer Sci., Part *21*, 5 (1968).

[109] *R. Beau, M. Le Page*, and *A. J. DeVries*, Appl. Polymer Sympos. *8*, 137 (1969).

[110] *W. B. Smith, J. A. May*, and *C. W. Kim*, J. Polymer Sci., Part A-2 *4*, 365 (1966).

[111] *N. Nakajima*, J. Polymer Sci., Part C *21*, 153 (1968).

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Chemistry and Logical Structures

By Ivar Ugi, Dieter Marquarding, Hans Klusacek, George Gokel, and Paul Gillespie[*]

The utility of the basic structures of modern mathematics for chemistry is discussed; general set theory, topology, and group theory are shown to pervade almost all static and dynamic aspects of chemistry. Chemical analogy, the systematic classification of molecules and a corresponding nomenclature system, conformational transformations, polyhedral rearrangements, and the relations between starting materials, transition complexes, and final products of chemical reactions are examples of where we apply the elements of modern mathematics to the solution of chemical problems.

"Die Moral dieser Geschichte ist offenkundig: man nehme solche vorläufigen kombinatorischen Schemata wie die Valenzdiagramme nicht zu wörtlich, so nützlich sie auch als erste Führung in einer scheinbar zusammenhanglosen Masse von Tatsachen sind. Von einem mit ein paar scharfen Strichen entworfenen Bild der Wirklichkeit kann nicht erwartet werden, daß es der Vielfalt all ihrer Schattierungen adäquat sei. Gleichwohl muß gerade der Zeichner den Mut haben, die Linien kräftig zu ziehen." – Hermann Weyl, on the chemical bond[1]

1. Introduction and General Considerations

1.1. Chemistry and Mathematics

Mathematics has recently undergone substantial reforms. A Paris group of mathematicians formalized the new approach to mathematics (see Section 1.3.1.) in their book "Eléments de Mathématique" published under the pseudonym *Nicolaus Bourbaki*[2i]. The organization of classical mathematics, which was strongly influenced by its applications, is now being oriented towards generating mathematics from the "basic structures", *i.e.* the *algebraic structures*, the *ordered sets*, and the *topological spaces*. The ideas of the Bourbaki group can be considered a consequential extension of the formalistic approach initiated by *Hilbert*.

Pure mathematics, from the contemporary viewpoint, is a general, hypothetical, deductive formalism of relations. This formalism, which may serve an objective, is created without any consideration of the objective. It provides us with a theory of logical structures which can be used as models for some characteristic properties of reality. It is our intention to develop a mathematical concept of molecules, confined and prejudiced as little as possible by our experience.

The relations between objects, rather than the objects themselves, are the primary concern of science. Usually, spatial relations are *prima facie* defined on the basis of the Euclidean space of our experience. It is, however, as physics illustrates, often advantageous for the solution of certain problems to use purely mathematical concepts of space, which have in common with Euclidean space only some formalistic characteristics.

The question of whether or not a certain mathematical concept provides the basis for the most suitable model of a phenomenon is consciously asked in physics. In chemistry, however, three-dimensional Euclidean space and classical mathematics have been so strongly favored by tradition that the use of the more abstract mathematical structures was confined to those who considered chemistry an extremely complicated special case of physics, and accordingly treated chemical problems with the advanced and sophisticated methods of theoretical physics. The use of mathematics in chemistry has been oriented almost exclusively towards generating numerical data in order to test the validity of some mathematical model of an experimentally observed phenomenon. Little use has generally been made of the fact that mathematics is formalized logical thought and can be used directly to gain insight into the intrinsic logical structure behind chemical problems.

The coming generation of scientists will have grown up with modern mathematics and it is safe to predict that this generation will use these fundamental concepts to an extent which we cannot even imagine. The present paper attempts to outline some aspects of chemistry where structure-oriented mathematics offers a promising approach.

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[1] *H. Weyl:* Philosophie der Mathematik und Naturwissenschaft, Oldenbourg, München, 1966, p. 352.

[2] See, *e.g.:* a) *M. Hamermesh:* Group Theory and its Application to Physical Problems. Addison-Wesley, Reading, Mass. 1962; b) *R. McWeeney:* Symmetry. Pergamon, New York 1963; c) *S. Lipschutz:* Set Theory. McGraw-Hill, New York 1964; d) *S. Lipschutz:* General Topology. McGraw-Hill, New York 1965; e) *H. J. Kowalski:* Topological Spaces. Academic Press, New York 1965; f) *H. Meschkowski:* Mathematisches Begriffswörterbuch. Bibliographisches Institut, Mannheim 1965; g) *J. Dugundji:* Topology. Allyn and Bacon, Boston 1966; h) *J. Schmidt:* Mengenlehre. Bibliographisches Institut, Mannheim 1966; i) *N. Bourbaki:* Elements of Mathematics. General Topology. Addison-Wesley, Don Mills, Ontario 1966; j) *A. J. Coleman* in *E. M. Loebl:* Group Theory and its Applications. Academic Press, New York 1968, p. 61; k) *R. H. Fox* and *R. Crowell:* Introduction to Knot Theory. Blaisdell, Waltham, Mass., 1963.

1.2. Chemical Topology

Among the mathematical structures, the group and topological space have the greatest potential for chemistry. The striking success of group theory in solving problems which are related to symmetry is well documented. Group theory is also a powerful mathematical tool for dealing with such deviations from geometrical symmetry which can be represented by algebraic symmetry [7, 15].

Topology has not found extensive application to the solution of chemical problems. It was pointed out during various pertinent discussions [3] that stereochemistry ought to be discussed in terms of topology, because some of the metric features of molecules are not essential for stereochemistry.

Prelog [4] proposed the term "chemical topology" to be used for the description of stereochemical entities in topological terms:

"Chemical topology deals with properties of geometrical figures that are either isomorphous or homomorphous with the momentary or time average topography of chemical particles."

"When I use a word", Humpty Dumpty said in rather a scornful tone, "it means just what I choose it to mean – neither more nor less". *Lewis Carroll*, Through the Looking-Glass [5].

It is difficult to predict whether this concept of chemical topology will ever provide a basis for an operational formalism in chemistry or lead to new insights.

Nonetheless, *Prelog*'s definition of chemical topology has initiated and stimulated the use of mathematical structures in chemistry, as discussed in the present paper.

The main difficulty in generating a topological theory of stereochemistry arises from chirality; it is not possible to distinguish between a geometrical system and its non-superimposable mirror image by the representation of molecules as topological spaces. Yet, it is possible to generate a framework of thought for the treatment of chemical problems by a combined application of basic concepts from topology and group theory.

1.3. Elements of Modern Mathematics [2, 6] [*]

1.3.1. Sets [2c, f–h]

A fundamental concept in all branches is that of a set. A set is any well defined collection or class of distinguishable objects of our experience or thought. These objects are called elements or members of the set. The theory of sets contains only one basic relation, usually denoted by $\in$ and expressed as *belongs to*. Examples pertinent to our discussion include not only sets of individual elements, numbers, and points, but sets (classes, families) of sets. A set A is a *subset* of a set B, or conversely B is a *superset* of A;

$$A \subset B \quad \text{or} \quad B \supset A$$

if each element in A also belongs to B.

Sets are specified by giving them a property P which can be used to test the claim of membership to a set by any object in the universe, the set of all objects having the property P is defined by $\{x|x \text{ has the property } P\}$. In the following specific applications of set theory, all sets under investigation are subsets of a fixed set. We call this set the *universal set*, U. The *empty* or *null set*, $\emptyset$, is the set which contains no elements; it is a subset of every other set. Important additional concepts are *intersections* and *unions*. The *intersection* of two sets A and B, symbolized $A \cap B$, is the set of elements which belong to both A *and* B, *i.e.*

$$A \cap B = \{x|x \in A \text{ and } x \in B\}$$

The *union* of two sets A and B, symbolized $A \cup B$, is the set of elements which belong to at least one, A *or* B, *i.e.*,

$$A \cup B = \{x|x \in A \text{ or } x \in B\}$$

Here, "or" is used in the sense of "and/or".

Two more important set operations are best introduced at this point. The *complement* of set B with respect to set A or simply the *difference* between A and B, denoted by $A \setminus B$, is the set of elements which belong to A but not to B, *i.e.*,

$$A \setminus B = \{x|x \in A, x \notin B\}$$

The *absolute complement* of set A, symbolized by A^c, is the set of elements which do not belong to A, *i.e.*,

$$A^c = \{x|x \in U, x \notin A\}$$

Or, A^c is the difference between the universal set U and the set A.

These four set operations can be further illustrated with the use of Venn-Euler diagrams. Here, the sets A and B are symbolized by circles and the universal set U shown as a rectangle. The indicated operations are shaded.

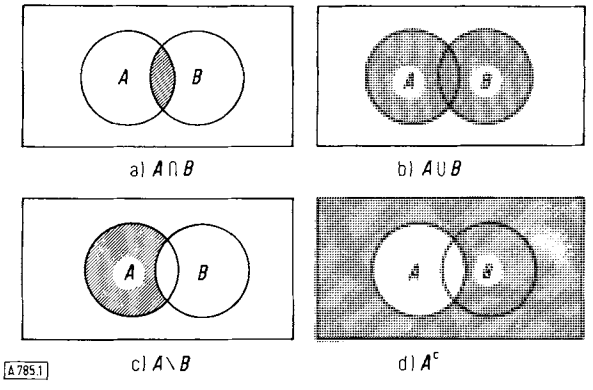


Fig. 1. Venn-Euler diagrams of set operations.

To each two objects, a and b, there corresponds a new object $\langle a,b\rangle$ called their *ordered pair*. Ordered pairs are required to satisfy:

$$\langle a,b\rangle = \langle c,d\rangle \text{ if and only if } a = c \text{ and } b = d.$$

The product set in set theory, written $A \times B$ and called the Cartesian product, is the set whose members are all ordered pairs $\langle a,b\rangle$ where $a \in A$ and $b \in B$, *i.e.*,

$$A \times B = \{\langle a,b\rangle | a \in A, b \in B\}$$

The product of a set with itself, *i.e.*, $A \times A$ is symbolized by A^2 and plays an important part in the definition of group structure (see Section 1.3.3.).

A rule f that assigns to each element of a set A a unique element of a set B is called a *mapping* f of A into B: $A \rightarrow B$ (or $A \xrightarrow{f} B$). The specific element $b \in B$ assigned to $a \in A$ by f is called the image $f(a)$ of a under f (or the value of f at a). Figure 2 illustrates the various types of mapping.

[3] Euchem Conferences on Stereochemistry, Bürgenstock.

[4] *V. Prelog*, Abstract of the Roger Adams Award Lecture on June 17, 1969, at the A.C.S. Meeting, Salt Lake City, Utah.

[5] *L. Carroll:* The Annotated Alice (edited and annotated by *M. Gardner*). World Publishing Company, New York 1969, p. 269; see also *M. Gardner:* The Ambidextrous Universe. Mentor Books, New York 1969, pp. 74, 118.

[6] For a review, see: Mathematical Aspects of Chemical Reactions – *R. Aris*, Ind. Eng. Chem. *61*, No. 6, p. 17 (1969), especially footnotes 17, 18, 27, 34, 35, 216.

[*] We suggest that readers familiar with elementary topology and group theory omit Section 1.3.

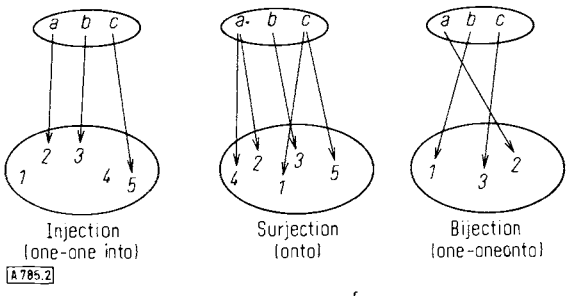


Fig. 2. Various types of mapping of sets $A \xrightarrow{f} B$.

A propositional function $P(x,y)$ on the Cartesian product $A \times B$ has the property that $P(a,b)$, a and b being substitutes for x and y in $P(x,y)$, is true or false for any ordered pair $\langle a,b\rangle \in A \times B$. If A is the set of all chemists and B is the set of all known chemical compounds, then $P(x,y) \equiv$ "x discovered y" is a propositional function on $A \times B$. For example, P(*Waksman*, streptomycin) = "*Waksman* discovered streptomycin", P(*Fischer*, streptomycin) = "*Fischer* discovered streptomycin" are true and false, respectively.

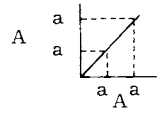
A binary relation R in the set A is, intuitively, a proposition such that for each ordered couple $\langle a,a'\rangle$ of elements of A one can determine whether aRa' (a is a relation, R, to a') is or is not true. Any subset R of $A \times B$ is called a binary relation, R, from A to B. Formally stated in terms of the set concept, the binary relation R of $A \times B$ is:

$R \subset A \times B$

$\langle a,b\rangle \in R = aRb$

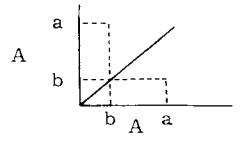
A binary relation R in A is called an *equivalence relation* if:

E I: $\forall a \in A : a\,R\,a$



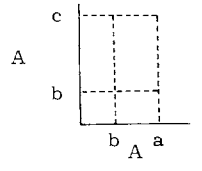
$(a,a) \in R$ (Reflexive) The relation R cortains the diagonal

E II: $(a\,R\,b) \Rightarrow (b\,R\,a)$



$(a,b) \in R$
$(b,a) \in R$ (Symmetric) The relation R is Symmetric about the diagonal

E III: $(a\,R\,b) \wedge (b\,R\,c) \Rightarrow (a\,R\,c)$



$(a,b) \in R$
$(b,c) \in R$ $\Big\}$ $(a,c) \in R$ (Transitive)

The equivalence class $[a]$ of any element $a \in A$ is the set of elements to which a is related. If the equivalence relation R is "x is congruent to y modulo 2" in the set N of integers, these are two distinctive equivalence classes, the *even* and the *odd* numbers. In chemistry most reasoning is done by analogy, *i.e.* by classification according to equivalence relations. For this to be meaningful, the pertinent equivalence relation must always be defined.

1.3.2. Topology [2d-g,i,j]

In modern mathematics the notion of a set is an undefined term whose use is governed by various axioms. This notion is used only as a framework from which mathematical theories are developed by defining axioms and applying logical deduction. Any mathematical structure has at its foundation a set, but one usually imposes an extra structure. Concepts of *neighborhood*, *open set*, *limit*, and *continuity*, necessary for the formalisms that follow, can be applied to a set A only if it has been supplied with a topology. A topological space is a set equipped with a topological structure.

If we let A be any non-empty set, a class T of subsets of A is called a topology on A if T satisfies the following axioms:

T I: A and $\emptyset$ belong to T.
T II: The *union* of any number of sets in T belongs to T.
T III: The *intersection* of any two sets in T belongs to T.

The pair (A,T) is called a topological space and the members of T are called the open sets of the topological space (A,T). If only one topology on A is considered we refer to the topological space A. Sometimes it is necessary to use different topologies on the same set to produce the formalism best suited for the solution of a problem. Here a comment by *Coleman* [2j] is appropriate. "... the chief skill needed is the ability to switch adroitly from one topology to another as rapidly as a quick change artist exchanges personalities. In such situations the old notations and habits of mind are very inhibiting ..."

If an open set T contains a point p, the open set T is called a neighborhood of p.

A family, $\{V_\alpha | \alpha \in T\}$, of sets is called a *basis* for a topology if the family of arbitrary unions of these sets forms a topology.

To illustrate the defined concept of topological space, one can see that a topological structure on the set of real numbers R is defined by using the open intervals and their unions as the open sets T. (R can be represented by a real line whose points are paired with the real numbers in a natural manner.) In this example, the neighborhood concept is obvious. The neighborhood of a point on a real line is any open interval which contains this point (compare the sequence rules discussed in Section 2.3.).

Open and *interior* are best illustrated with the concept of the open interval of real numbers.

Open interval from a to b: $]a,b[= \{x | a < x < b\}$
Closed interval from a to b: $[a,b] = \{x | a \leqq x \leqq b\}$

We can further define our topology to include the Hausdorff separation property:

T IV: Any two points of a space A have disjoint neighborhoods M and N whose intersection is the empty (null) set, *i.e.*, $M \cap N = \emptyset$.

A set A is called a metric set if there is given for any two points a and b a real number $D(a,b)$, the distance between a and b. A metric in a set A is a function $D : A \times A \rightarrow R$ such that:

T V: $D(a,a) = 0$
T VI: $D(a,b) = D(b,a) > 0$, for $a \neq b$
T VII: $D(a,b) \leq D(a,c) + D(c,b)$

Each metric D induces a topology. For example, by using the balls $\boldsymbol{B}_{(a,\gamma)} = \{x|D_{(a,x)} < \gamma\}$ for all $\gamma > 0$, $a \in \boldsymbol{A}$, the balls and all their unions are the topology on $\boldsymbol{A}$.

Let $(\boldsymbol{A}_i, \boldsymbol{T}_i)$ be a finite family of topological spaces where $i \in \boldsymbol{I}$ with $\boldsymbol{I}$ being a finite set of indices. The Cartesian *product topology* $\prod_1^n \boldsymbol{T}_i$ of $\prod_1^n \boldsymbol{A}_i$, is that topology having the open sets $\boldsymbol{U}_i \times \ldots \times \boldsymbol{U}_n$, where $\boldsymbol{U}_i \in \boldsymbol{T}_i$, as a basis.

The mutual neighborhood relations within families of intersecting sets can be described graphically by the nerve of the family. The nerve of an n-fold non-empty intersection is given by an $n-1$ dimensional graph (simplex); the non-empty intersection of two sets is represented by a line, a non-empty intersection of three sets by a triangle (see Fig. 3).

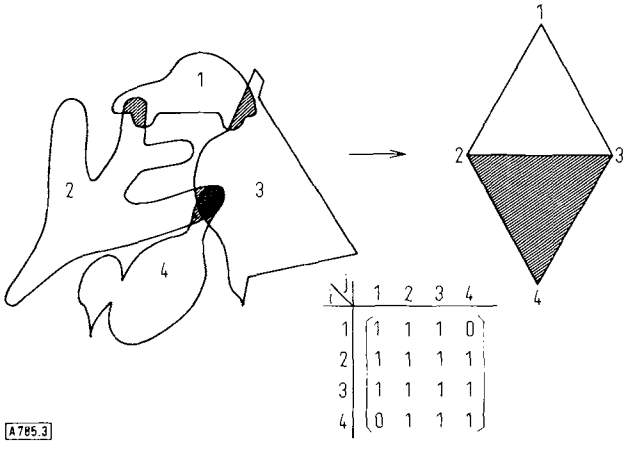


Fig. 3. Graph and matrix representation of neighborhood relations of a family of intersecting sets (nerve).

Such graphs can also be represented by matrices, using zero and one to indicate whether two sets are disjoint or have a non-empty intersection respectively. If matrix element $a_{ij} = 0$, this indicates that sets i and j are disjoint, and $a_{ij} = 1$ means their intersection is not empty (cf. Fig. 3). The secular determinants of the HMO theory are based upon such topological matrices. By their very definitions, these matrices are symmetrical across the main diagonal. If one replaces the connecting lines between pairs of points by arrows (as in category theory) the direction of the connection can be expressed by the indices of the matrix elements; $a_{12} = 1$, $a_{21} = 0$ means point one is connected with point two by an arrow $1 \rightarrow 2$. A formalism for the representation of molecules including all the steric features could be based upon category theory. However, such a treatment would afford a formalism which, except for computer use, is too complicated for practical purposes (see Section 4).

For the description of complicated reaction mechanisms with consecutive and parallel reactions (see ref. [6,7]), the category theory offers interesting possibilities. If we represent the reactants, products and all the observed and hypothetically assumed intermediates of a reaction by points and represent the observed and assumed reaction by arrows, the mapping of the sets of arrows onto the sets of points describes the reaction kinetic scheme. Here, the recent discussion[6] of topological (homology theoretical) concepts of "chemical reaction" and "reaction mechanism" is of particular interest. In this context, thermodynamic equilibria can be viewed as equivalence relations.

1.3.3. Groups[2a,b,g,j]

Another structure that can be imposed upon a set is the group structure. A set is called a group $\boldsymbol{G} = (\boldsymbol{A},\varphi)$ if there is a mapping $\varphi: \boldsymbol{A} \times \boldsymbol{A} \rightarrow \boldsymbol{A}$ (we write $\varphi(a \cdot a') = a \cdot a'$) satisfying the following conditions:

G I: The associative law is obeyed, *i.e.*, $(a \cdot a') \cdot a'' = a \cdot (a' \cdot a'')$ for all $a, a', a'' \in \boldsymbol{A}$.

G II: There exists an element $e \in \boldsymbol{A}$ (called the *unit element*) such that $e \cdot a = a$ for all $a \in \boldsymbol{A}$.

G III: For each $a \in \boldsymbol{A}$ there exists an element a^{-1} (called the *inverse element*) such that $a^{-1} \cdot a = e$.

The group $\boldsymbol{G} = (\boldsymbol{A},\varphi)$ is characterized by the set $\boldsymbol{A}$ and the mapping φ. Two groups are compared by mappings of the underlying sets that comprise the structures, *i.e.*,

$$(\boldsymbol{A},\varphi) \xrightarrow{f} (\boldsymbol{B},\psi)$$

If the condition

$$f(a \cdot a') = f(a) \cdot f(a')$$

is satisfied, such mappings are called *homomorphous*. A special case is a homomorphism which is a one to one mapping of a group onto another group, a bijection (see Fig. 2). Such a map is called an *isomorphism*. In this case the two groups have the same structure. Any homomorphism of a given group into the general linear group $\boldsymbol{GL}(n,\boldsymbol{R})$ of non-singular $(n \times n)$ matrices with real entries

$$(\boldsymbol{A},\varphi) \xrightarrow{f} \boldsymbol{GL}(n,\boldsymbol{R})$$

is a *representation* of the group $(\boldsymbol{A},\varphi)$. If this mapping is an isomorphism into $\boldsymbol{GL}(n,\boldsymbol{R})$ we have a *faithful representation*.

A group is characterized by its multiplication table, a square array of group elements arranged to show the results of the combination of group elements. If we have a group of order two with elements A and B and let the combination of these elements be defined such that

$$AA = BB = A$$
$$AB = BA = B$$

this statement could be represented by the multiplication table

	A	B
A	A	B
B	B	A

If we take the real number $+1$ as the element A and the real number -1 as element B, and make multiplication the group operation, we have a particular realization of the above group with the multiplication table

	$+1$	-1
$+1$	$+1$	-1
-1	-1	-1

The concept of a symmetry group is illustrated by Fig. 4.

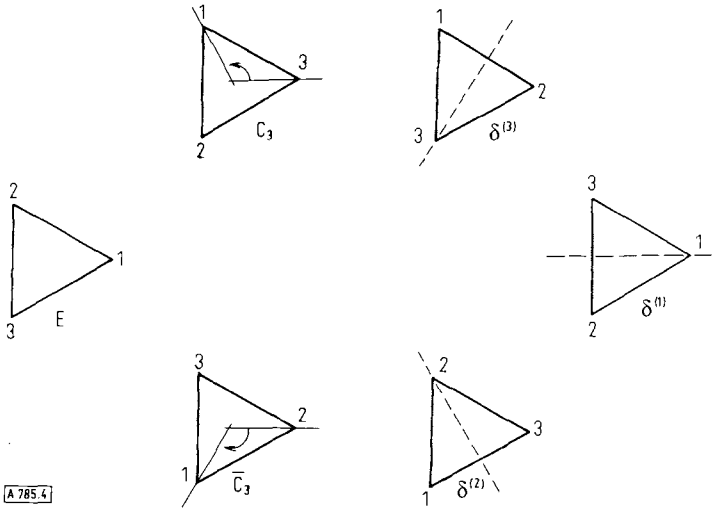
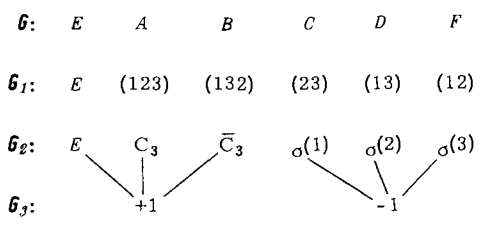


Fig. 4. Rotations C_n and reflections σ.

[7] *E. Ruch* and *I. Ugi*, Theor. Chim. Acta *4*, 287 (966); Top. in Stereochem. *4*, 99 (1969).

The operations that bring this triangle in Fig. 4 into a position indistinguishable from its original position, *i.e.* self-coincidence, are called *symmetry operations*. Symmetry operations may be performed sequentially. We define, for any set of symmetry operations R and S, a law of combination φ symbolized by RS, meaning first apply S, then R. Sequentially performed symmetry operations obeying the combination law φ form groups $G = (A,\varphi)$.

If we map the symmetry operations G_2 of Fig. 4 on the letters $A-F$



the multiplication table obtained is that of the group symmetry operations.

	E	A	B	C	E	F
E	E	A	B	C	D	F
A	A	B	E	F	C	D
B	B	E	A	D	F	C
C	C	D	F	E	A	B
D	D	F	C	B	E	A
F	F	C	D	A	B	E

Notice that the group $\{(+1)(-1)\}$ also satisfies the same multiplication table, but that the latter group is homomorphic to the first two.

Order, subgroup, and coset are further basic concepts of group theory essential for our discussion. In a group G containing g elements, g is called the *order* of the group. Any collection of the elements of G which by themselves form a group H is a *subgroup* of G. Every group contains two trivial or *improper subgroups*, the unit element, E, and the whole group itself, the rest of the subgroups considered *proper*. The set of subgroups does not correspond to a partition of the original group as E must be a member of *every* subgroup.

Let $H = \{A_1, A_2 \ldots A_h\}$ and R_1, R_2 .... be elements of G not contained in H; then the collection defined by

$$HR_k = \{A_1R_k, A_2R_k \ldots A_hR_k\}$$

is called the *right coset* of H with respect to R_k. Analogously, the double coset HR_kH' ($R_i \in G$, $R_i \notin H$, $R_i \notin H'$) is obtained from the two subgroups H and H' and their relative complement. Notice that the coset HR_k is not a group as it does not contain the identity element E, the same also applying to HR_kH'.

The symmetry group of a regular polygon with n vertices is of the order $2n$. It contains n rotations and n reflections.

$$G = \{E = C_n^n, C_n, C_n^2 \cdots C_n^{n-1} = \bar{C}_n, \sigma, \sigma C_n \cdots \sigma C_n^{n-1}\}$$

Since this group G can be generated from the rotations C_n and the reflections σ, these are called the *generators* of G.

Symmetry operations that leave one point of a figure unmoved form a *point group*.

Three dimensional point groups are characterized by the following generators:

C_n = positive rotations moving 360°/n (C_n axis normal to the plane of the paper).
σ_v = reflection across a vertical plane.
σ_h = reflection across horizontal plane.
σ_d = reflection across a vertical plane bisecting the angle between two C_2' axes.
C_2' = rotation through 180° about axes normal to the principal C_n axis.
S_n = improper positive rotations through 360°/n.

The Schoenflies notation is used to denote the point group symmetries in terms of their generators. C_n: $\{C_n\}$, C_{nv}: $\{C_n,\sigma_v\}$, C_{nh}: $\{C_n,\sigma_h\}$, S_n: $\{S_n\}$, D_n: $\{C_n,C_2'\}$, D_{nd}: $\{C_n,C_2',\sigma_d\}$, D_{nh}: $\{C_4, C_2',\sigma_h\}$, T: $\{C_2^z, C_3^{xyz}\}$, T_d: $\{\bar{S}_4^z, C_3^{xyz}\}$, T_h: $\{C_2^z, C_3^{xyz}, i\}$, O: $\{C_4^z, C_3^{xyz}\}$, O_h: $\{C_4^z, C_3^{xyz}\}$, Y: $\{C_3, C_5\}$.

The trajectory followed by a given point resulting from sequentially applied group operations is called its orbit. One can use this concept for numbering a symmetrical set of points (see Fig. 6).

An informative mapping of one three-dimensional Euclidean space E^3 onto another $\bar{E}^3$ can be represented by an orthogonal matrix

$$A = \begin{pmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{pmatrix} \quad ; \quad A \begin{pmatrix} x \\ y \\ z \end{pmatrix} = \begin{pmatrix} a_{11}x + a_{12}y + a_{13}z \\ a_{21}x + a_{22}y + a_{23}z \\ a_{31}x + a_{32}y + a_{33}z \end{pmatrix} = \begin{pmatrix} \bar{x} \\ \bar{y} \\ \bar{z} \end{pmatrix}$$

Each row in the resulting matrix is the new coordinate of the original point. The distance relation between the points as well as the origin is maintained. A has the following properties:

M I: $a_{11}^2 + a_{12}^2 + a_{13}^2 = 1$
$a_{21}^2 + a_{22}^2 + a_{23}^2 = 1$
$a_{31}^2 + a_{32}^2 + a_{33}^2 = 1$

M II: $a_{11}a_{21} + a_{12}a_{22} + a_{13}a_{23} = 0$
$a_{11}a_{31} + a_{12}a_{32} + a_{13}a_{33} = 0$
$a_{21}a_{31} + a_{22}a_{32} + a_{23}a_{33} = 0$

M I and M II state: The product of the matrix A and its transpose A^T (the 'mirror image" of A across its main diagonal) is equal to the unit matrix E_3 symbolized:

$$AA^T = E_3$$

The product of any two orthogonal matrices is an orthogonal matrix and the inverse of such a matrix is its transpose:

$$AA^{-1} = E_3 = A^{-1}A$$
$$A^{-1} = A^T$$

A set of all orthogonal matrices is a group $O(n)$. We define the group operation as multiplication.

If we define:

$$SO(n) = \{A \in O(n) \mid \text{Det } A = +1\}$$

as that group, resulting from the transformation, whose determinants are equal to +1, it can be shown that a three-dimensional figure retains its "handedness" as a result of the operation (see Sections 2.2. and 2.5.) and the result can be defined as a rotation. If the Det $A = -1$ a three-dimensional figure reverses its "handedness" upon transformation, this result corresponding to a reflection.

We have a choice as to the number of dimensions allowed in the representation space E^n of a molecule. An E^2 space would allow some molecules to be chiral [*e.g.. (2a) – (2c)*] when they would not be so in E^3. However, since all E^1 and E^2 can be embedded into E^3, we use the E^3 space to describe chemical systems. Further, we will consider achirality as equivalent to $O(3)$ invariance.

The symmetric group S_n of n letters or symbols consists of the $n!$ mappings of a set of n letters on itself.

$$\left\{\begin{matrix} 1\ 2\ 3\ \ldots\ n \\ \downarrow\ \downarrow\ \downarrow\ \quad \downarrow \\ 1\ 2\ 3\ \ldots\ n \end{matrix}\right\} \quad \left\{\begin{matrix} 2\ 1\ 3\ \ldots\ n \\ \downarrow\ \downarrow\ \downarrow\ \quad \downarrow \\ 1\ 2\ 3\ \ldots\ n \end{matrix}\right\} \textit{ etc.}$$

These mappings are transformations from one arrangement of the numbers $1 \ldots n$ to another and are called permutations. The symmetric group S_n, the group of all permutations on n letters is of great general importance in mathematics and science. Permutations play a central role in this paper.

φ is an action, φ:
$g \times X \rightarrow X$, such that the transformation g (elements of the group G) on the set X reproduce the set X where g (all $g \in G$) acting on $x \equiv (gx)$ and $g[g'x] = [gg']x$. Each $g \in G$ is a bijection of X onto X. A family of such bijections is called a symmetry. A Cartesian product $(X_1 \times X_2 \times \ldots \times X_n)$ which is symmetrized with respect to the permutational transformation (permutation of the indices) of the group S_n is called the symmetrized Cartesian product of $X = SP^n X$.

$$SP^n X = \frac{(X_1 \times X_2 \times \cdots \times X_n)}{S_n}$$

2. Classification of Molecules

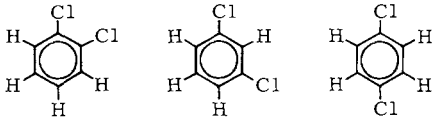
2.1. Isomers

An equivalence relation in a set divides that set into pairwise disjoint classes. The members of an equivalence class are "the same" with reference to the defining relation.

Equivalence relations are the basis for many useful classifications in chemistry whereby order is achieved. This order provides for the possibility of a systematic nomenclature for chemical systems. A clear example of the utility of a classification for chemical systems according to equivalence relations is the periodic system of elements.

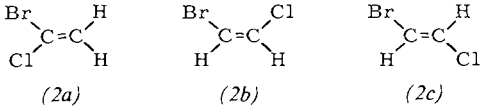
The set of all chemical compounds can be divided into those classes which have the same empirical formula, *i.e.*, the isomers. Those compounds classified according to the criterion of molecular skeletal similarity form a further class, *i.e.*, topologically similar compounds. We can now define the concept of *permutational isomers*, chemical compounds which have in common the same molecular skeleton and set of ligands, differing only by the distribution of the ligands on the skeletal positions.

Chemical constitution can be defined as a set of neighborhood relations between the atoms of a molecule [7]. This can be visualized in terms of bonds and bonded neighbors. Those permutational isomers which differ only by ligand permutations at constitutionally equivalent positions are the subclass of stereoisomers [8].



(1a) *(1b)* *(1c)*

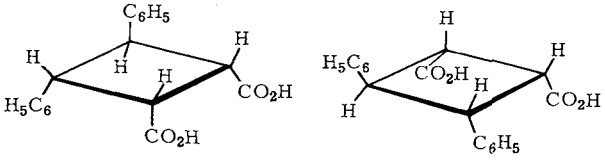
The three isomeric dichlorobenzenes *(1a)–(1c)* are permutational isomers having skeleton VI (see Section 2.4.2), but are not stereoisomers.



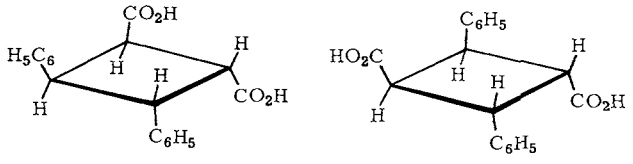
(2a) *(2b)* *(2c)*

[8] a) *E. L. Eliel:* The Stereochemistry of Carbon Compounds. McGraw-Hill, New York 1962; Stereochemie der Kohlenstoffverbindungen. Verlag Chemie, Weinheim 1966; b) *K. Mislow:* Introduction to Stereochemistry. Benjamin, New York 1965; Einführung in die Stereochemie. Verlag Chemie, Weinheim 1967.

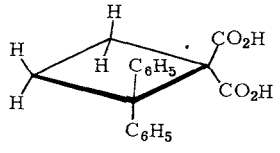
All the bromochloroethylenes *(2a)–(2c)* are permutational isomers because they have the same skeleton I, and they differ only by permutations of the ligand set. *(2a)* differs in chemical constitution from *(2b)* and *(2c)*, which are stereoisomers.



(3a) *(3b)*

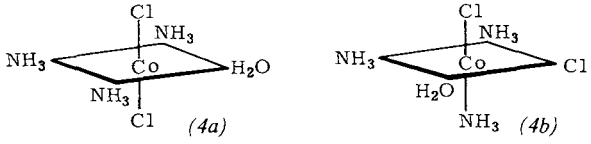


(3c) *(3d)*



(3e)

The isomers *(3a)*[$\equiv$*(3b)*], *(3c)–(3e)* are all permutational isomers; *(3a)* is identical with *(3b)* and can be brought into coincidence with *(3b)* by rotation and translation. Of these permutational isomers, the truxinic acids *(3a)* and *(3c)* are mutual stereoisomers, whereas α-truxillic acid [9] *(3d)* and the reference isomer *(3e)* (see Section 2.4.4.) differ in chemical constitution from the other species.



(4a) *(4b)*

The determination of whether *(4a)* and *(4b)* are stereoisomers or non-stereoisomeric permutational isomers is relevant only to some problems, and involves an arbitrary decision as to whether the two "axial" chloro ligands distort the O_h symmetry of the skeleton sufficiently to create a distinction between "axial" and "equatorial" skeletal positions [10]. If such a distortion occurred, the constitutional equivalence of the ligand positions would be destroyed, violating a precondition for *(4a)* and *(4b)* being stereoisomers.

The non-stereoisomeric permutational isomers arise from molecular skeletons whose equivalent skeletal positions become non-equivalent on attachment of a ligand. In fact, those skeletons with a symmetry that precludes the non-equivalence of skeletal positions regardless of the ligand

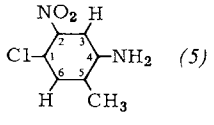
[9] *A. Mustafa*, Chem. Rev. *57*, 1 (1952).

[10] *E.g.: J. Lewis* and *R. G. Wilkins:* Modern Coordination Chemistry. Interscience, New York 1960; *F. A. Cotton* and *G. Wilkinson*, Advanced Inorganic Chemistry, Interscience, New York 1966; Anorganische Chemie. Verlag Chemie, Weinheim 1967; *C. K. Jørgensen:* Inorganic Complexes, Academic Press, New York 1963; *R. F. Gould*, Werner Centennial, A.C.S. Publ. Washington, D.C., 1967.

distribution (like XXVII) are rather the exception than the rule. Likewise, those skeletons with a symmetry (like VI) which allow only constitutionally different, non-stereoisomeric permutational isomers, are also in the minority. A consistent nomenclature for permutational isomers would simultaneously be a solution to the remaining unsolved problems of stereochemical nomenclature.

Any isomer nomenclature must be so devised that there is a well defined and clear correspondence between names and isomers. One must be able to determine, unequivocally and, if possible, easily, all constitutional and stereochemical features of a given isomer from its name, and be able to classify a given isomeric species according to unambiguous criteria. It would be a convenient feature of such a nomenclature if it contained both the (*R*),(*S*) [11] and the (*E*),(*Z*)-nomenclature [12] and related nomenclatures [13] as special cases (subsets).

The simplest type of unequivocal assignment of nomenclature names to molecules with a given skeleton and set of ligands is the kind of nomenclature which is used, for instance, for benzene derivatives. Thus an adequate description of a given molecule is achieved by numbering the skeletal positions and including the position numbers with the ligands (which substitute hydrogen) in the nomenclature name. For instance, *(5)* would be 1-chloro-2-nitro-4-amino-5-methylbenzene.



(5)

A variety of other names could be found for *(5)*, however, by the same procedure (if no further definitions were included in the nomenclature) depending upon which ligand occupied skeleton position number one, and whether the numbering was carried out clockwise or counterclockwise. However, no matter how the numbering is selected, the resulting name can always be used to reconstruct *(5)*. Such simple nomenclatural procedures cannot be applied to chiroids and molecules with highly symmetrical three-dimensional molecular skeletons, *e.g.*, XXII–XXIX, as no simple unequivocal correlations of molecules and names can be achieved.

2.2. Chirality Problems

In order to establish a basis for such a universal nomenclature some implications of chirality must be discussed. *Lord Kelvin* [14] introduced the concept of chirality as follows: "I call any geometrical figure or group of points *chiral* and say it has *chirality* if its image in a plane mirror ideally realized, cannot be brought to coincide with itself."

Achiral objects have symmetries which include reflections and improper rotations. Whether an object is chiral in Euclidean space or not depends also upon its dimensionality and the dimensions of the space in which it is observed (see Section 1.3.3.). For example, a two-dimensional chiral object, such as an idealized, suitably substituted ethylene [*e.g.*, *(2a)–(2c)*] is chiral in two dimensional space E^2, but achiral in three dimensional space, E^3.

Lord Kelvin's intuitive definition of chirality serves most purposes of stereochemistry well, although in certain exceptional cases (see below) it does not provide an unambiguous basis for the mathematical treatment of chirality problems.

The mathematical description of chirality is related to representations of orientation-preserving transformations by orthogonal matrices (see Section 1.3.3.).

Along with the objects classified as chiral and achiral, there is a class of objects called *amphichiral* [2k]. These are characterized by the fact that they are chiral according to *Kelvin*'s definition but achiral according to orientation-preserving transformations from $\boldsymbol{O}(n)$.

We call an object *K* amphichiral if there exists an orientation-preserving mapping, *h*, such that, h: $E^3 \rightarrow E^3$ with $h(K) = \rho(K)$, *i.e.*, *K* is amphichiral if there is an orientation-preserving homomorphism of E^3 taking *K* into its mirror image. For example, the twisted loop and the trefoil knot are amphichiral objects.



Amphichiral systems might be of significant importance in chemistry and biochemistry. The discovery of cyclic and catenated nucleic acid structures leads one to suspect that amphichiral superstructures of nucleic acids are responsible for neoplastic processes by interfering with the transfer of information on chirality.

We propose to make the distinction between chiroids and achiroids only with respect to the action of orthogonal matrices rather than the criterion of the superimposibility of an object and its mirror image by reflection in a plane mirror and rigid motions.

The set of operators $A = \{e =$ "leave the object as it is", $i =$ "convert the object into its mirror image"$\}$ with the combination law $\varphi =$ "apply the operation to the result of the preceding operation", forms a group $I = (A,\varphi)$. Converting the mirror image of an object into its mirror image leads back to the original object $(i \cdot i = e)$.

The inversion group *I* is isomorphic to, and is represented by, the group $V = (\{(+1),(-1)\}$, multiplication) (see below). With regard to achiral objects it is isomorphic to $(\{(+1)\}$, multiplication). In stereochemistry a chiroid χ_R with an (*R*)-configuration as the standard situation can produce the (*S*)-chiroid χ_S as the result of the operator *i* acting upon an (*R*)-chiroid.

$$\{\chi_S\} = i \cdot \{\chi_R\}$$

A chiroid with two elements of chirality χ and χ' occurs in four stereoisomeric forms.

$$\{\chi_R,\chi'_R\}\ \{\chi_S,\chi'_S\}\ \{\chi_R,\chi'_S\}\ \{\chi_S,\chi'_R\}$$

[11] *R. S. Cahn, C. K. Ingold,* and *V. Prelog,* Angew. Chem. *78,* 413 (1966); Angew. Chem. internat. Edit. *5,* 385 (1966), and preceding papers cited there.

[12] *J. E. Blackwood, C. L. Gladys, K. L. Loening, A. E. Petrarca,* and *J. E. Rush,* J. Amer. chem. Soc. *90,* 509 (1968).

[13] *I. Ugi,* Jahrb. 1964 Akad. Wiss., Vandenhoeck and Rupprecht, Göttingen 1965, p. 21; Z. Naturforsch. *20b,* 405 (1965); *I. Ugi, K. Offermann,* and *H. Herlinger,* Chimia (Aarau) *18,* 278 (1964).

[14] *Lord Kelvin,* Baltimore Lectures, 1884 and 1893. C. J. Clay and Sons, London 1904, pp. 436, 619.

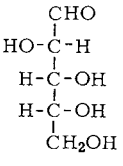
This class of stereoisomers is generated from $\{\chi_R, \chi'_R\}$ by the direct product group $I \times I'$ where I (see above) acts upon χ and I' acts upon χ'. The above set is isomorphic with

$$V \times V' = \{(+1)(+1)', (-1)(-1)', (+1)(-1)', (-1)(+1)'\}$$ and is ahomomorphism onto: $V = \{(+1), (-1)\}$.

This relation can be used for the classification of diastereoisomers [13].

The (*R*),(*S*)-nomenclature of chiroids with many elements of chirality essentially corresponds to a mapping of the direct products of the group I onto the group V or its direct products.

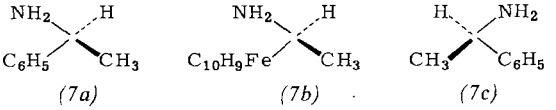
The nomenclatural designation (2(*S*),3(*R*),4(*R*),5)-tetrahydroxypentanal [8a] for D-arabinose *(6)* is based upon the direct product group $I_2 \times I_3 \times I_4$ and corresponds to $(-1)(+1)(+1)$. The classification of sugars into D- and L-sugars makes use of a mapping of the set of sugars into V rather than an ordered product of the V's.



(6)

The (*R*),(*S*)-nomenclature is currently accepted for chiral stereoisomers. It is far superior to the classical D,L-nomenclature [8] which is not based upon rigorous definitions. The (*R*),(*S*)-nomenclature was conceived in order to discriminate between enantiomers and to classify the absolute configurations of chiral molecules or elements of chirality unambiguously according to the criterion of either *homochirality* or *heterochirality*, concepts originated by *Lord Kelvin* and further refined by *Ruch* [15c] for chiroids of category *a* (see below).

Two chiral objects χ and χ' are termed homochiral if it is possible to define a criterion by which χ and χ' are similar, whereas, by the same criterion, χ' and $\bar{\chi}$, the antipode of χ, are dissimilar. If one finds, by the same criterion, that χ' and $\bar{\chi}$ are similar (and χ and χ' are not) $\bar{\chi}$ and χ' are heterochiral. As it is used here, the term "chiral" does not refer to the action of an orthogonal matrix. It is used only to discuss a suitably defined series of compounds in a manner some chemists find useful. In the following figure *(7a)* – *(7c)* the criteria for comparison is that three ligands must be identical and distributed in a like manner. As C_6H_5 and $C_{10}H_9Fe$ are different yet on equivalent skeletal positions, *(7a)* and *(7b)* are homochiral, whereas *(7c)* is heterochiral to *(7a)* and *(7b)*.



(7a) *(7b)* *(7c)*

[15] a) *E. Ruch, A. Schönhofer*, and *I. Ugi*, Theor. Chim. Acta *7*, 420 (1967); b) *E. Ruch* and *A. Schönhofer*, Theor. Chim. Acta *10*, 91 (1968); c) *E. Ruch*, Theor. Chim. Acta *11*, 183 (1968); d) *E. Ruch* and *A. Schönhofer*, Theor. Chim. Acta, in press; e) *E. Ruch*, personal communication; f) *E. Ruch, W. Hässelbarth*, and *B. Richter*, Theor. Chim. Acta, in press; see also *G. Polya*, Acta Math. *68*, 145 (1937); g) *E. Ruch*, Lectures at Zürich and Los Angeles 1969.

Accordingly, the classification of a chiral object with regard to homochirality is possible only by comparison with a chiral reference system.

It is possible to communicate the fact that some object is "right handed", only by making the statement that it is homochiral to some other comparable "right handed" object.

Despite its obvious merits, the (*R*),(*S*)-nomenclature is not the ultimate solution to the problem of stereochemical nomenclature for the following reasons:

First, it is limited to configurational assignments.

Second, in the case of molecules with complex molecular skeletons, its underlying definitions do not provide a basis for dealing with the molecule as an entity, but require consideration of the molecule by (tetrahedral) subunits and thus sometimes makes additional definitions necessary.

Third, and most serious, the (*R*),(*S*)-nomenclature is confined to chiroids of *class* ***a*** [15b,c], for chiroids of *class* ***b*** [15b,c] its definitions become meaningless unless they are arbitrarily extended. The (*R*),(*S*)-nomenclature does not therefore allow for the consequence of two different *chirality classes* ***a*** and ***b***. This nomenclature was conceived before *Ruch* [15] showed by the group theoretical analysis of chemical chirality that there are two different classes, ***a*** and ***b***, of chiroids.

A class of chiroids for which there is a non-arbitrary right-left classification is termed a class of category *a*, otherwise a class of category *b*. A molecule belongs to category *a* if and only if it has either only two skeletal positions, or if each skeletal plane of reflection contains $n-2$ skeletal positions, $n > 2$ being the number of skeletal positions [15e].

Let us now consider *Ruch*'s [15b,c] classification:

By definition, any transformation of a chiroid χ_a of *class* ***a*** into its antipode $\bar{\chi}_a$ must pass through some state in which all differences between χ_a and $\bar{\chi}_a$ vanish. This can be visualized in terms of a sharp achiral border without loopholes between χ_a and $\bar{\chi}_a$, such that all compounds on the χ_a-side of the border are homochiral to χ_a, and that beyond that achiral border any chiroid is homochiral to $\bar{\chi}_a$.

For chiroids of *class* ***b*** there is no such sharp border between the antipodes χ_b and $\bar{\chi}_b$ (*class* b_β) or the border has loopholes (*class* b_α). Accordingly, chiral molecules of *class* ***a*** are subject to classification by statements of homochirality, like right- and left-handedness or the D,L or (*R*),(*S*)-nomenclature, and chiroids of *class* ***b*** are not.

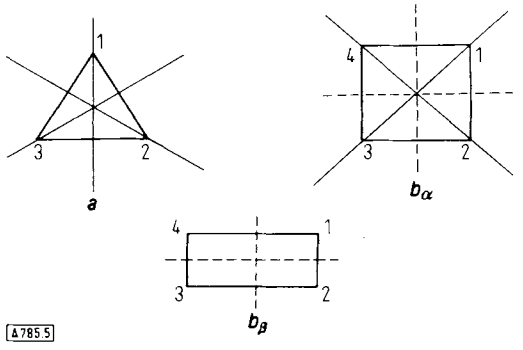
Let a chiral molecule be represented by an achiral skeleton with n ligand bearing positions and n ligands (groups) attached to the framework. Then, the following applies:

Chiroids of *class* ***a*** do not contain any skeletal planes of reflection or improper axes of rotation where more than two non-equivalent ligands are attached to skeletal positions not coincident with the stated fixes of symmetry. For these chiroids of *class* ***a*** there are no reflections or improper rotations of the skeletal symmetry group which exchange more than two non-equivalent ligands when the chiroid is transformed into its antipode. For the molecules in *class* ***a*** to become achiral, it is necessary and sufficient to remove or to make equal two non-equivalent ligands which do not

occupy skeletal positions not coinciding with skeletal planes of reflection or improper axes of rotation (see Section 1.3.3.).

For chiroids of *class* $\boldsymbol{b}_\beta$ there are only those skeletal planes of reflection or improper axes of rotation that allow more than two non-equivalent ligands to occupy skeletal positions outside any of these skeletal planes or improper axes of symmetry. It is not possible to transform a chiroid of *class* $\boldsymbol{b}_\beta$ into its mirror image by permuting only two differing ligands; more than two non-equivalent ligands must be exchanged in order to generate the antipode. More than two ligands must be removed or equalized in order to destroy chirality.

Chiroids of *class* $\boldsymbol{b}_\alpha$ have at least one skeletal plane of reflection or improper axis of symmetry of type $\boldsymbol{a}$ and at least one of type $\boldsymbol{b}_\beta$. This classification is illustrated by the two-dimensional examples shown below.



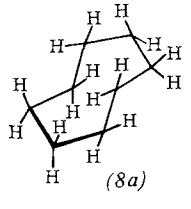
A785.5

Fig. 5. Reflection across the lines —— or ------ transforms the laminae into their mirror images. Two of the distinguishable vertices (, ..., 4 lie outside the lines ——, more than two lie outside the lines -------.

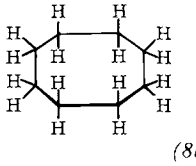
Class $\boldsymbol{b}$ contains various types of molecules. For some, the concept of handedness has no meaning. However, it is possible to dissect others into elements of chirality of *class* $\boldsymbol{a}$. For example, the cyclopropane (XI) and prismane derivatives (with D_{3h} skeleton and six ligands) can be dissected into tetrahedral elements of chirality which can be described in terms of the (*R*),(*S*)-nomenclature. Conversely, it is not possible to apply the (*R*),(*S*)-nomenclature meaningfully to a molecule whose skeleton consists of a central atom with valencies directed towards the vertices of a trigonal prism with six different ligands.

2.3. The Nerve and Beyond

Now the various types of mathematical structures can be combined to represent molecules in a detailed manner. We will describe a cyclooctane molecule *(8a)* first in topological terms.

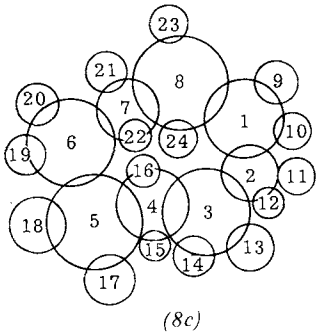


(8a)

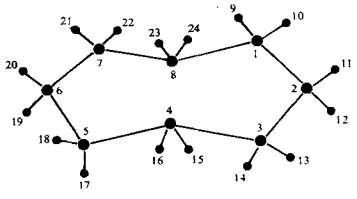


(8b)

Neighborhood relations provide the chemical constitution of cyclooctane. They are given by bonds and bonded neighbors and can be described by an indexed family of 24 intersecting sets, *e.g.* a family of open spheres *(8c)*. The *nerve* of this family *(8d)* represents the chemical constitution of cyclooctane.



(8c)



(8d)

No information beyond the neighborhood relations is included in the nerve of the molecule. All stereochemical features of a molecule are lost when it is represented by its nerve. Cyclooctane's behavior is that of a molecule possessing D_{8h} symmetry. This is usually described by stating that cyclooctane has a D_{8h} *time average symmetry*. While this notion serves some purposes well it is not at all well founded. Geometrical properties cannot be averaged like scalar properties. We will make use of the highest symmetry which a molecule or its skeleton can be imagined to attain within its given constraints. The constraints of a given molecule and its skeleton can depend upon the time scale inherent to the method of observation. Symmetrical molecules suffering distortion, as well as those having none of the symmetry described as time average symmetry in any of its vibrational, internal rotational or conformational states can all be represented without auxiliary hypotheses using the highest available symmetry concept.

The highest attainable D_{8h} symmetry of the cyclooctane molecule can be described by a permutation group. The indexed open spheres of *(8c)* are employed as the coordinates of the carbons and hydrogens of cyclooctane. Then the permutational transformation properties of the coordinate system represent not only the skeletal symmetry, considering the equivalence of the hydrogens, but the symmetry of the whole molecule. When the necessity arises to differentiate between the hydrogen atoms of the various molecular ligands in substituted cyclooctanes one must further define a mapping process. This mapping must correlate the various parts of the molecule with suitably chosen coordinates. The coordinates of the eight equivalent carbon atoms of cyclooctane are not needed for the description of the steric features of the molecule and its derivatives. Therefore, the partially symmetrized product, $\boldsymbol{SP^{D_{8h},16}}\ \boldsymbol{X}$, of sixteen indexed copies of one set is adequate as a coordinate system for the idealized D_{8h} skeleton of cyclooctane. The subgroup $\boldsymbol{H_{16}}$ of the symmetric group $\boldsymbol{S_{16}}$ is used as a partial symmetrizer of the product set $\{\boldsymbol{X_{16}} \times \boldsymbol{X_2} \times \ldots \times \boldsymbol{X_n}\}$. The indexed set $\{p_1, \ldots, p_{16}\}$ of points with disjoint neighborhoods, $p_i \in \boldsymbol{X_i}$, can be used as the set $\{\boldsymbol{X_1}, \boldsymbol{X_2}, \ldots, \boldsymbol{X_{16}}\}$. This is obtained from one point p_1 by sequentially applying the generators C_8 and σ_h to p_1 and assigning odd indices, $2s-1$ ($s = 1, \ldots, 8$), to the points on the orbit of C_8. We then reflect this set of points (Fig. 6a) across a plane parallel to and above the

plane of the paper. Now, assign the even indices $2s$ to σ_h mirror images of the points with $2s-1$ indices (Fig. 6b).

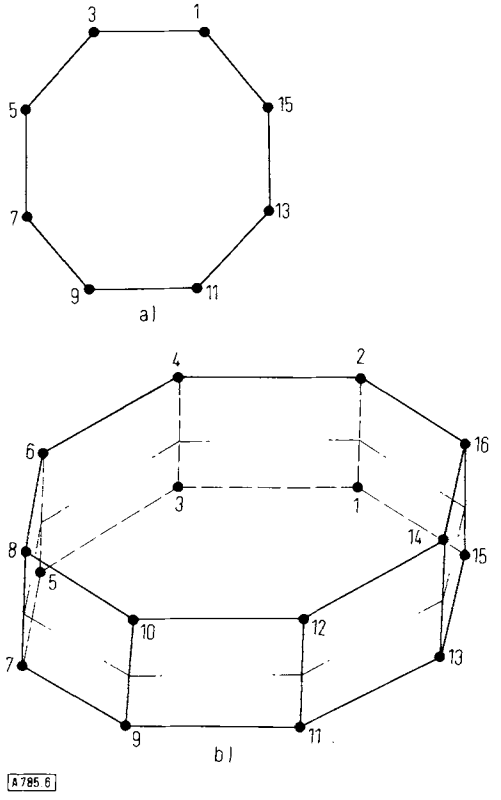


Fig. 6. Sequential application of the point group symmetry operations (generators) C_8 and σ_h to a point (odd indices $2s-1$ ($s = 1, \ldots, 8$) assigned to orbit of C_8).

We may now formally consider the carbon atoms. The carbon atom with the index one belongs to a distinguished point, the cross-section of the neighborhoods of those atoms to which the carbon is directly connected. Thus, the assignment is in accord with skeletal symmetry.

In principle, as is illustrated by Fig. 7, the simultaneous use of product sets and the descriptions of neighborhood relations by non-empty intersections of τ_1, τ_2, and τ_3 of $\prod_{1}^{3}\tau_i$ is possible. To accomplish this, sets must be used at different "levels" and symbolized by double indexing.

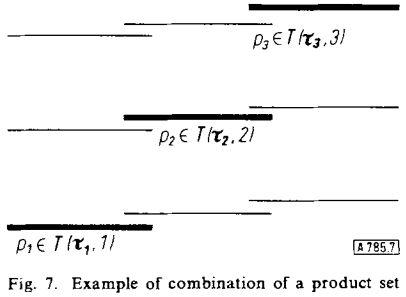


Fig. 7. Example of combination of a product set with the description of neighborhood relations by non-empty intersections.

A physical feeling for these operations can best be visualized by looking upon neighborhood relation operations as vertical projections and product topological and group theoretical operations as horizontal projections. This approach avoids violation of the product of sets definition by the intersections.

Representation of cyclooctanes substituted by a numbered set of sixteen distinguishable ligands $L = \{L_1, L_2, \ldots, L_{16}\}$ is achieved through the bijective mapping of the ligands on the skeleton and thus assigning the skeletal coordinate of each ligand. By using the partially symmetrized set of coordinates $SP^{D}{}_{8h,16}$ X the fact that some skeletal coordinates are symmetry equivalent is accounted for and one is allowed to select that one among the equivalent bijections which is the best according to some criterion. The latter may be defined as that mapping where the highest number of ligand and coordinate indices match.

$$\begin{array}{ll} L_i\colon & i = 1\ 2\ 3\ \ldots\ 16 \\ & \downarrow\ \downarrow\ \downarrow\ \ldots\ \downarrow \\ X_i\colon & i = 1\ 2\ 3\ \ldots\ 16 \end{array}$$

Since the ligands of molecules are not *per se* indexed, a procedure must be established for assigning the indices to the n ligands of a molecule. This produces, for example, a one to one mapping of a set of n ligands onto the numbers $1, 2, \ldots, n$ that we call the indices of the coordinates Y_l of the ligands such that $L_1 \in Y_1$, $L_2 \in Y_2$, $\ldots$ $L_l \in Y_l$ $\ldots$ $L_n \in Y_n$. This is equivalent to the statement that the set of ligands belongs to the product of the coordinates. We propose to assign the ligand coordinates l according to the sequence rule of *Cahn, Ingold,* and *Prelog* [11], which permits the ordering of a set of distinguishable ligands. The coordinate index $l = 1$ is assigned to the ligand with the highest sequential priority, $l = 2$ to the second highest priority ligand, ... and $l = n$ to the ligand with the lowest priority.

If there are several equivalent ligands then the corresponding index interval is assigned as illustrated by the following example:

Let L be the sequentially ordered set of ligands for a given molecule [like *(3a)*]. The coordinate indices are

L_i: HO_2C^-, HO_2C^-, $C_6H_5^-$, $C_6H_5^-$, H^-, H^-, H^-, H^-

Y_i: $[1 \leq 1 \leq 2]$ $[3 \leq 1 \leq 4]$ $[5 \leq 1 \leq 8]$

The equivalence of ligands (see the example above) is taken into account, just as the symmetry equivalence of skeletal positions is, by partially or fully symmetrizing the Cartesian product $\{Y_1 \times Y_2 \times \ldots \times Y_n\}$ of the ligand coordinates Y. The ligand coordinate spaces Y_i correspond to open intervals in a line of sequential points. This line of points represents the sequence of all ligands that can occur in permutational isomers. Sequential intervals are the open sets of the topology on the linear sequential manifold. The partially symmetrized Cartesian product.

$$SP^{m'n}Y = \frac{(Y_1 \times Y \times \ldots \times Y_n)}{H'_m}$$

refers to the subgroup H'_m of permutations of non-distinguishable ligands, a subgroup of S_n, and becomes equal to S_n, if all ligands are equals as in the case of cyclooctane.

The bijective mapping of the index set of the partially (or fully) symmetrized ligand coordinates Y_l onto the index set of partially (or fully) symmetrized skeletal coordinates X_s permits unequivocal classification of topological isomers and is introduced by us as the basis of a permutational nomenclature.

There is a bijective mapping from the set of these mappings onto the given class of isomers. According to *Ruch* and *Schönhofer* [15d] the total number of isomers in such a class

can be calculated from the number of double cosets of H_m and H_n in S_n [15d]. The use of the permutational nomenclature system is illustrated by the flow sheet shown in Fig. 8.

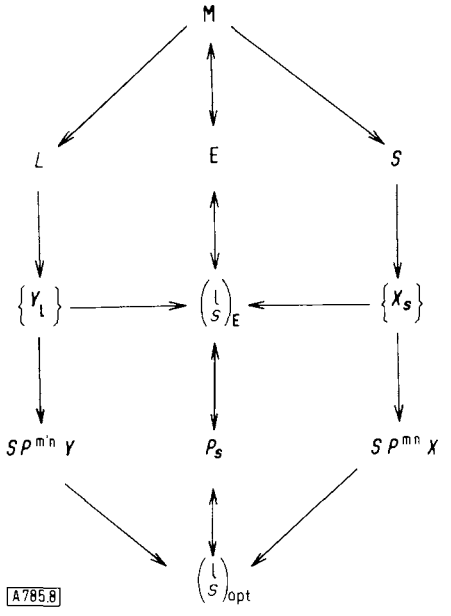


Fig. 8. Flow sheet for generation of the descriptor of permutation isomers.

Here, $L \leftarrow \mathbf{M} \rightarrow S$ symbolizes the division of a molecule into a skeleton and a set of ligands. Coordinate assignment and numbering is represented by $\{Y_l\}$ and $\{X_s\}$.

The n ligand and skeletal indices l and s of the set $\{Y_l\}$ and $\{X_s\}$ are correlated by mapping in a $(2 \times n)$ unit matrix, the $\binom{l}{s}_E$ matrix. We use the term matrix for any rectangular array of mathematical symbols. If these mappings are represented by permutations, this corresponds to the identity permutation e (see 2.4).

$$\binom{l}{s}_E = \begin{pmatrix} 1 & 2 & \ldots & n \\ 1 & 2 & \ldots & n \end{pmatrix}.$$

Among the $\binom{l}{s}$ matrices of equivalent mappings $SP^{m'n}Y \rightarrow SP^{mn}X$ that matrix $\binom{l}{s}_{opt}$ which is obtained from $\binom{l}{s}_E$ by the most simple s permutation, P_s, is chosen as the descriptor of a given molecule.

In the context of their solution of the Polya problem, *Ruch et al.* [15f,g] demonstrated that the number of distinguishable isomers of a given class of isomers corresponds to the number of double cosets PxG ($x \in S_n$); P and G are the subgroups which correspond to the skeletal symmetry of the skeleton with n positions and the permutation of equivalent ligands. The various isomers correspond to systems of representatives of the double cosets PxG. Therefore, a nomenclature system for permutational isomers can only be adequate and non-arbitrary if it corresponds to a system of the above double coset representatives.

Ruch et al. will soon report on a proof that the descriptions of the present paper (which are here derived according to a mapping formalism – which is closer to chemistry – rather than by a formalism that is in immediate relation to the double cosets) are indeed equivalent to a representation system of the PxG double cosets.

2.4. Describing Molecules by Permutations[16]

2.4.1. Descriptor

The permutational isomers are described by mapping the indexed set of ligands L_l onto the indexed set of permutational coordinates X_s, the equivalent of the molecular skeleton. This mapping is represented by a $(2 \times n)$ matrix notation using the $\binom{l}{s}$ matrices of the indices l and s. An effective nomenclature for permutational isomers results from this matrix representation. That permutational transformation, P_s, of the permutational coordinates s which generate the matrix $\binom{l}{s}_M$ of a given molecule **M** from the matrix $\binom{l}{s}_E$ of a reference molecule **E** according to

$$\binom{l}{s} = P_s \binom{l}{s}_E \qquad (1)$$

is called the descriptor of the molecule **M**. The descriptor is an unambiguous symbolism for the nomenclatural classification of the permutational isomers [16].

2.4.2. Skeleton

The permutational descriptors are based upon the following definitions:

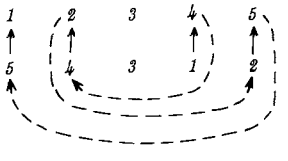
S I: A molecule **M** is represented by an achiral skeleton S_n with n ligand positions and a corresponding set of n ligands $L_1 \ldots . L_n$.

S II: A permutational coordinate system is introduced to represent the molecular skeleton, such that the permutational transformation properties of the coordinates correspond to the symmetries of the skeleton.

S III: A set of skeletal position numbers $s = 1, 2, 3, \ldots, n$ is assigned to the n skeletal positions of S_n by a convention which is defined for each type of skeleton, and is characteristic of the given class of permutational isomers according to the rules S I – S IX. The result is a standard skeleton (see I – XXIX) whose skeletal numbers correspond to the indices of the skeletal coordinates.

---

[16] The following may serve to illustrate permutations and descriptors: The permutation $P_s = (1425)$ represents the cycle $5 \leftarrow 2$ ($\downarrow$ $\uparrow$ and means 1 replaces 4 (or is the image of 4) and similarly, $1 \rightarrow 4$ $4 \rightarrow 2$, $2 \rightarrow 5$, $5 \rightarrow 1$. The ordered set $A = \{12345\}$ is transformed into and mapped onto $B = \{54312\}$ by the permutation $P_s = (1425)$. Given that permutation P_s, which represents the mapping of set A onto set B, is found from the matrix $\binom{A}{B} = \begin{Bmatrix} 12345 \\ 54312 \end{Bmatrix}$; following the arrows



gives the operator $P_s = (1425)$. When used as a descriptor, the operator $P_s = (1425)$ generates $\binom{1}{s} = \begin{Bmatrix} 12345 \\ 54312 \end{Bmatrix}$ from $\binom{1}{s}_E = \begin{Bmatrix} 12345 \\ 12345 \end{Bmatrix}$ according to $\binom{1}{s} = P_s \binom{1}{s}_E$. Now, the descriptor (1425) expresses the following mapping: Skeletal position 1 carries the ligand with the sequential number 4, position 4 carries ligand 2, position 2 carries ligand 5, and position 5 carries ligand 1; at position 3, unaffected by P_s, the ligand number 3 matches the skeletal number.

S IV: The skeletal numbers are assigned such that, whenever possible, the configurations of the reference isomers **E** of *class* ***a*** have the (*R*)-configuration (see XVII and XXVII).

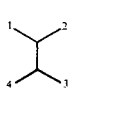
S V: If the observer looks along a principal C_n axis [2b] the assigned skeletal numbers increase in a clockwise manner.

S VI: If there are several C_n cycles, belonging to the same principal C_n-axis, the cycle which is closer to the observer has the lower numbers *s* (see XVI). The portion of the cycle with the lowest *s* lies within a plane that includes the principal axis and is the same for each one. If this is not possible, the lowest *s* lies in a clockwise direction, less than 90° from this plane.

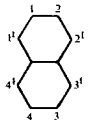
S VII: Pairs of skeletal positions which belong to the same atom have consecutive *s* (see XI).

S VIII: If there are several non-equivalent sets of symmetry equivalent skeletal positions, separate sets of skeletal position numbers $s = 1 \ldots\ldots n$, $s' = 1' \ldots\ldots n'$, $s'' = 1'' \ldots\ldots n''$, *etc.*, are assigned. Similarly separate sets of ligand numbers $1 = 1 \ldots\ldots n$, $1' = 1' \ldots\ldots n'$, $1'' = 1'' \ldots\ldots n''$ are associated with these.

S IX: Skeletal positions and ligands on a principal symmetry axis of the skeleton are described by primed or multiply primed 1 and *s* (see VII).



I (D_{2h})



II (D_{2h})



III (D_{3h})



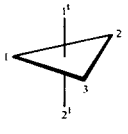
IV (D_{4h})



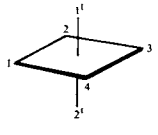
V (D_{5h})



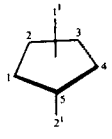
VI (D_{6h})



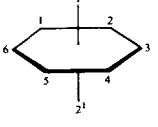
VII (D_{3h})



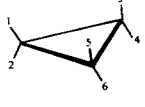
VIII (D_{4h})



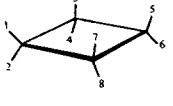
IX (D_{5h})



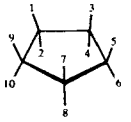
X (D_{6h})



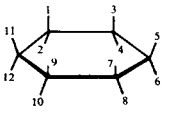
XI (D_{3h})



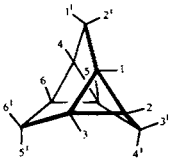
XII (D_{4h})



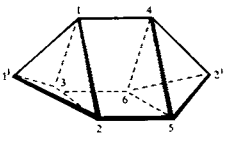
XIII (D_{5h})



XIV (D_{6h})



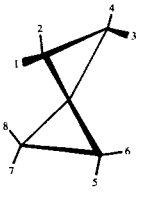
XV (D_{3h})



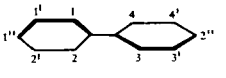
XVI (D_{3h})



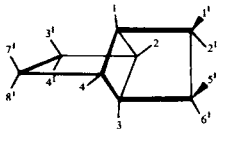
XVII (D_{2h})



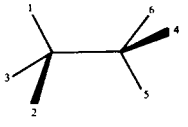
XVIII (D_{2h})



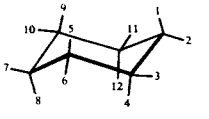
XIX (D_{2d})



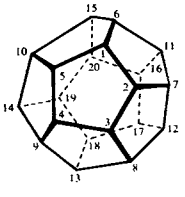
XX (D_{2d})



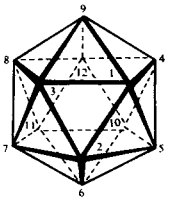
XXI (D_{3d})



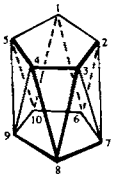
XXII (D_{3d})



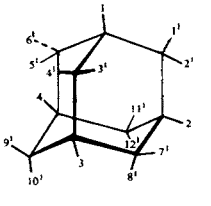
XXIII (Y)



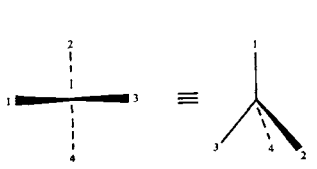
XXIV (Y)



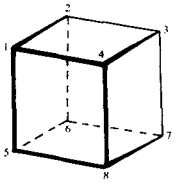
XXV (D_{5d})



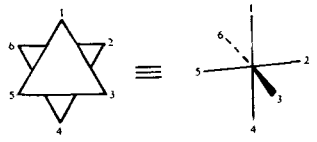
XXVI (T_d)



XXVII (T_d)



XXVIII (O_h)



XXIX (O_h)

2.4.3. Ligands

L I: A set of ligand numbers $l = 1, 2, 3, \ldots n$ is assigned to the ligands $L_1 \ldots L_n$ of **M** according to the *sequence rule* [8,11], in the order of the sequential priorities of the ligands. The number 1 is assigned to the ligand which has the highest sequential priority and n to the ligand with the lowest sequential priority [11].

L II: If there are n_i ligands ($L_i = L_{i+1} = L_{i+2} \ldots = L_{i+n_i-1}$) of the same kind in the set, they are given the corresponding n_i ligand numbers $l = i, i+1, \ldots, i+n_i-1$.

2.4.4. Reference Isomer

E I: The reference isomer **E** is that permutation isomer in which the ligands $L_1 \ldots L_n$ of **M** are attached to the positions of the standard skeleton (see I–XXIX) so that the ligand numbers l and the skeletal position numbers *s* match. We represent this mapping by the *unit matrix* $\binom{l}{s}_E$ of the set of isomers.

$$\binom{l}{s}_E = \begin{Bmatrix} 1\ 2\ 3\ 4 \ldots\ldots n \\ 1\ 2\ 3\ 4 \ldots\ldots n \end{Bmatrix}$$

E II: The reference matrix with more than one set of equivalent skeletal positions is that matrix in which the ligand numbers l, l′, l″, *etc.* of all sets are superimposed upon all corresponding skeletal numbers *s*, *s′*, *s″*, *etc.*

$$\binom{l}{s}_E = \begin{Bmatrix} 1 \ldots\ldots n\ 1' \ldots\ldots n'\ 1'' \ldots\ldots n'' \ldots\ldots \\ 1 \ldots\ldots n\ 1' \ldots\ldots n'\ 1'' \ldots\ldots n'' \ldots\ldots \end{Bmatrix}$$

The mapping of $l \rightarrow s$ of a set of n indexed ligands onto an indexed set of n skeletal coordinates can be particularly well represented by $(2 \times n)$ matrices. An $(n \times n)$ matrix will also represent this mapping. In the latter case, all matrix elements a_{sl} are *zero* except for a *one* in each row and column. $a_{sl} = 1$ expresses that *s* and l belong together, and $a_{sl} = 0$ means *s* and l are not mapped onto each other. The $(n \times n)$ matrices of the reference isomers are unit matrices E_n.

$$E_n = \begin{array}{c|c} \begin{matrix} 1 & 2 & 3 & 4 & \ldots & n \end{matrix} & l/s \\ \hline \begin{pmatrix} 1 & 0 & 0 & 0 & \ldots & 0 \\ 0 & 1 & 0 & 0 & \ldots & 0 \\ 0 & 0 & 1 & 0 & \ldots & 0 \\ 0 & 0 & 0 & 1 & \ldots & 0 \\ \vdots & & & & & \vdots \\ 0 & 0 & 0 & 0 & \ldots & 1 \end{pmatrix} & \begin{matrix} 1 \\ 2 \\ 3 \\ 4 \\ \vdots \\ n \end{matrix} \end{array}$$

2.4.5. Optimum Projection

A molecule **M** can generally be described by many equivalent mappings (see Section 2.4.7.) in which the l and *s* belong together in different ways. This is due to the equivalence of some skeletal positions ***S*** (topological coordinates) and, in certain cases, the equivalence of some of the ligands $L_1 \ldots L_n$. Some of these different mappings correspond to different spatial orientations of **M**. These different arrangements can be compared to the different *Fischer projections* [8a] of a molecule. For the comparison of **M** with its reference isomer **E** the optimum mapping, $\mathbf{M}_{opt}$ of **M** is chosen.

O I: The optimum mapping $\mathbf{M}_{opt}$ is that mapping of **M** whose matrix $\binom{l}{s}_{opt}$ is most similar to $\binom{l}{s}_E$.

O II: We consider that mapping of **M** to be most similar to $\binom{l}{s}_E$ whose matrix $\binom{l}{s}_{opt}$ can be transformed into $\binom{l}{s}_E$ by the simplest permutation of the skeletal numbers, *s*. The *s*-permutations correspond to permutations of the rows of the $(n \times n)$ matrices. The simplest permutation is the permutation which involves the smallest number of *s*, if possible in small cycles. Accordingly, $\mathbf{M}_{opt}$ is that arrangement of **M** in whose matrix there is a maximum set of superimposable ligand and skeletal numbers $l = s$.

In terms of an $(n \times n)$ matrix representation the optimum arrangement is that one in which as many *ones* as possible are matrix elements of the main diagonal, and those *ones* which are off the main diagonal can be brought into it by the simplest permutation of rows.

O III: If there is more than one such matrix the alphanumerically lowest set of non-matching l and *s* is preferred. If this is not sufficient to identify the optimum matrix $\binom{l}{s}_{opt}$, then that matrix is preferred for which the difference $l - s$ is the smallest. This corresponds to a $(n \times n)$ matrix where the diagonal zeros are as close to the upper left corner of the matrix as possible.

O IV: The optimum matrix $\binom{l}{s}_{opt}$ of an isomer with non-equivalent sets of equivalent skeletal positions is that matrix which is generated from $\binom{l}{s}_E$ by the simplest, alphanumerically lowest permutation of the unprimed *s*.

If **M** does not happen incidentally to be given in its optimum arrangement, its matrix $\binom{l}{s}_{opt}$ can be determined as follows:

O V: First, the ligand and skeleton numbers, l and *s* are determined according to L I – S IX for the particular arrangement of **M**, and are then represented by the $\binom{l}{s}$ matrix.

O VI: If **M** contains sets of equal ligands (like $n_i \geq 2$ equal ligands $L_i = L_{i+1} \ldots + L_{i+n_i-1}$), then, at first, only a corresponding range $i \leq l \leq i + n_i$ of the ligand numbers is "reserved" for these ligands:

$$\begin{matrix} i,\ i+1 \ldots\ldots i+n_{i-1} \\ L_i,\ L_{i+1} \ldots\ldots L_{i+n_i-1} \end{matrix}$$

In the corresponding $(n \times n)$ representation the matrix element $a_{sl} = x = \{^1_0$ is used for $i \leq l \leq i + n_{i-1}$ if the skeletal position *s* carries one of the equal ligands $L_i = L_{i+n_i-1}$.

O VII: The ligand and skeleton numbers, l and *s* of **M** are adjusted to an optimum matrix, $\binom{l}{s}_{opt}$ by permuting

the skeletal numbers s in the $\binom{l}{s}$ matrix or the rows in the (n × n) matrix. Only those permutations of s are permitted which correspond to transformations of the permutational coordinates into equivalent coordinates, *i.e.*, permutations which correspond to the rotational symmetry operations (of the subgroup $\boldsymbol{H}$) of the skeletal symmetry group $\boldsymbol{G}$.

O VIII: If not all of the ligands $L_1 \ldots L_n$ are different, *i.e.*, if there is at least one set of $n_i \geq 2$ of equal ligands ($L_i = L_{i+1} \ldots = L_{i+n_i-1}$), and some of the ligand numbers l had only been pre-assigned by O VI (for final assignment after establishing $\binom{l}{s}_{pre}$), a *pre-optimum* matrix $\binom{l}{s}_{pre}$ is obtained by applying O VII. The pre-optimum matrix $\binom{l}{s}_{pre}$ is transformed into $\binom{l}{s}_{opt}$ by assigning the n_i individual numbers ($i \leq l \leq n_i$) of the ligands $L_i \ldots L_j \ldots L_{i+n_i-1}$ in such a manner that as many as possible of them match the skeletal numbers of $\binom{l}{s}_{pre}$. In the (n × n) representations this is done by simply replacing that x in each row which is on the main diagonal or that is permutationally "closest" to it by a one, and all other x's by zero.

2.4.6. Assigning Descriptors

The conversion of the reference matrix $\binom{l}{s}_E$ (see Section 2.4.4.) into the $\binom{l}{s}$-matrix of a given permutational isomer **M** is given by a permutation $\boldsymbol{P_s}$, the *descriptor* of **M**, according to equation (1),

$$\text{with } \boldsymbol{P_s} = (\ldots n_i\ 1\ n_1 \ldots n_j\ 2\ n_2 \ldots n_k\ 3\ n_3 \ldots n\ n_n) \qquad (2)$$

$$\text{and } \binom{l}{s} = \begin{Bmatrix} n_1 & n_2 & n_3 \ldots 1 & \ldots 2 & \ldots 3 & \ldots n_n \\ 1 & 2 & 3 \ldots n_i \ldots n_j \ldots n_k \ldots n \end{Bmatrix} \qquad (3)$$

We propose to use the *descriptor* $\boldsymbol{P_s}$ of **M** as the nomenclature name of the isomer **M**, because the set of permutational isomers is in an unequivocal relation to the set of these operators $\boldsymbol{P_s}$. The operator $\boldsymbol{P_s}$ gives unequivocal instructions as to how to construct its corresponding isomer from a given molecular skeleton $\boldsymbol{S_n}$ (see I–XXIX) and a set of ligands $L_1 \ldots L_n$. The identity operator $\boldsymbol{P_s} = (e)$ represents the reference isomer **E**, according to $(e)\binom{l}{s}_E = \binom{l}{s}_E$.

The set of descriptors of a set of isomers is not a group, but the set of permutations which interconvert all the isomers is a group $\boldsymbol{G}$. Those permutations which interconvert the stereoisomers among the permutational isomers, belong to a subgroup of $\boldsymbol{G}$.

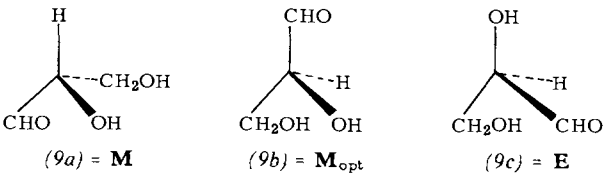
2.4.7. Examples

2.4.7.1. Simple Skeletons

One might infer from the preceeding definitions that use of this nomenclature involves lengthy and complicated operations. This is however, not the case, as one can readily demonstrate with the examples of Section 2.4.7. Any systematic nomenclature which appears less complicated is bound to contain arbitrary rules and oversimplifications which will severely limit its generality and accuracy (see Section 2.3 and footnotes [15d–15g]).

Example 1

The spatial arrangement of *(9)*, ($s = 1, \ldots, 4$, see XXVII, $l = 1, \ldots, 4$ with OH = 1, CHO = 2, CH_2OH = 3, and H = 4) is represented by $\binom{l}{s}_{(9a)}$ which is converted into $\binom{l}{s}_{(9b)}$ by the s-permutation *(1 3 4)* or the equivalent l-permutation (1 4 3) [16].



(9a) = **M** *(9b)* = $\mathbf{M}_{opt}$ *(9c)* = **E**

$$\left\langle \tfrac{1}{s} \right\rangle_{(9a)} = \begin{Bmatrix} 4 & 1 & 2 & 3 \\ 1 & 2 & 3 & 4 \end{Bmatrix} \qquad \left\langle \tfrac{1}{s} \right\rangle_{(9c)} = \begin{Bmatrix} 1 & 2 & 3 & 4 \\ 1 & 2 & 3 & 4 \end{Bmatrix}$$

$$(1\ 3\ 4)\ \left\langle \tfrac{1}{s} \right\rangle_{(9a)} = \left\langle \tfrac{1}{s} \right\rangle_{(9b)} = \begin{Bmatrix} 4 & 1 & 2 & 3 \\ 4 & 2 & 1 & 3 \end{Bmatrix} = (1\ 2)\ \left\langle \tfrac{1}{s} \right\rangle_{(9c)}$$

oder:

$$(1\ 3\ 4) \begin{bmatrix} 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \end{bmatrix}_{(9a)} = \begin{bmatrix} 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}_{(9b)} = (1\ 2) \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}_{(9c)} = (1\ 2)\ \boldsymbol{E_4}$$

The l-permutation (1 4 3) corresponds to a counterclockwise 120° rotation (C_3) of the ligands, L_1, L_3, L_4.

The permutation *(1 2)* converts *(9c)* into *(9b)* and is therefore the descriptor of *(9b)* [≡*(9a)*]. The steric formula of *(9b)* is reconstructed from the descriptor *(1 2)* as follows: The ligands OH, CHO, CH_2OH, and H are written in this sequence. When these ligands are attached to the *(1 2)*-transform of the standard framework in their sequential order, OH → 2, CHO → 1, CH_2OH → 4, the formula *(9b)* results.

The matrix

$$\begin{matrix} \beta \\ \alpha \\ \gamma \end{matrix} \left| \begin{Bmatrix} 4 & \mathbf{1} & \mathbf{2} & 3 \\ 1 & 2 & 3 & 4 \\ 4 & \mathbf{2} & \mathbf{1} & 3 \end{Bmatrix} \right| \left\langle \tfrac{1}{s} \right\rangle_{(9b)} \equiv (1\ 2)$$

contains an abbreviated formalism for deriving the descriptor *(1 2)* for *(9a)*. The rows are written in the order α, β, γ. The α-row contains the s in their natural order. The sequential numbers of the ligands are mapped upon the numbers of the skeletal positions to which the individual ligands are attached (row β). The γ-row is obtained from the α-row by the permutation *(1 3 4)*; this permutation (which corresponds to a 120° rotation around *2*) brings 3 and 4 into coincidence with *3* and *4*. The β- and γ-rows correspond to $\binom{l}{s}_{opt}$ which is transformed into $\binom{l}{s}_E$ by the permutation *(1 2)*.

The descriptor *(1 2)* is obtained by permuting row γ such that it matches row β. Since the pairs 3–*3* and 4–*4* match already, only *1* and *2* must be permuted in order to transfer those mappings 1–*2*, 2–*1* into 1–*1*, 2–*2*.

Example 2 (see XII) [9]

The molecule of *(3a)* (=**M**) contains three sets of equivalent ligands for which the corresponding intervals of l are "reserved" (*i.e.*, CO_2H = 1,2; C_6H_5 = 3,4; H = 5–8), according to Section 2.4.3. Then, if {l} is mapped onto {s} (see above) the pre-optimum matrix $\binom{l}{s}_{pre}$ (see Section 2.4.5) is generated by the permutation *(1 3 5 7) (2 4 6 8)* which represents a 90° rotation of the skeleton. A comparison of the s in γ, and the l in β make the assignments of all the l except 5 and 8 obvious. The aim is simply to match as many l and s as possible. The assignment of 5 and 8 is not so simple. Since an optimum assignment of an isomer should be, whenever possible, that assignment which leads to the reference isomer *via* the most simple permutation of s, 8 is assigned to *1* and 5 to *3* so that these interchanges may be made directly. Then, the $\binom{l}{s}_{opt}$ is $\binom{6}{7}$.

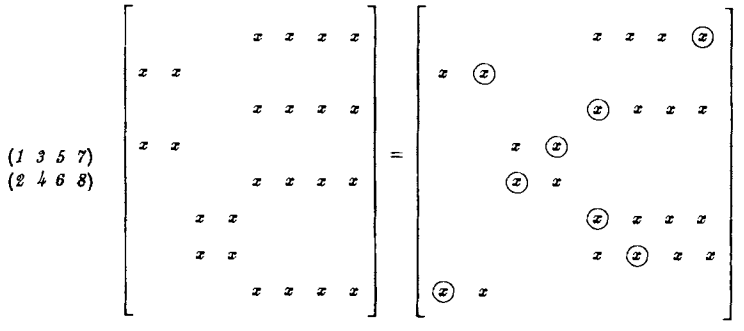
δ	7	**1**	**8**	2	**5**	4	**3**	6
β	5-8	1, 2	5-8	1, 2	5-8	3, 4	3, 4	5-8
α	*1*	*2*	*3*	*4*	*6*	*6*	*7*	*8*
γ	*7*	*8*	*1*	*2*	*3*	*4*	*5*	*6*

$\left\{\begin{matrix}\delta\\ \gamma\end{matrix}\right\} \equiv \left\{\begin{matrix}1\\ s\end{matrix}\right\} \equiv (1\,8)\,(3\,5)$

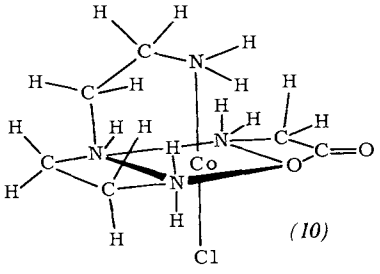
The only non-matching ($^{\delta}_{\gamma}$) mappings are $1-8$, $8-1$, and $3-5$, $5-3$. By this nomenclature *(3a)* is thus *(1 8)(3 5)*-dicarboxy-diphenylcyclobutane.

The (8 × 8) representation for this is as follows (see XII) (those matrix elements which are zero are left out; those *x* which become one are encircled):

(1 3 5 7)
(2 4 6 8)



$\equiv (1\,8)\,(3\,5)\,E_8$



(10)

Example 3 (see XII)

The steric formulas *(3c)* and *(3d)* of the *(1 7)(3 5)*- and *(1 5)(3 7)*-dicarboxy-diphenyl-cyclobutanes are derived from the *descriptors* as follows:

The permutations (1 7)(3 5) and (1 5)(3 7) of the ligands 1 (CO_2H) and 7 (H) as well as 3 (C_6H_5) and 5 (H) of the reference isomer *(3e)* generate *(3c)* and *(3d)*. In this case the l- and the *s*-permutations have the same effect.

For comparison, try naming the truxinic acids *(3c)* and *(3d)* by any other nomenclature, and then reconstruct their steric formulas!

Example 4

The steric formula *(4a)* of the *(2 4)*-dichloro-aquo-triammino-cobalt(III) ion is obtained by first writing down the ligands in sequential order (Cl = 1,2; H_2O = 3; NH_3 = 4,5,6) and then attaching them to the *(2 4)*-transform of the skeleton XXIX to form *(4a)*. The reference isomer is *(4b)*.

Example 5

For the purpose of assigning ligand numbers, the coordinating moieties of the multidentate ligands of *(10)* are treated as separate ligands.

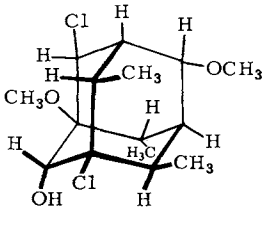
Accordingly, the ligand numbers of *(10)* are,

Cl	$^{\ominus}O_2C\text{-}CH_2\text{-}NH_2$			$NH(CH_2CH_2NH_2)_2$	
1	2		3	4	5,6

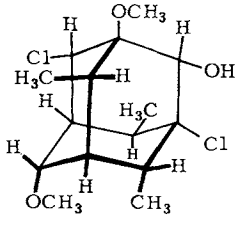
δ	**5**	3	2	1	6	**4**	$\equiv \left\{\begin{matrix}1\\ s\end{matrix}\right\}_{opt}$
β	5,6	3	2	1	5,6	4	
α	*1*	*2*	*3*	*4*	*5*	*6*	
γ	*4*	*3*	*2*	*1*	*6*	*5*	

and the descriptor of the chiral complex *(10)* is *(4 5)*-chloro-aminoacetato-diethylenetriamine-cobalt.

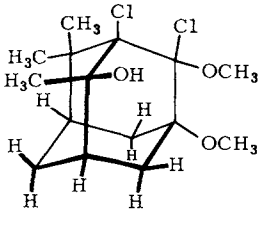
Example 6



(11a) = **M**



(11b) = $\mathbf{M}_{opt}$



(11c) = **E**

δ	4	3	**1**	**2**	9'	**2'**	**5**	12'	**11'**	**1'**	**6'**	7'	**8'**	**3'**	**10'**	**4'**
β	3,4	3,4	1	2	7'-12'	2'	4'-6'	7'-12'	7'-12'	1'	4'-6'	7'-12'	7'-12'	3'	7'-12'	4'-6'
α	*1*	*2*	*3*	*4*	*1'*	*2'*	*3'*	*4'*	*5'*	*6'*	*7'*	*8'*	*9'*	*10'*	*11'*	*12'*
γ	*4*	*3*	*2*	*1*	*9'*	*10'*	*11'*	*12'*	*6'*	*5'*	*8'*	*7'*	*1'*	*2'*	*3'*	4'

(7' 8')

The unprimed and primed skeletal numbers of XXVI are arranged in one line (α), and the (assigned or preassigned) sequential numbers of the ligands (1: Cl; 2: OCH_3; 3,4: H; 1': Cl;

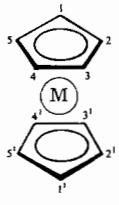
2′: OCH_3; 3′: OH; 4′–6′: CH_3; 7′–12′: H) are paired with their positions (β). The unprimed part of the matrix is optimized by a permutation which corresponds to a C_2-rotation [≡(7′ 8′)]. The pre-optimal matrix is converted into the optimal matrix (δ) by assigning the final ligand numbers l. The upper and the lower rows are the rows of $\binom{l}{s}_{opt}$ of *(11b)*. The permutation *(12)* *(1′ 8′ 6′ 11′ 5′) (2′ 3′ 10′)* is therefore the descriptor of *(11a)* ≡ *(11b)*, a chiroid of *class b*. Admittedly, it involves some work to find the descriptor of *(11a)*, but it takes, even in this complicated case, very little effort to reconstruct *(11b)* [≡*(11a)* = **M**] from its descriptor and the reference isomer *(11)* (≡**E**). The attempt to treat a compound like *(11a)* by any other nomenclature would lead to a rather frustrating experience.

2.4.7.2. Composite Skeletons

There are molecules whose skeletons have internal rotational degrees of freedom. These skeletons can be treated as if they were combinations of independent simpler skeletons.

Example 7

The metallocenes [17a] with their internal rotation are considered to be a combination of two C_{5v} skeletons (V).

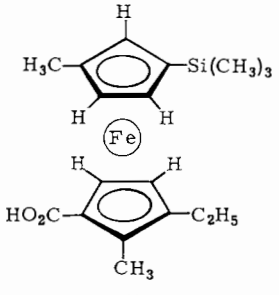


(12)

In the case of permutational isomers with these composite skeletons containing independent equivalent parts, the unprimed skeletal numbers *s* are assigned to that moiety which carries the greatest number of different ligands.

The assignment of the skeletal numbers *s* is done as shown in formula *(12) i.e.*, the metal is coordinated to those sides of the rings from which the skeletal numbers appear to be numbered in a counter-clockwise sequence. This definition is intended to have general validity for metal complexes which contain symmetrical subskeletons whose skeletal positions lie in a plane or whose idealized representations lie in a plane.

Example 8



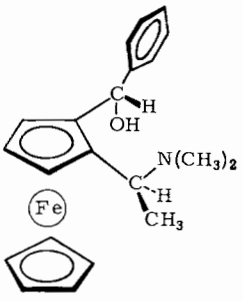
δ	3′	**1′**	5′	**4′**	2′	≡(1′ 4′)
β	3′-5′	1′	3′-5′	3′-5′	2′	
α	*1′*	*2′*	*3′*	*4′*	*5′*	
γ	*3′*	***4′***	*5′*	***1′***	*2′*	
β	**3**	**2**	4,5	4,5	1	≡(2 3)
α	*1*	*2*	*3*	*4*	*5*	
γ	***2***	***3***	*4*	*5*	*1*	

(13)

The primed l and *s* are assigned to the upper ring which has three equal ligands (H). Both rings are represented by their skeletal number *s* and *s′* (α), and the ligand numbers l are assigned and the l′ are preassigned to their corresponding *s*- and *s′* (β). Then the optimum matrices of *(13)* $\binom{l}{s}_{opt}\binom{l'}{s'}_{opt}$ are generated (*via* the pre-optimum of $\binom{l'}{s'}_{pre}$) by cyclic permutations of the *s* and *s′* (γ). The resulting descriptor of *(13)* is *(23)(1′ 4′)*.

[17] a) *K. Schlögl*, Top. in Stereochem. *1*, 39 (1967); b) *D. Marquarding, H. Klusacek, G. Gokel, P. Hoffmann*, and *I. Ugi*, Angew. Chem. *82*, 360 (1970); Angew. Chem. internat. Edit. *9*, 371 (1970).

Example 9



(14)

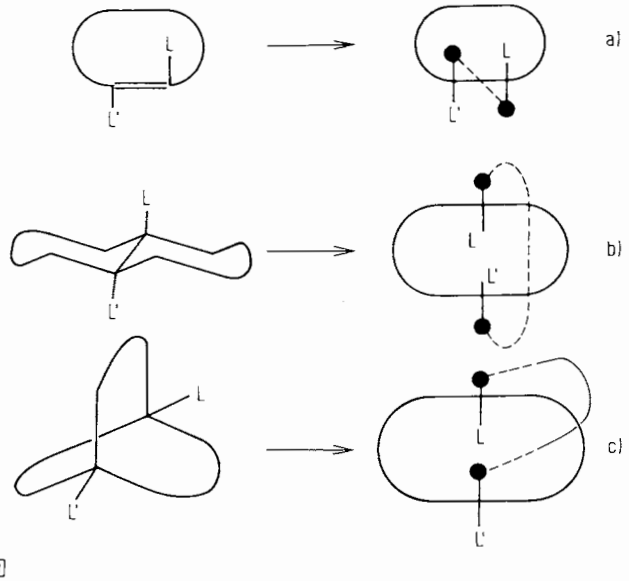
β	1	2	3-5	3-5	3-5	≡ (e)
α	*1*	*2*	*3*	*4*	*5*	
β	3*	**1***	4*	**2***		≡ (1 2)*
α	*1**	*2**	*3**	*4**		
γ	*3**	***2****	*4**	*1**		
β	**2****	4**	**1****	3**		≡ (1 2)**
α	*1***	*2***	*3***	*4***		
γ	*1***	*4***	***2*****	*3***		

In example 9, chiral side chains are attached to the ferrocene system. In order to describe the permutation of the ligands of those side chains in the description of the whole molecule and in order to differentiate that part of the descriptor which belongs to the side chain, we used starred ligand numbers and starred skeletal numbers for the side chain. If there is more than one side chain which belongs to the system, we use double starred ligands and skeleton numbers. The priorities follow the sequence rule. Accordingly, in *(14)*, the unstarred ligands belong to the ferrocene skeleton; l, *s* with one star belong to the benzyl alcohol group and those l and *s* which are doubly starred belong to the dimethylamino group.

According to the usual procedure, we find the descriptor to be (cf. example 1) *(e) (1 2)* (1 2)***. This is equivalent to the designations which have been used in the past, and corresponds to *(S)(S)(R)* [17b].

2.4.7.3. The Use of Nil

Cyclic molecules which contain multiple bonds, annellations, or bridges can be included in the present concept of permutational nomenclature by dissecting bonds and representing the resulting free valencies by *nils* (= ↑). By this dissection procedure (see Fig. 9), a cycloalkane derivative results with a D_{nh} skeleton which carries 2 z nils if z bonds were dissected. The positions of the nils are determined by the stereochemistry of the dissected molecule.



A 785.9

Fig. 9. Formal dissection of cyclic and polycyclic compounds with multiple bonds (a) or bridges (b, c), the resulting free valencies being represented by nils.

Whether a given skeletal position number of a D_{nh} (cycloalkane) skeletal representation is odd or even is usually obvious. In complicated cases, the solution is obtained unequivocally as shown in Fig. 10.

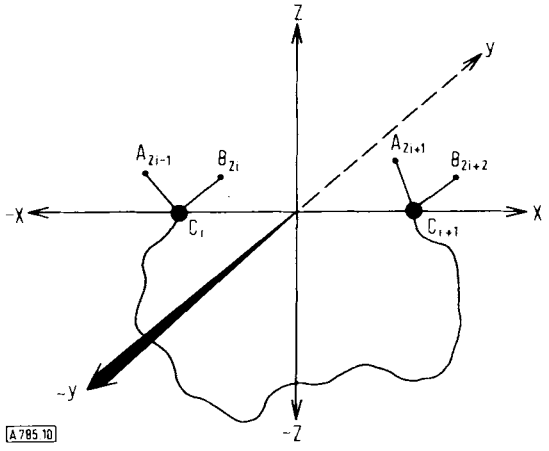


Fig. 10. Unequivocal assignment of skeletal position numbers to a D_{nh} skeleton.

An idealized Cartesian coordinate system is drawn so that two neighboring members, C_i and C_{i+1} of a ring belong to the $-x$ axis and the $+x$ axis. The ring belongs to the space with $y \leq 0$. Ligand positions A_{2i-1} and B_{2i+2} belong to $y \geq 0$. A_{2i-1} and A_{2i+1} have odd s (are above the clockwise ring) B_{2i} and B_{2i+2} have even s (are below) if

$A_{2i-1}, B_{2i} : z_{2i-1} : y_{2i-1} > z_{2i} : y_{2i}$
$A_{2i+1}, B_{2i+2} : z_{2i+1} : y_{2i+1} > z_{2i+2} : y_{2i+2}$

The descriptors of unsaturated and/or polycyclic compounds are assigned according to these definitions. Whenever the stereochemistry is unknown or purposely neglected, the topological coordinates of the nils are chosen such that the most simple, alphanumerically lowest descriptor results.

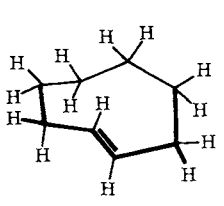
a) *Multiple and Transannular Bonds*

For unsaturated compounds and a wide variety of polycyclic compounds the permutational nomenclature in combination with the concept of nils provides a satisfactory solution to the nomenclature problem, even if chiral skeletons are involved.

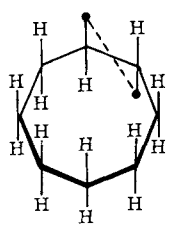
The bonds which are considered to be formed from the nils are designated by attaching the suffixes *ene*, *yne*, and *con*, respectively, to the name of M for double and triple bonds and transannular connections and, in brackets ⟨⟩, the numbers s of the skeletal positions in $\mathbf{M}'_{opt}$ which are connected by these bonds.

Example 10 [18]

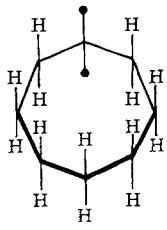
The chiral *trans*-cyclooctane *(15a)* is, for descriptor purposes, considered as a cyclooctane (with an idealized D_{8h} symmetry, see Section 2.3.); the two nils in *(15b)* in adjacent skeletal positions characterize the formation of a *trans* double bond.



(15a)



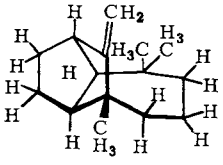
(15b) (≡ **M** ≡ $\mathbf{M}_{opt}$)



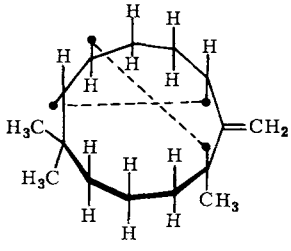
(15c) (= **E**)

The reference isomer of *(15a)* [= *(15b)*] is *(15c)* and the descriptor is *(2 16)*. Therefore *(15a)* is *(2 16)*-cyclooctene-⟨2 – 15⟩.

Example 11 [19]



(16a)



(16b)

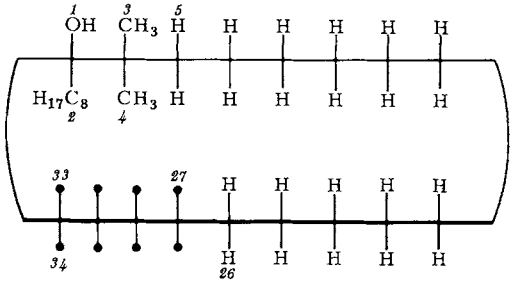
Longifolene *(16a)* is dissected, as shown by *(16b)*, into a cycloundecane derivative with the ligands CH_2 = : 1,2; CH_3: 3 – 5; H: 6 – 18; ↑ : 19 – 22, and the matrix is

$$\left(\begin{matrix}1\\s\end{matrix}\right)_{opt} = \left\{\begin{matrix} 1 & 2 & \mathbf{19} & 4 & \mathbf{11} & 6 & 7 & 8 & 9 & 10 & \mathbf{3} & \mathbf{5} & 13 & \mathbf{20} & \mathbf{21} & 16 & 17 & 18 & \mathbf{12} & \mathbf{14} & \mathbf{15} & 22 \\ \mathit{1} & \mathit{2} & \mathbf{\mathit{3}} & \mathit{4} & \mathbf{\mathit{5}} & \mathit{6} & \mathit{7} & \mathit{8} & \mathit{9} & \mathit{10} & \mathbf{\mathit{11}} & \mathbf{\mathit{12}} & \mathit{13} & \mathbf{\mathit{14}} & \mathbf{\mathit{15}} & \mathit{16} & \mathit{17} & \mathit{18} & \mathbf{\mathit{19}} & \mathbf{\mathit{20}} & \mathbf{\mathit{21}} & \mathit{22} \end{matrix}\right\}$$

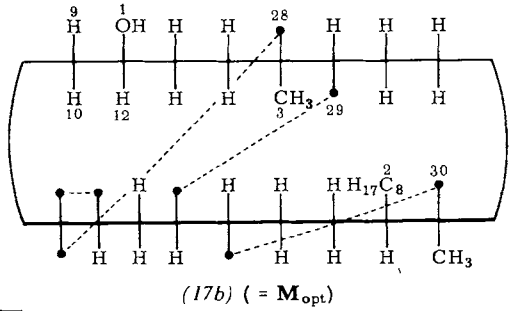
From this follows the descriptor *(3 19 12 5 11) (14 20) (15 21)*-methylene-trimethyl-cycloundecane-*dicon*-⟨3 – 15, 14 – 22⟩.

Example 12 [20]

The steric formula of *(1 9 28 17 30 19 2 10 3) (4 12 29 18) (26 32)*-hydroxy-[*(1′ 2′)*-α,ε-dimethyl-hexyl]-dimethyl-cycloheptadecene-⟨31 – 33⟩-*tricon*-⟨9 – 34, 12 – 27, 17 – 26⟩ is derived by the following steps.



(17a) (= **E**)

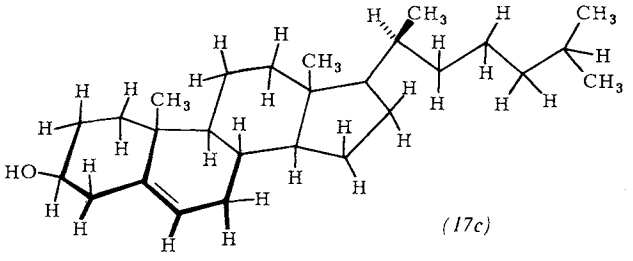


(17b) (= $\mathbf{M}_{opt}$)

[18] *A. C. Cope, C. R. Ganellin*, and *H. W. Johnson, Jr.*, J. Amer. chem. Soc. *84*, 3191 (1962); *A. C. Cope, C. R. Ganellin, H. W. Johnson, Jr., T. V. Van Auken*, and *H. J. S. Winkler, ibid. 85*, 3276 (1963); *A. C. Cope* and *A. S. Mehta, ibid. 86*, 5626 (1964).

[19] *P. Naffa* and *G. Ourisson*, Chem. Ind. (London) *1953*, 917; *R. H. Moffett* and *D. Rogers, ibid. 1953*, 916.

[20] *J. W. Cornforth, F. Youhotsky*, and *G. Popjak*, Nature *173*, 536 (1954); *B. Riniger, D. Arigoni*, and *O. Jeger*, Helv. Chim. Acta *37*, 546 (1954).



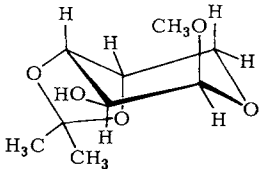
(17c)

The molecule is based upon the skeleton of cycloheptadecane with an idealized D_{17h} symmetry. The 34 skeletal positions are numbered according to the rules of Section 2.4.2. and the reference isomer *(17a)* is generated by attaching the ligands (1: OH, 2: C_8H_{17}, 3,4: CH_3, 5–26: H, 27–34: *nils*). The descriptor *(1 9 28 17 30 19 2 10 3) (4 12 29 18) (26 32)* permutes the coordinate indices of *(17a)* and transforms it into *(17b)*. Then the nils of the skeletal positions *31* and *33* are used to make a double bond, and the pairs of nils at *9* and *34*, *12* and *27*, *17* and *26* are connected to produce the tetracyclic framework of *(17c)*, which is cholesterol.

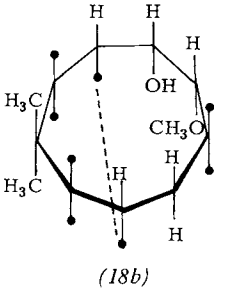
b) *Heterocycles*

The concept of nils is useful for the description of the aza-, oxa-, and thia-derivatives of the carbocyclic permutational isomers. If the covalency of the heteroatom is lower than four $(4 - x)$, this is taken into account by attaching x nils to the heteroatom. Further, the positions of heteroatoms must be specified. For this purpose the (carbon) atoms of the skeleton are numbered by skeletal nuclear numbers $s_N = 1_N \ldots n_N$, differentiated from the skeletal position numbers s by the subscript N. The nuclear number 1_N is assigned to the skeletal nucleus with the skeletal position number *1* (or numbers *1* and *2*, respectively); number 2_N belongs to the nucleus with the position number *2* (or *3* and *4*, respectively), *etc.* The nature and position of a heteroatom is indicated in the descriptor (see example 13).

Example 13 [21]



(18a)



(18b)

The methyl-3,4-*O*,*O'*-isopropylidene-β-D-arabinopyranoside *(18a)*, an intermediate in the synthesis of gentosamine is treated as a trioxa-cyclononane.

The optimal matrix $\left(\begin{smallmatrix}1\\s\end{smallmatrix}\right)_{opt}$ of *(18b)* yields the descriptor *(1 5 13 3 6 14 4) (10 17)-con-⟨10–18⟩-3$_N$,6$_N$,8$_N$*-trioxa-methoxy-dimethyl-cyclononanol for *(18a)*.

$$\left(\begin{smallmatrix}1\\s\end{smallmatrix}\right)_{opt} = \left\{\begin{array}{cccccccccccccccccc} \mathbf{5} & 2 & \mathbf{6} & \mathbf{1} & \mathbf{13} & \mathbf{14} & 7 & 8 & 9 & \mathbf{17} & 11 & 12 & \mathbf{3} & \mathbf{4} & 15 & 16 & \mathbf{10} & 18 \\ \mathbf{1} & 2 & \mathbf{3} & \mathbf{4} & \mathbf{5} & \mathbf{6} & 7 & 8 & 9 & \mathbf{10} & 11 & 12 & \mathbf{13} & \mathbf{14} & 15 & 16 & \mathbf{17} & 18 \end{array}\right\}$$

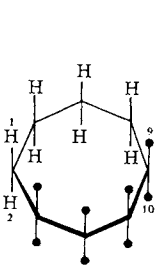
[21] *H. Maehr* and *C. Schaffner*, J. Amer. chem. Soc. *92*, 1697 (1970).

c) *Bridged Molecules*

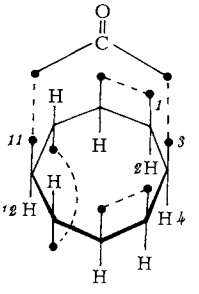
The nil method can be extended to bridged systems, by simply considering the bridges as connections between nils, and describing them by attaching to the name of $\mathbf{M}'_{opt}$ the suffix *pon* (lat.: *pons* = bridge), and in brackets⟨⟩ the numbers s of the skeletal positions which are connected and (between those numbers) the name of the bridge.

Example 14 [22]

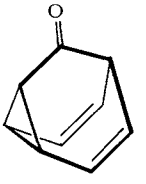
The formula of *(19c)*, *(19) (3 12) (5 13) (7 16)*-cyclooctadiene-⟨*1–15, 5–7*⟩-*con*-⟨*10–14*⟩-*pon*-⟨*3*-carbonylo-*11*⟩ follows from *(19a) via (19b)* by generating *(19c)* with the permutation operator *(1 9)(3 12)(5 13)(7 16)* and then connecting the nil ligands as indicated by diene-⟨*1–15, 5–7*⟩-*con*-⟨*10–14*⟩-*pon*-⟨*3*-carbonylo-*11*⟩. The result is barbaralone *(19c)*.



(19a)



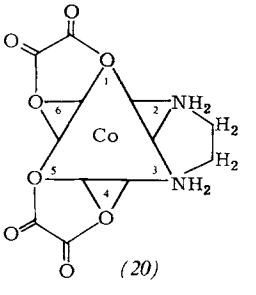
(19b)



(19c)

The concept of bridged skeletal positions can, in a slightly modified form, be extended to the chelated metal complexes. As a rule, it suffices to indicate the skeletal positions of the central atoms that are connected by chelating ligands. Permutation of the skeletal positions in a complex having chelating ligands might easily lead to confusion regarding the original skeletal position-ligand relationship. In order to retain the information provided by the original $\left(\begin{smallmatrix}1\\s\end{smallmatrix}\right)$ matrix, those columns of skeletal positions which belong together because of chelation are indicated by brackets and these brackets are retained during s-permutations.

Example 15 [10]



(20)

$$\begin{array}{lc} \delta & \left\{\begin{array}{cccccc} 1 & 5 & 6 & 4 & 2 & 3 \\ 1\text{-}4 & 5,6 & 5,6 & 1\text{-}4 & 1\text{-}4 & 1\text{-}4 \end{array}\right. \\ \beta & \\ \alpha & \left\{\begin{array}{cccccc} 1 & 2 & 3 & 4 & 5 & 6 \end{array}\right. \\ \gamma & \left\{\begin{array}{cccccc} 1 & 5 & 6 & 4 & 2 & 3 \end{array}\right. \end{array} \equiv \left(\begin{smallmatrix}1\\s\end{smallmatrix}\right)_{opt}$$

[22] *W. v. E. Doering, B. M. Ferrier, E. T. Fossel, J. H. Hartenstein, M. Jones, Jr., G. Klumpp, R. M. Rubin*, and *M. Saunders*, Tetrahedron *23*, 3943 (1967).

According to $(^{1}_{3})_{opt}$ the descriptor of the chiral complex *(20)* is dioxalato-⟨*1*−*3*, *2*−*4*⟩-ethylenediamine-⟨*5*−*6*⟩-cobalt, and the ⟨*1*−*2*, *3*−*4*⟩-⟨*5*−*6*⟩-isomer is the antipode of *(20)*.

The descriptors of multinuclear metal complexes indicate the connecting bridges and the numbers of the nils of the nuclei which are used for bridging. Ligands inserted into faces of complexes as bridges are symbolized by *pon* and in ⟨ ⟩ brackets the numbers of those ligands between which the additional ligand is inserted (see some of the hepta-coordinate complexes).

A wide variety of polycyclic molecules could not be adequately represented by descriptors unless further operations were defined for the treatment of complications arising from the bridges of certain polycyclic systems.

A bridge of a polycyclic molecule that is capable of existing in various isomeric forms requires a nomenclatural procedure which allows one to describe unequivocally the topology of this bridge in relation to the rest of the molecule. A one-membered bridge of a molecule **M** such as *(21)*

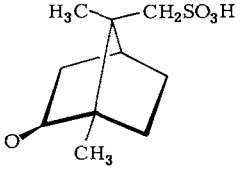


(21)

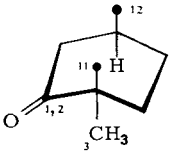
can be adequately represented by a tetrahedral skeleton XXVII. Positions *1* and *2* carry the ligands L_1 and L_2 and positions *3* and *4* are empty, *i.e.*, occupied by nils, and are used for attaching this bridge to the rest of the molecule **M**, in a manner indicated by the descriptor.

Example 16 [23]

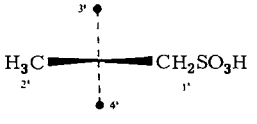
The camphor π-sulfonic acid *(22a)* is an example for compounds with bridges capable of existing in different "epimeric" forms.



(22a)



(22b)



(22c)

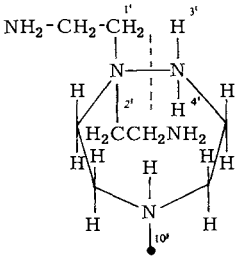
For nomenclatural purposes *(22a)* is "dissected" into *(22b)* and *(22c)*, which leads through the $(^{1}_{3})$-matrices of *(22b)* and *(22c)* to the descriptor (*3 5 12*)-*pon*-⟨*3'*−*5*, *4'*−*11*⟩-[sulfonylmethyl-methyl-methano]-methyl-cyclohexanone for *(22a)*.

Two-membered bridges are derived from I by attaching this system in a specified manner (see above), with its clockwise side toward the positions which must be connected. The most convenient way to describe bridges with three or more members is to describe a corresponding cyclic system and open the ring between two of its members. The resulting chain is fully described by the descriptor of the cyclic system and further, by specifying which bond was transformed into two nils by the prefix *se* (lat.: *secare*) and finally, in brackets ⟨ ⟩, the numbers of skeletal nuclei whose bond was broken.

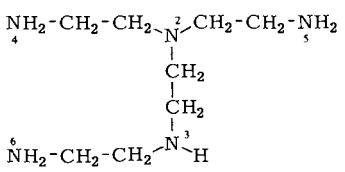
[23] *F. S. Kipping* and *W. F. Pope*, J. chem. Soc. *63*, 549 (1893); *67*, 357 (1895); *A. M. T. Finch* and *W. R. Vaughan*, J. Amer. chem. Soc. *91*, 1416 (1969).

Example 17 (see XXIX) [24]

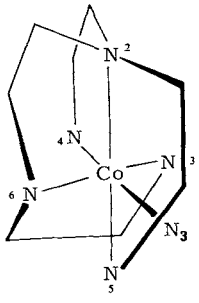
The (*2 4 3*)-azido-{(*10' 14'*)-*se*-⟨$1'_N$ $2'_N$⟩-1_N, 2_N, 5_N-triaza-bis-[β-aminoethyl]-cycloheptane}-cobalt ion is *(23d)*.



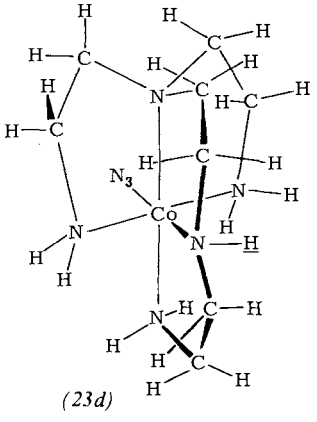
(23a)



(23b)



(23c)



(23d)

The trenen ligand *(23a)* of the complex *(23d)* is obtained from its reference isomer **E'** = (*1' 2'*)-bis-(β-aminoethyl)-*14'-nil*-cycloheptane by applying its descriptor and attaching a nil to the skeletal position *10'* according to (*10' 14'*), and replacing the carbon atoms at the nuclear positions $1'_N$, $2'_N$, and $5'_N$ by nitrogen. The chirality of the asymmetric nitrogen at *10'* is stabilized by complexation in *(23a)* [= *(23b)*] in the configuration indicated.

The azido group has the highest sequential priority (1) among the ligands of the complex *(23d)*, and the chelating nitrogen atoms of the amine groups are sequentially numbered as indicated in *(23b)*. Hence the reference isomer for the octahedral complex is *(23c)*, a structure that is only conceptual and could not exist for ring strain reasons. The permutation (*2 4 3*) transforms *(23c)* into *(23d)*.

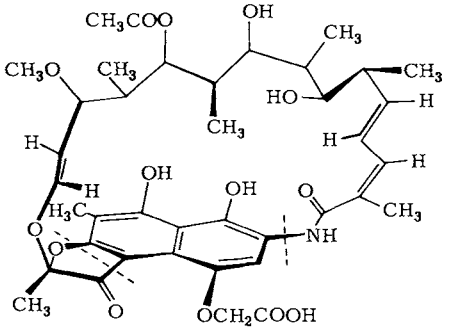
Example 18 [25]

Rifamycin B *(24a)* is treated as a naphthalene derivative with a *se*-azacyclononadecane bridge and an additional oxa-bridge. The combination of the description of the aliphatic bridge *(24d)* and the naphthalene moiety *(24c)* leads to the descriptor (*1 29 26 12 38 2 16 7 17 10 19 8 36 13 24 5 9 37*) (*11 21*) (*6 32 27*)-*se*-⟨1_N−19_N⟩-1_N-aza-17_N-oxa-dioxo-acetoxy-methoxy-dihydro-

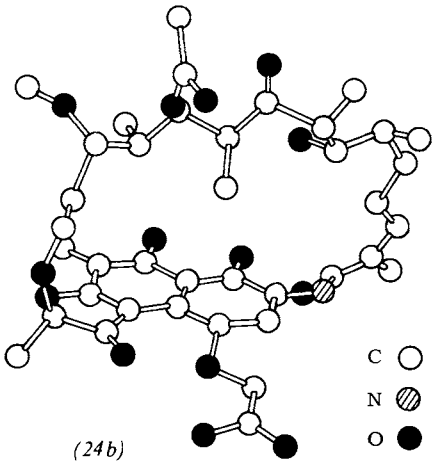
[24] *D. A. Buckingham*, *P. A. Marzilli*, and *A. M. Sargeson*, Inorg. Chem. *8*, 1595 (1969).

[25] *W. Oppolzer*, *V. Prelog*, and *P. S. Sans*, Experientia *20*, 336 (1964); *M. Burfoni*, *W. Fedeli*, *G. Giacomello*, and *A. Vaciago*, *ibid. 20*, 339 (1964); *J. Leitlich*, *W. Oppolzer*, and *V. Prelog*, *ibid. 20*, 343 (1964).

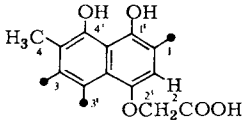
xy-hexamethyl-nonadecatriene-⟨6–8, 10–12, 30–31⟩-dipon-⟨1_N-$1'_N$, 19_N-$3''_N$, 18_N-oxa-$3'_N$⟩-(1′2″)(1″2′)(3′4″)-carbomethoxy-dihydroxy-methyl-naphthalene. On reconstructing Rifamycin B with Dreiding models, according to the descriptor, one obtains a model which is strikingly similar to the model of the molecule as determined by X-ray methods.



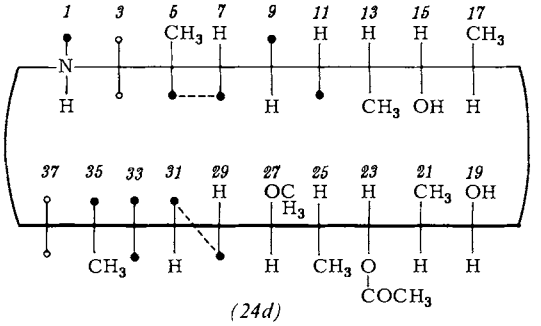
(24a)



(24b)



(24c)



(24d)

2.5. Chiral Descriptors

An observation of chirality relates to a measurement of some property of a chiral system, the numerical value of which will (by definition) be the same for the two antipodes but each will have the opposite algebraic sign [15b,c].

With respect to a class of molecules, we may call a function F_χ a *chirality function* [7,13,15] if it is capable of expressing these numerical values in terms of the nature of the particular molecules, *i.e.*, in terms of the ligands by which the molecules of the given class differ. For chiral permutational isomers with n places for the ligands and a skeletal symmetry S the chirality function F_χ is of the form

$$F_\chi = F_\chi (L_1 \ldots\ldots L_n)$$

The operations of the group S produce permutations P_s, of the L_s. Here the L_s are used as symbols for the ligands, and the indices s refer to the skeletal positions to which L_s is attached.

We use the symbol H' for the subgroups of all permutations belonging to rotations H of S (group order = g). The function F_χ is invariant towards the operations of H and changes its algebraic sign on permutations, S', which correspond to the improper rotations and reflections of S. Accordingly, F_χ vanishes for achiral molecules.

In order to describe observations of chirality, such as optical rotation, ORD, CD, as well as the logarithms of the product ratios of stereoselective syntheses, we use approximations F_χ of chirality functions F_χ [15].

$$F_\chi \simeq F_\chi = F_\chi (\lambda_1 \ldots\ldots \lambda_n) \qquad (4)$$

In the approximated $F_\chi (\lambda_1 \ldots\ldots \lambda_n)$ the variables λ_i represent those properties of L_i which are relevant for a given observation of chirality. The value of the ligand parameter λ_i of L_i differs for the description of different types of chirality observations. The approximation of F_χ by F_χ is achieved by two methods [15b]; 1) the method of the polynomials of the lowest degree, and 2) the method of linear combinations of functions of a minimum set of ligands.

The approximated chirality function $F_\chi(\lambda_1 \ldots\ldots \lambda_n)$ is such that F_χ is invariant towards those permutations P of the variables λ_i which belong to the subgroup H and changes its algebraic sign by permutations representing the coset C. Accordingly, these chirality functions F_χ are invariant towards the projection operator P_A of the antimetric representation of the permutation group S' of the variables $\lambda_1 \ldots\ldots \lambda_n$.

$$P_A F_\chi (\lambda_1 \ldots\ldots \lambda_n) = F_\chi (\lambda_1 \ldots\ldots \lambda_n) \qquad (5)$$

with

$$P_A = \frac{1}{g}\left(\sum_{s\in H} P - \sum_{s\in H} P\right) \qquad (6)$$

This antimetric projection operator (6) can also be used to generate the approximation functions F_χ from monomials (1) or functions of a minimum set of ligands (2) [15b].

Example 19

The subgroup H of the skeletal symmetry group S of XII is

$$H = \{E, C_4^{(1357)}, C_4^{(7531)}, C_2^{(12)}, C_2^{(14)}, C_2^{(15)}, C_2^{(16)}, C_2^{(18)}\},$$

and its coset is

$$C = \{\sigma^{(12)}, \sigma^{(13)}, \sigma^{(15)}, \sigma^{(17)}, \sigma^{(37)}, i, S_4^{(14)}, S_4^{(18)}\}.$$

Therefore, projection operator $P_{A,\mathrm{XII}}$ of the standard skeleton XII is

$$\begin{aligned} P_A = \tfrac{1}{16}\{&E + (1357)(2468) + (7531)(8642) + (12)(38)(47)(56)\\ &(14)(23)(76)(85) + (15)(26)(37)(48) + (16)(25)(34)(78)\\ &(18)(27)(36)(45) - (12)(34)(56)(78) - (13)(24)(75)(86)\\ &(15)(26) - (17)(28)(35)(46) - (16)(25)(38)(47) - \\ &(14)(23)(36)(45)(58)(67)(78)(81) - (18)(27)\\ &(37)(48)(78)(54)(63)(32)(41)\} \end{aligned} \tag{7}$$

The lowest degree, homogeneous polynomial $F_{\chi,\mathrm{XII}}$ is an approximation chirality function of compounds with the skeleton XII. It is generated by applying $P_{A,\mathrm{XII}}$ to the monomial $\lambda_1\lambda_4$ (or an equivalent monomial).

$$\begin{aligned} F_{\chi,\mathrm{XII}} &= P_{A,\mathrm{XII}}\lambda_1\lambda_4 = \\ &= \tfrac{1}{16}\{\lambda_1\lambda_4 + \lambda_7\lambda_2 + \lambda_3\lambda_6 + \ldots\ldots + \lambda_4\lambda_5 + \lambda_8\lambda_1\} = \\ &= \tfrac{1}{8}\{(\lambda_1 - \lambda_5)(\lambda_4 - \lambda_8) - (\lambda_2 - \lambda_6)(\lambda_3 - \lambda_7)\} \end{aligned} \tag{8}$$

This chirality function, based upon the skeletal numbers of XII, can also be obtained from the previously published function $F'_{\chi',\mathrm{XII}'}$ [15b] by applying the permutation $P' = (2'\ 5'\ 3')(6'\ 7'\ 4')$, which converts the original skeletal numbers s' (indices of the XII') into the standard skeletal numbers of XII.

$$\begin{aligned} P'F'_{\chi,\mathrm{XII}} &= (2'\,5'\,3')(4'\,6'\,7')\\ &\{(\lambda'_1 - \lambda'_3)(\lambda'_6 - \lambda'_8) - (\lambda'_2 - \lambda'_4)(\lambda'_5 - \lambda'_7)\}\tfrac{1}{8} = F_{\chi,\mathrm{XII}} \end{aligned} \tag{9}$$

In the reference matrix $\binom{1}{s}_{\mathbf{E}}$ the ligand numbers l and the skeletal numbers s are superimposed. Therefore, in the *standard chirality function*, the skeletal indices i of the λ_i can be replaced by ligand indices i ($\lambda_i \rightarrow \lambda_i'$), by which the standard chirality functions F_χ is transformed into the chirality function $F^{\mathbf{E}}_{\chi,n}$ of the reference isomer. The descriptor $\boldsymbol{P}_s$ of a given permutational isomer generates the specific chirality function $F_{\chi,n}$ of this particular isomer from the reference chirality function $F^{\mathbf{E}}_{\chi,n}$

$$\bar{\boldsymbol{P}}_s F^{\mathbf{E}}_{\chi,n} = F_{\chi,n} \tag{10}$$

The isomer functions $F_{\chi,n}$ are easier to use than the original chirality functions, because the indices i of the λ_i in the isomer functions are the sequential ligand numbers of the ligands of the given set of permutation isomers. With the isomer functions there is no need to draw the particular isomer with numbered skeletal positions in order to assign the indices of the variables λ_i'.

Without knowledge of the particular numerical values of the ligand parameters λ_i the isomer functions can be used to determine whether a descriptor belongs to a chiral or an achiral molecule.

Example 20

The isomer function F_χ of *(17)(46)*-dicarboxy-diphenyl-cyclobutane is (with: $CO_2H = 1,2$; $C_6H_5 = 3,4$; $H = 5\ldots8$),

$$\begin{aligned} \mathbf{P}_S F^{\mathbf{E}}_\chi = F_\chi &= \tfrac{1}{8}(17)(46)\{(\lambda_1 - \lambda_5)(\lambda_4 - \lambda_8) - (\lambda_2 - \lambda_6)(\lambda_3 - \lambda_7)\}\\ &= \tfrac{1}{8}\{(\lambda_7 - \lambda_5)(\lambda_6 - \lambda_8) - (\lambda_2 - \lambda_4)(\lambda_3 - \lambda_1)\}\\ &= \tfrac{1}{8}\{(\lambda_H - \lambda_H)(\lambda_H - \lambda_H) -\\ &\quad (\lambda_{CO_2H} - \lambda_H)(\lambda_{C_6H_5} - \lambda_{CO_2H})\} \neq 0 \end{aligned} \tag{11}$$

and is different from zero; therefore *(3c)* is chiral, whereas its *(15)(48)*-isomer is achiral, because of:

$$\begin{aligned} F_\chi = (15)(48)F^{\mathbf{E}}_\chi &= \tfrac{1}{8}\{(\lambda_5 - \lambda_1)(\lambda_8 - \lambda_4) - (\lambda_2 - \lambda_6)(\lambda_3 - \lambda_7)\}\\ &= \tfrac{1}{8}\{(\lambda_H - \lambda_{CO_2H})(\lambda_H - \lambda_{C_6H_5}) -\\ &\quad (\lambda_{CO_2H} - \lambda_H)(\lambda_{C_6H_5} - \lambda_H)\} = 0 \end{aligned} \tag{12}$$

Another way of determining whether a descriptor $\boldsymbol{P}_s$ describes a chiral or an achiral molecule, without drawing a steric formula, is to generate the matrix $\binom{1}{s}_{\mathrm{opt}} = \boldsymbol{P}_s\binom{1}{s}_{\mathbf{E}}$ and then apply an s-permutation from the coset $\boldsymbol{C}'$ of $\boldsymbol{H}'$ to $\binom{1}{s}_{\mathrm{opt}}$. If the resulting $\binom{1}{s}$-matrix can be brought into "coincidence" with $\binom{1}{s}_{\mathrm{opt}}$ by s-permutations of $\boldsymbol{H}'$, the molecule that is described by the descriptor $\boldsymbol{P}_s$ is achiral, otherwise it is chiral.

3. Dynamic Chemistry

3.1. Permutational Isomerization

3.1.1. General Formalism

Redistribution of ligands on a polytopal framework is called a polytopal rearrangement [26]. The mutual transformations of permutational isomers, called polytopal rearrangements, involve a permutation of at least two skeletal sites, or ligands, respectively.

We wish to differentiate between two types of polytopal isomerizations, regular and irregular. The regular polytopal isomerizations are those that occur without breaking and reforming bonds, conserving neighborhood relations, as in the closely related process of interconversion of conformers. The irregular polytopal rearrangements occur with bond fission and reformation. While irregular rearrangements can be easily treated with this formalism, we restrict ourselves, in this paper, to regular processes.

Polytopal rearrangements, $\mathbf{M} \rightleftharpoons \mathbf{M}'$, can be described by transforming the matrix $\binom{1}{s}$ into $\binom{1}{s}'$ or the reverse by the operation of the ligand or coordinate isomerizer [eq. (13)] on the appropriate matrix.

$$\binom{1}{s}' = I_l\binom{1}{s} = I_s\binom{1}{s} \tag{13}$$

The s permutations are used as descriptors. In order to differentiate those permutations used to describe isomerization reactions from the descriptors, we will use l-permutations, I_l of equation (13) to represent the isomerizations. I_l will be called the *isomerizer*. The isomerizer which describes the transformation of a molecule $\mathbf{M}$ to $\mathbf{M}'$ is derived from their descriptors $\boldsymbol{P}_s$ and $\boldsymbol{P}'_s$ as follows: $\mathbf{M}$ and $\mathbf{M}'$ are generated from their reference isomer $\mathbf{E}$ according to equations (14a) and (14b).

$$\binom{1}{s} = \boldsymbol{P}_s\binom{1}{s}_{\mathbf{E}} = \mathbf{P}_l\binom{1}{s}_{\mathbf{E}} \tag{14a}$$

$$\binom{1}{s}' = \boldsymbol{P}'_s\binom{1}{s}_{\mathbf{E}} = \mathbf{P}'_l\binom{1}{s}_{\mathbf{E}} \tag{14b}$$

In these equations the equivalent s and l permutations $\boldsymbol{P}_s$ and $\mathbf{P}_l$ as well as $\boldsymbol{P}'_s$ and $\mathbf{P}'_l$ are numerically reversed. For example, one obtains $\mathbf{P}_l$ from the inverse $\bar{\boldsymbol{P}}_s$ of $\boldsymbol{P}_s$, by replacing its s with l, *i.e.*, by "deitalicizing" its numbers. The inverse $\bar{\boldsymbol{P}}_s$ of $\boldsymbol{P}_s$ is defined by equation (15).

$$\bar{\boldsymbol{P}}_s \times \boldsymbol{P}_s = e \tag{15}$$

Equation (15) states that if you first apply the permutation $\boldsymbol{P}_s$ and then $\bar{\boldsymbol{P}}_s$ upon the elements of a set, the result is the identity operation, e. Inverse permutations are numerically

[26] We use the term polytopal rearrangements in a more general sense than it has been used by previous authors (cf. [27]).

reverse; for instance if $\bar{P}_s = (1\ 2\ 3\ 4)$, then $\bar{P}_s = (4\ 3\ 2\ 1) = (1\ 4\ 3\ 2)$. Multiplying equation (14a) by $\bar{P}_I$ and equation (14b) by $\bar{P}'_I$ produces equation (16)

$$\bar{P}'_I \begin{pmatrix} 1 \\ s \end{pmatrix}' = \bar{P}_I \begin{pmatrix} 1 \\ s \end{pmatrix} = \begin{pmatrix} 1 \\ s \end{pmatrix}_E \qquad (16)$$

from which equation (17) is obtained by multiplication with P'_I.

$$\begin{pmatrix} 1 \\ s \end{pmatrix}' = P'_I \times \bar{P}_I \begin{pmatrix} 1 \\ s \end{pmatrix} \qquad (17)$$

Combining equations (16) and (13) yields equation (18).

$$I_I = P'_I \times \bar{P}_I \qquad (18)$$

The *isomerizer* I_I can be directly obtained from the descriptor, by reversing the sequence of and "de-italicizing" $[\bar{P}_s \times P'_s]$. The product of the isomerizers of a closed cycle of reactions corresponds to the identity operation (*e*).

$$\overset{\circlearrowleft}{\prod} P_I = (e) \qquad (19)$$

3.1.2. Conformations

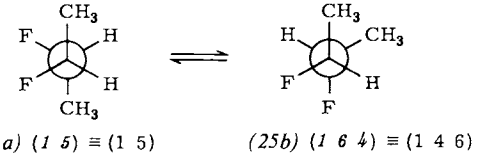
The energetically preferred geometrical configurations of molecules which can be interconverted by movements of some of their parts without breaking bonds are the conformers of a given molecular species (see below) and can be treated by the following methods. The skeletal coordinate systems and their transformations must be chosen taking into account the peculiarities of the conformational interconversions.

Example 21

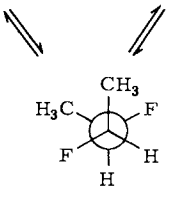
The conformational interconversions of *(25a) – (25c)* are treated on the basis of the (D_{3d}) skeleton *(25d)* and the reference isomer *(25e)*; the isomerizers

$I_{ab} = (1\,4\,6)(1\,5) = (1\,4\,6\,5)$ $\quad I_{ba} = (1\,5\,6\,4)$
$I_{ac} = (2\,5\,3)(1\,5) = (1\,5\,3\,2)$ $\quad I_{ca} = (1\,2\,3\,5)$
$I_{bc} = (2\,5\,3)(1\,6\,4)$ $\quad I_{cb} = (1\,4\,6)(2\,3\,5)$

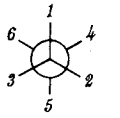
follow from the description according to Section 2.4.6.



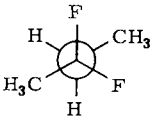
(25a) (1 5) ≡ (1 5) *(25b)* (1 6 4) ≡ (1 4 6)



(25c) (2 3 5) ≡ (2 5 3)

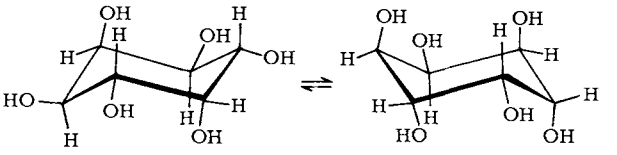


(25d) (≡ XXI)

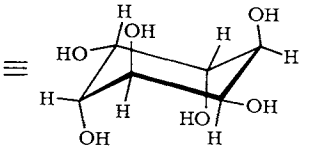


(25e)

Example 22



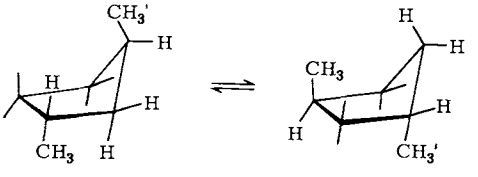
(26a) (1 7) (3 9) (5 11) *(26b)*



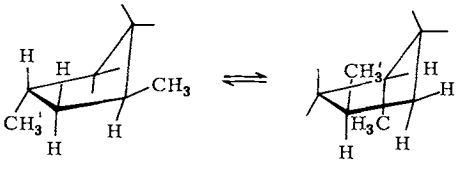
(26b)' (2 8) (4 10) (6 12)

The isomerizer (1 7) (2 8) (3 9) (4 10) (5 11) (6 12) of the conformational equilibrium *(26a)* ⇄ *(26b)* of neoinositol is derived in a straight forward manner on the basis of skeleton XIV.

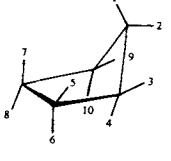
Example 23



(27a) (2 6) *(27b)* (1 4) (2 7)



(27c) (1 8) (2 3) *(27d)* (1 5) (2 10)



(27e)

The conformation independent descriptor (2 6)-dimethyl-cyclopentane refers to the skeleton XIII whereas the descriptors of *(27a) – (27d)* and the isomerizers of their interconversions (*e.g.*, I_{ab} = (1 4) (2 7) (2 6) = (1 4) (276)) are derived from *(27e)* when $CH'_3 \equiv 1$, $CH_3 \equiv 2$.

3.1.3. Trigonal Bipyramidal Molecules[27,28][*]

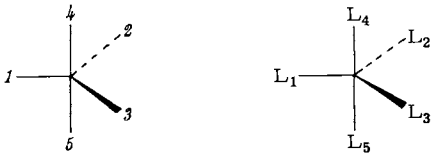
3.1.3.1. General Remarks

A polyhedral skeleton is that molecular skeleton with ligand positions equivalent to the n vertices of a polyhedron (see *e.g.* VII–XIV). There have been several recent attempts to determine the number of interconvertible polyhedral isomers (*Muetterties*[27d] calls these polytopal stereoisomers) and the number of steps needed for the interconversions of these isomers by graph theoretical methods[27b,c] or some matrix equivalent thereof[27f]. In all of these contributions particular attention was focused upon the isomerizations of the pentacoordinate phosphorus compounds by the generally accepted pseudorotation[28] mechanism.

Isomerizations of polyhedral molecules are treated according to the general procedure of Section 3.1.1. If an isomerization process leads to an exchange of ligands between non-equivalent skeletal positions, it must be represented by transformations involving skeletal coordinates of different, non-equivalent sets. The separate treatment of the ligands of non-equivalent coordinates, suitable for nomenclature purposes, can be given up, and the combination of the unprimed and the primed sets of ligands used instead.

Application of this permutational formalism to the rearrangements of pentacoordinate compounds *(28b)* with the skeleton *(28a)* and skeletal coordinates 1 . . . 5 shows, in a straightforward manner, which mechanisms are conceivable[29].

If the ligands of *(28b)* are indexed in sequential order *(28b)* is the reference isomer **E** and is represented by the descriptor (*e*).

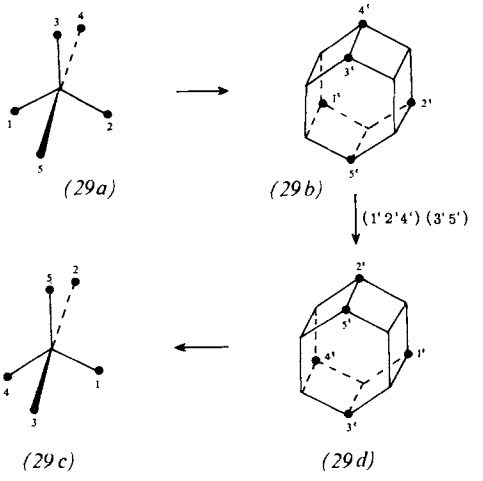


(28a) **a** (≡ S_5) *(28b)* **b** (≡ **E**)

3.1.3.2. (2+3)-Turnstile Processes[29]

Of the formal possibilities invoked to explain regular pentacoordinate isomerization, the one alternative to the (1+4)-pseudorotation mechanism that satisfies *all* experimental data is the (2+3)-internal rotation process shown in example 24. We call this process the (2+3)-*turnstile mechanism.*

Example 24



(29a) *(29b)* *(29c)* *(29d)*

This scheme can be viewed as an attempt to illustrate the topological concept of the (2+3)-turnstile process (1 2 4) (3 5) in geometrical terms[*] by a 120 ± 180° relative internal

[27] a) *E. L. Muetterties*, J. Amer. chem. Soc. *90*, 5097 (1968); b) *J. D. Dunitz* and *V. Prelog*, Angew. Chem. *80*, 700 (1968), Angew. Chem. internat. Edit. *7*, 725 (1968); c) *P. C. Lauterbur* and *F. Ramirez*, J. Amer. chem. Soc. *90*, 6722 (1968); d) *E. L. Muetterties, ibid. 91*, 1636 (1969); e) *E. L. Muetterties* and *A. T. Storr, ibid. 91*, 3098 (1969); f) *M. Gielen, M. DeClerq*, and *J. Nasielski*, J. Organometal. Chem. *18*, 217 (1969); *M. Gielen* and *J. Nasielski*, Bull. Soc. Chim. Belges, in press; *M. Gielen, C. Depasse-Delit*, and *J. Nasielski, ibid.*, in press; g) *R. G. Pearson*, J. Amer. chem. Soc. *91*, 4947 (1969); h) *F. N. Tebbe, P. Meakin, J. P. Jesson*, and *E. L. Muetterties*, J. Amer. chem. Soc. *92*, 1068 (1970).

[28] a) *R. S. Berry*, J. Chem. Phys. *32*, 933 (1960); b) see also: *L. H. Sommer:* Stereochemistry, Mechanism, and Silicon. McGraw-Hill, New York 1964; c) *R. F. Hudson:* Structure and Mechanism in Organophosphorus Chemistry. Academic Press, New York 1965; d) *R. Schmutzler*, Advan. Fluorine Chem. *5*, 31 (1965); e) *E. L. Muetterties*, Inorg. Chem. *6*, 635 (1967); f) *G. Wittig*, Bull. Soc. Chim. France *1966*, 1162; g) *D. Hellwinkel*, Chem. Ber. *99*, 3668 (1966); h) *E. L. Muetterties* and *R. A. Schunn*, Quart. Rev. (London) *20*, 245 (1966); i) *J. H. Letcher* and *J. R. van Wazer*, J. Chem. Phys. *45*, 2926 (1966); j) *D. Gorenstein* and *F. H. Westheimer*, Proc. Nat. Acad. Sci. U.S. *58*, 1747 (1967); k) *R. R. Holmes* and *R. M. Deiters*, J. Amer. chem. Soc. *90*, 5021 (1968); l) *F. Ramirez*, Accounts Chem. Res. *1*, 168 (1968); m) *F. Ramirez, J. F. Pilot, O. P. Madan*, and *C. P. Smith*, J. Amer. chem. Soc. *90*, 1275 (1968); n) *F. Ramirez*, Trans. N.Y. Acad. Sci. *30*, 410 (1968); o) *M. Sanchez, R. Wolf, R. Burgada*, and *F. Mathis*, Bull. Soc. Chim. France, *1968*, 733g; p) *F. H. Westheimer*, Accounts Chem. Res. *1*, 70 (1968); q) *G. M. Whitesides* and *H. L. Mitchell*, J. Amer. chem. Soc. *91*, 5384 (1969).

[*] *F. Ramirez* is co-author of Section 3.1.3.

[29] a) *I. Ugi, D. Marquarding, H. Klusacek, P. Gillespie*, and *F. Ramirez*, Accounts Chem. Res., in press; b) *F. Ramirez, S. Pfohl, E. A. Tsolis I. Ugi D. Marquarding P. Gillespie* and *P. Hoffman*, J. Amer. chem. Soc., in press.

[*] *Note added in proof:* The mechanistic alternatives for the positional exchange of pentacoordinate molecules belong to different classes of the permutation group S_5. Pseudorotation of D_{3h} trigonal bipyramidal molecules correspond to the alternating permutations (a e a' e') of the apical a and a' and equatorial e, e'' and e''' ligand indices whereas turnstile processes by permutations (a e) (e'' e' a') from the class of (2 + 3) cycles. As a consequence of the skeletal symmetry of VII the permutations (a e) (e'' e' a'), (a' e) (e'' e' a), (a' e') (e'' e a) and (a e a' e') are equivalent. For instance, the pseudorotation isomerizer (2435) as well as the four different but equivalent turnstile isomerizers (24) (135), (25) (134), (34) (125) and (35) (124) all transform *(28b)* (≡**E**) into the same isomer. During the equivalent turnstile process, the pivot L_1 of the pseudorotation mechanism replaces one of the equatorial ligands (L_2 or L_3). It must be noted that during a turnstile process, the pair has an approximate local C_2 skeletal symmetry and undergoes a corresponding rotation about the local C_2 axis while the trio has an approximate local C_3 skeletal symmetry and simultaneously undergoes a rotation about the local C_3 axis with opposite angular momentum.

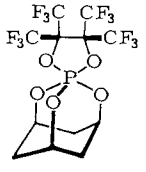
The BPR (Berry pseudorotation or (1+4)-pseudorotation) and TR ((2+3)-turnstile rotation) differ fundamentally by the pathways by which they occur and by the intermediate species involved. The BPR, as it is defined, is the combination of two synchronized bending motions of a pair of equatorial and a pair of apical bonds respectively, and does not involve any internal rotation. The TR process, by contrast, involves internal rotation.

In cyclic pentacoordinate compounds, enforcing BPR upon a molecule invariably involves internal rotation of the cyclic moiety *vs.* the remaining ligands and thus becomes a TR unless the BPR involves the interconversion of a diequatorial ring and an apical-equatorial or a diapical ring respectively which is quite unlikely and only reasonably conceivable for sufficiently large rings.

rotation of the ligands 1, 2, and 4 *vs.* 3 and 5. We propose that the regular pentacoordinate isomerizations occur by a (2+3)-internal rotation through a (2+3)-intermediate or an interconvertible set of (2+3)-intermediates rather than by the generally accepted (1+4)-pseudorotation mechanism. Both processes can, in the idealized case, occur with conservation of angular momentum. While there is experimental evidence which contradicts the (1+4)-pseudorotation mechanism, all data are in accordance with the (2+3)-turnstile concept.

Intermediate species of the type *(29b)* or *(29d)* in the (2+3)-internal rotation concept can only be characterized in terms of the permutational symmetry of the skeletal coordinates and not by a particular geometry. Species *(29b)* for instance, is characterized only by the fact that it can be represented by five skeletal coordinates of which a pair (3′ and 5′) and a triple (1′, 2′, and 4′) are equivalent and permutable. If all of the possible (2+3)- intermediates of a given set of 20 pentacoordinate topological isomers are interconvertible, this is represented by complete equivalence of the five skeletal coordinates which are interconverted by 5! permutations. Such a state cannot be described by geometry or the conventional concept of symmetry because it is not possible to place five points mutually equidistant on the surface of a sphere. Since it can be assumed that the (2+3)-intermediates are short-lived species, a geometrical description loses its meaning in any case, due to the uncertainty principle.

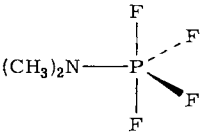
Example 25



(30)

The ^{1}H- and ^{19}F-NMR data of *(30)* [29b] indicate rapid positional exchange (permutational isomerization) of the ligands of the pentacoordinate phosphorus. This can only be interpreted by a (2+3)-turnstile process; the (1+4)-pseudorotation is not possible as a consequence of the structure and the strain it imposes. Even if one forces *(30)* into the pseudorotation pathway by overcoming the structural limitations, the result would involve relative internal rotation of the adamantanoid moiety *vs.* the five membered ring, a superposition of the turnstile upon pseudorotation.

Whitesides and *Mitchell* [28q] analyzed the temperature dependence of the ^{31}P-NMR spectrum of *(31)*, and were able to show that at low temperatures ($T \leq -100\,°C$) structure *(31)* is frozen, *i.e.*, the dimethylamino group and two of the fluorines occupy equatorial positions, and two of the P–F bonds are apical, without any exchange of the equatorial and apical fluorines. Above $-50\,°C$ all four fluorines become completely equivalent, but there is an intermediate temperature range in which the equatorial pair of fluorines replaces the apical pair of fluorines and *vice versa* in a single concerted step. This result was invoked by the authors as proof that none of the published ("non-Berry") alternatives to the (1+4)-pseudorotation mechanism of pentatopal rearrangements could be responsible for the F-exchange of *(31)*. However, the (2+3)-process corresponds exactly, like the (1+4)-pseudorotation process, to all the assumptions that entered *Whitesides'* and *Mitchell's* evaluation of their experimental data.



(31)

If such a (2+3)-internal rotation is terminated with the dimethylamino group in the equatorial position, the result is an exchange of the equatorial and apical pairs of fluorine atoms.

3.2. Chemical Reactions and Transition States

3.2.1. General Considerations

The mechanisms of chemical reactions can be described on various levels and in a variety of terms [30]. In any detailed discussion of the mechanisms of a chemical reaction the transition complex, which is often called the transition state, plays a central role [31]. The transition state corresponds to a complex which contains all participants in a reaction such that the reactants have already lost some of their characteristics, and in which the characteristics of the products are not yet fully developed. The transition complex is a short-lived state, or better, a statistical ensemble of short-lived states, which corresponds to the peak of an energy barrier between starting materials and products. These transition complexes, as statistical entities, cannot be characterized in geometrical terms (as has been attempted, often with admirable imagination), since they do not represent a uniform long-lived species, but a collection of different, short-lived states.

Even if we could observe one single, isolated transition complex of an "ultimate kinetic unit" [31b], a geometrical description would not be possible. As a consequence of the *uncertainty principle*, the geometrical features (distance) of short-lived species are not subject to an accurate observation [32].

The reader of current chemical literature could be led to believe that there exists a wealth of detailed knowledge on transition complexes. However, a critical analysis of the statements often reveals assertions which go far beyond the evidence or, in some cases, even contain violations of basic principles.

There seems to be a tradition, among mechanistically oriented chemists, to describe reaction mechanisms ac-

[30] *A. Streitwieser, Jr.*: Molecular Orbital Theory. Wiley, New York 1962, p. 310.

[31] a) *H. Eyring*, J. Chem. Phys. *3*, 107 (1935); *W. F. K. Wynne-Jones* and *H. Eyring*, *ibid.* *3*, 492 (1935); *S. Glasstone*, *K. J. Laidler*, and *H. Eyring*: The Theory of Rate Processes. McGraw-Hill, New York 1942; b) *H. Eyring*, *D. Henderson*, *B. J. Stover*, and *E. M. Eyring*: Statistical Mechanics and Dynamics. Wiley, New York 1964, p. 29.

[32] *O. K. Rice*, J. Phys. Chem. *65*, 1588 (1961).

cording to accepted terminologies and formalisms, without ascertaining the pertinence of the proceedings. The occurrence of a chemical reaction is frequently expounded in detailed geometrical terms. Conclusions are drawn about the transition complex from the so-called "reaction coordinate diagram", in which the only thing less certain than the ordinate is the abscissa.

To interpret and predict the steric course of stereoselective reactions, often one arbitrarily chosen conformation of the transition complex is discussed. The geometrical distribution of nuclei and electrons of this choice, of which at best, only its relative free energy, origin, and destination are known, is quite often the basis of interpretation and prediction of the steric course of stereoselective reactions.

3.2.2. Relations between Reacting Entities

These current extrapolations of the transition state theory [31] result from the fact, that there are many things which can and should be said about transition states, but no formalized framework of thought has been available to support these statements. The quantum mechanical description of reacting systems must be interpreted with caution as the assumptions one requires are not made on the basis of a complete understanding of the phenomenon [**]. Further, with the proper choice of assumptions, one can produce the result one intuitively feels is the most adequate.

A description of chemical reactions and their states employing mathematical structures, offers less to visualize but substantially avoids unjustifiable statements. It is beyond the scope of this article to discuss, in a detailed manner, the major objectives of mechanistic chemistry. We wish to generate a partially symmetrized topological coordinate system in order to discuss some examples of reactions whose mechanisms have previously been critically analyzed on the basis of sound experimental evidence.

A topological description yields some information on reaction mechanisms because the coordinates of the relevant particles, including the phase of the wave functions of the reacting species can be chosen in such a manner that there is conservation of coordinates during the reaction.

It is possible to choose the coordinates of certain parts of the reacting species in such a manner that the reactions can be described by permutation operators in analogy to the "isomerizer" description of isomerizations. Relative to the description of isomerization mechanisms, by virtue of the partitioning of the permutation groups S_n into their distinct classes [29a] of conjugate elements, it will also be possible to classify the mechanisms of the reaction between two (and more) reactants.
On this basis, it will be possible to establish rules concerning mechanistic alternatives in certain types of reactions.

The following brief discussion of certain symmetrical sets of lattice points will also be useful for the latter discussion of the topology of chemical reactions.

The lattice points |000|, |022|, |202|, and |220| are the vertices of a regular tetrahedron (T_d), as are the points |002|, |200|, |020|, and |222|. These eight points are also the vertices of a cube (O_h) or two interlocking tetrahedra, the di-dodecahedron (T_h). The six points |011|, |101|, |110|, |112|, |121|, and |211| lie in the centers of the faces of that cube and at the vertices of an octahedron (O_h). There are also sets of points which correspond to the vertices of a trigonal bipyramid (D_{3h}), *e.g.* |000|, |222| (the apical points), |021|, |102|, and |210|; if the points |012|, |120|, and |201| are added to the latter set, we have a hexagonal bipyramid (D_{6h}).

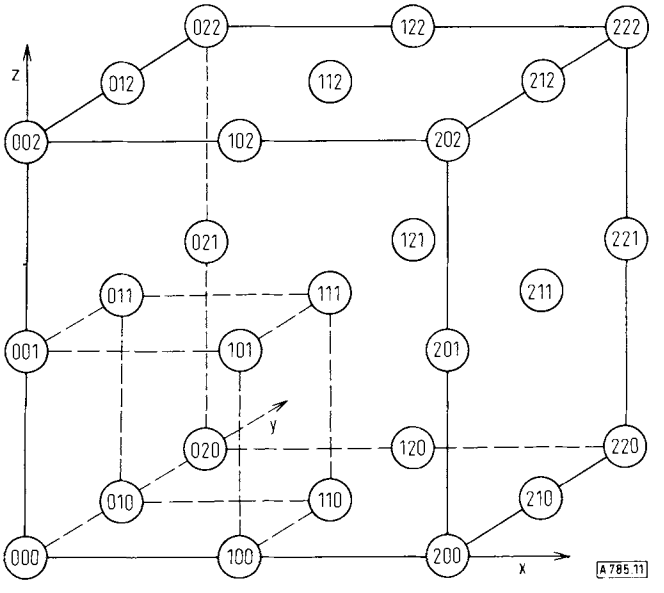
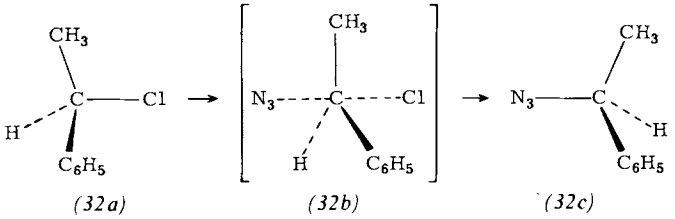


Fig. 11. Sets of points in a cubic lattice.

Finite sets of points belonging to the cubic point lattice and lattices which are contained within the cubic lattice are useful for the construction of coordinate systems with suitable permutational transformation properties and neighborhood relations to be applied to chemical reactions. A topology whose open sets contain the above mentioned finite sets of points as internal points can be chosen as a topological coordinate system for chemical reactions such that the coordinates of all relevant parts of the molecule are preserved throughout the reaction, from the starting material through the transition state to the final products.

Example 26



(32a) *(32b)* *(32c)*

The classical configurational correlation [33] of (+)-α-phenylethyl chloride *(32a)* and (−)-α-phenylethyl azide *(32c)* is chosen to illustrate the topological approach to a chemical reaction and its transition state.

[**] Cf., *e.g.*, Chem. Eng. News *48*, No. 22, 12 (1970).

[33] *E. D. Hughes, C. K. Ingold,* and *C. S. Patel,* J. Chem. Soc. *1933*, 526; see also: *E. D. Hughes* and *C. K. Ingold, ibid. 1933*, 1571; *1935*, 244; *J. L. Gleave, E. D. Hughes,* and *C. K. Ingold, ibid. 1935*, 255.

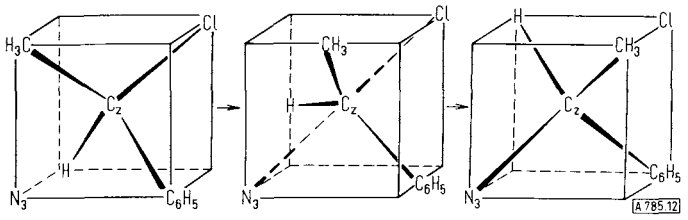


Fig. 12. Reaction *(32a)* → *(32b)* → *(32c)* in a topology oriented coordinate system.

The process whereby *(32a)* → *(32b)* → *(32c)* can be described in terms of a topology oriented skeletal coordinate system that applies to all participating species is pictured using the cubic lattice point set as follows:

$C_6H_5 \in \tau_1$, $CH_3 \in \tau_2$, $H \in \tau_3$, $Cl \in \tau_4$, $N_3 \in \tau_5$
$[000] \in \tau_5$, $\{[002], [102], [202]\} \in \tau_2$
$\{[020], [021], [022]\} \in \tau_3$
$\{[200], [210], [220]\} \in \tau_1$, $[222] \in \tau_4$

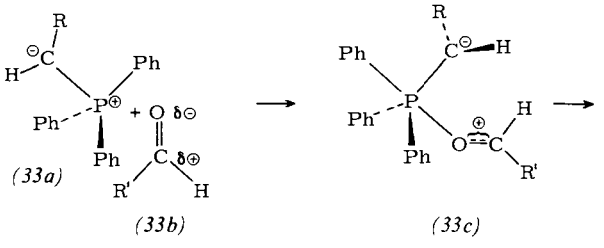
The central atom C_Z is represented by a distinguished point at the cross-section of the coordinates $\tau_1 - \tau_5$. Conservation of these coordinates throughout the process *(32a)* → *(32b)* → *(32c)* is characteristic of the S_n2 mechanism and is equivalent to a correlation of the configuration of *(32a)* and *(32c)*.

Example 27

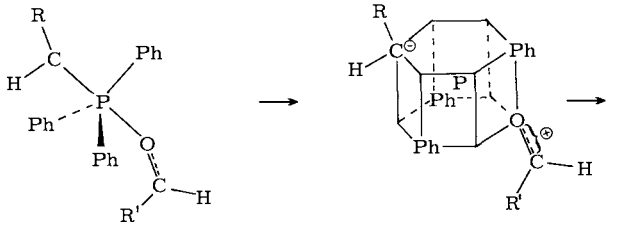
A trigonal bipyramidal adduct of the ylide *(33a)* and aldehyde *(33b)* has been suggested as an intermediate in the Wittig olefin synthesis [28f, 34]. This concept was recently invoked in an attempt to explain the preferential formation of *cis* isomers *(33i)* by *Wittig*'s kinetically controlled synthesis of 1,2-disubstituted olefins [34b].

Here it was assumed that the nucleophilic oxygen of an aldehyde *(33b)* attacks the electrophilic phosphorus of the ylide *(33a)* such that a trigonal bipyramidal adduct *(33c)* with an apical P–O bond and an equatorial P-carbanion bond was formed directly. It was further assumed that the *erythro*-intermediate *(33d)* was formed from *(33c)* by "a small anticlockwise rotation about the C–O bond" [28f]. A corresponding clockwise rotation would yield the *threo*-isomer of *(33c)* and thus the *trans*-olefin. Employment of the (2+3)-turnstile process (see Section 3.1.3.2) provides an alternate interpretation for the formation of these *cis*-olefins *(33i)* by the Wittig reaction in salt free, non-polar solvents at low temperatures [35].

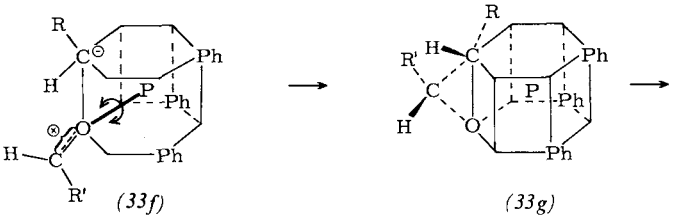
If the hypothesis of the "open-pyramid mechanism" is invoked at all, it is reasonable to assume that the nucleophilic oxygen of the aldehyde *(33b)* attacks the electrophilic phosphorus of the ylide *(33a)* on the side opposite the P-carbanion bond to give the trigonal bipyramidal intermediate *(33d)*.



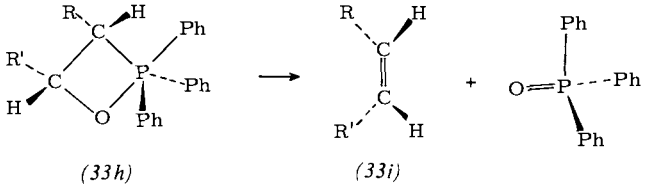
(33a) *(33b)* *(33c)*



(33d) *(33e)*



(33f) *(33g)*



(33h) *(33i)*

This is analogous to formation of an S_N2 transition state. The primary adduct *(33d)* is transformed by the (2+3)-turnstile mechanism into the intermediate species *(33f)* *via* *(33e)*. It is reasonable to assume that the conformations of *(33e)* and *(33f)* occur such that the (2+3)-turnstile process suffers minimal steric hindrance from the bulky groups R and R'. The stereochemical transformation of *(33f)* into *(33g)* arises from the fact that the carbonium ion moiety of *(33f)* can approach its carbanion moiety only through a rotation about the P–O bond. This is explained by observing that while resonance stability of the carbonium ion moiety of *(33f)* exists, groups H, C, R', O, and P must occupy a coplanar set of positions. A clockwise rotation about the P–O bond of *(33f)* leads to *(33g)*, the counterclockwise rotation generates the antipode of *(33g)*. Both *(33g)* and its antipode are intermediates of the *cis*-olefin formation. As long as there is no rotation about the C–O bond of the carbonium ion moiety, there can be no formation of the *trans*-olefin *via* the *threo*-isomer of *(33g)* or *(33h)* respectively.

The isocyanide-nitrile rearrangements [36] (and the S_Ni reactions) probably also occur through an intermediate state which resembles topologically the intermediate states of the (2+3)-turnstile rearrangement. It is even conceivable that some [37] of the reactions which have heretofore been considered to occur by an S_N2 mechanism do involve a (2+3)-turnstile type process. The topological consideration of this section may also be useful for the discussion of the pentacoordinate carbon systems [38].

We will refer to *Dewar*'s PMO formulation of the more than 30 year old Evans' rule as the Dewar-Evans' rule [39,40] of electrocyclic and related reactions:

[34] a) *L. D. Bergelson* and *M. M. Shemyakin*, Pure and Appl. Chem. *9*, 271 (1964); Angew.Chem. *76*, 113 (1964); Angew. Chem. internat. Edit. *3*, 250 (1964); b) *W. P. Schneider*, Accounts Chem. Res. *2*, 785 (1969).

[35] *M. Schlosser* and *K. F. Christmann*, Liebigs Ann. Chem. *708*, 1 (1967).

[36] *F. W. Schneider* and *B. S. Rabinovitch*, J. Amer. chem. Soc. *84*, 4215 (1962); *85*, 2365 (1963); *K. M. Maloney* and *B. S. Rabinovitch* in *I. Ugi*: Isonitrile Chemistry. Academic Press, New York 1970, in press.

[37] See *e.g.*: *J. L. Fry*, *C. J. Lancelot*, *L. K. M. Lam*, *J. M. Harris*, *R. C. Bingham*, *D. J. Raber*, *R. E. Hall*, and *P. v. R. Schleyer*, J. Amer. chem. Soc. *92*, 2540 (1970).

[38] *G. A. Olah*, *G. Klopman*, and *R. H. Schlosberg*, J. Amer. chem. Soc. *91*, 3261 (1969); *J. J. C. Mulder* and *J. S. Wright*, Chem. Phys. Lett. *5*, 445 (1970).

[39] *M. G. Evans*, Trans. Faraday Soc. *35*, 824 (1939).

[40] *M. J. S. Dewar*: The Molecular Orbital Theory of Organic Chemistry. McGraw-Hill, New York 1969 a) p. 319; b) p. 323; c) p. 335, 339.

"Thermal electrocyclic reactions take place *via* aromatic transition states. Photochemical electrocyclic reactions take place through excited forms of aromatic transition states" [40c].

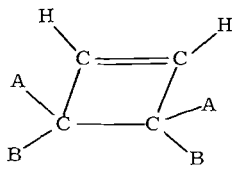
The thermal electrocyclic reactions can be considered as that class of reactions whose transition states are topologically equivalent to the aromatic hydrocarbons. Although *Dewar* did not use a topological formalism as the basis of his treatment of electrocyclic reactions, he was fully aware of the topological nature of the problem. He describes the transition states of the Diels-Alder reactions as "delocalized systems – topologically equivalent to, or isoconjugate with the π system in benzene" [40a]. The Dewar-Evans' Rule can be applied to an individual case by selecting such a topological coordinate system for the transition state that this system also applies to the isoconjugate hydrocarbon. By conserving the topology and suitably choosing coordinates throughout a chemical reaction one can correlate the features of interest (*e.g.* the stereochemistry) in the starting materials and products of the electrocyclic process.

Both in their essential content and consequences, the Dewar-Evans' rules are roughly an equivalent to the frontier-orbital [41] or correlation diagram [42] based Woodward-Hoffmann rules of orbital symmetry conservation [43].

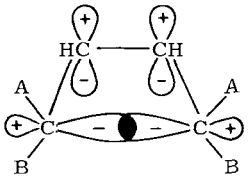
Yet, in some aspects, these rules differ. There are cases in which the application of the essentially topological Dewar-Evans' rules seem to be more simple and allow one to analyze a chemical situation more clearly, as in the case of the Cope rearrangement [40b] and the Diels-Alder synthesis [40,43]. Recently, *Mulder* and *Oosterhoff* [44] announced rules concerning the conservation of permutational symmetry which seem to be particularly clear, general, and theoretically well founded in their application to electrocyclic reactions and related processes.

The Woodward-Hoffmann rules [43] are primarily oriented towards geometrical symmetry. They can also be stated in the form of topological skeletal coordinate conservation.

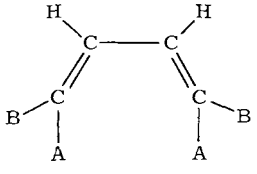
Example 28



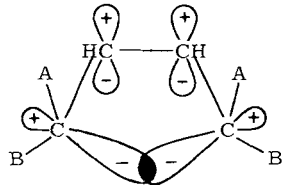
(34a)



(34b)



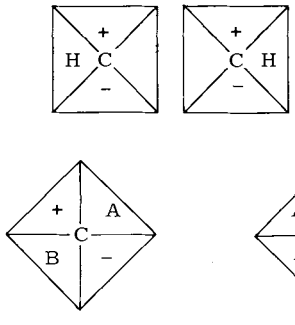
(34d)



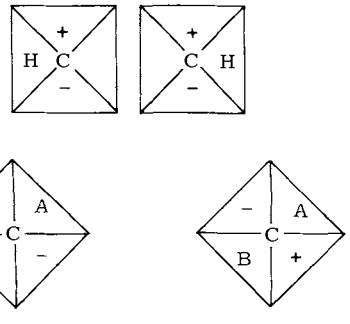
(34c)

The prediction of the stereochemistry of the process *(34a)* to *(34d)* by the Woodward-Hoffmann frontier orbital treatment is symbolized by the disrotatory opening *(34c)* → *(34d)*.

The topological equivalent of the process *(34a)* → *(34d)* results from the conservation of the topological coordinates during the entire reaction.



(34e)



(34f)

As can be seen immediately, the set of coordinates of *(34e)* apply to the transition state *(34c)* of the disrotatory process as well as the initial and final states *(34a)* and *(34d)*. This treatment could also be represented algebraically by mapping the set of indices to those parts of the involved species of interest onto the set of their coordinates but in this case the simple graph suffices.

There is no set of coordinates conserved during the contrarotatory analog of the process *(34a)* → *(34d)* if one forbids the overlap of orbitals which are not in phase. For example, if one takes the coordinates of *(34f)* of a conrotatory transition state, the in-phase overlap of the C–C σ bond of *(34a)* that is being opened has as a consequence an out-of-phase π overlap of *(34d)* and *vice versa*.

4. Conclusion

The authors' intention was clearly not to expound and exemplify all the aspects and applications of modern mathematics to chemistry. Neither is this an effort to present a complete and perfect discussion of the utility of mathematical structures to chemistry. In many areas, our treatment is open to profound improvement. Often, only the surface is scratched, hopefully deeply enough to stimulate interest and to point in a promising direction for further develop-

[41] *K. Fukui, T. Yonezawa,* and *H. Shingu,* J. Chem. Phys. *20,* 722 (1952); *K. Fukui, T. Yonezawa, C. Nagata,* and *H. Shingu, ibid. 22,* 1433 (1954); *K. Fukui* and *O. Sinanoglu:* Modern Quantum Chemistry. Academic Press, New York 1965, Vol. 1, p. 49.

[42] *R. Hoffmann* and *R. B. Woodward,* J. Amer. chem. Soc. *87,* 2046 (1965); *H. C. Longuet-Higgins* and *E. W. Abrahamson, ibid. 87,* 2045 (1965).

[43] *R. Hoffmann* and *R. B. Woodward,* Science *167,* 825 (1970); *R. B. Woodward* and *R. Hoffmann,* Angew. Chem. *81,* 797 (1969), Angew. Chem. internat. Edit. *8,* 781 (1969), and preceding papers cited there; see also: *J. J. Vollmer* and *K. L. Servis,* J. Chem. Educ. *45,* 214 (1968); *47,* 491 (1970).

[44] *J. J. C. Mulder* and *L. J. Oosterhoff,* Chem. Commun. *1970,* 305, 307.

ment. It should be noted that this paper is a compromise between imperative mathematical rigor and the desire to present a document that will be readable and comprehensible.

The apparent overemphasis of classification problems and nomenclature resulted from the obvious application of elementary topological and group theoretical concepts to these problems, and the desire to illustrate the direct applications of basic mathematical structures. Further, the definition of a nomenclature is only useful if it is complete with regard to its whole scope and its limitations, which, for our case, is all of chemistry. Macromolecules could have been included by some additional definitions, but the authors feel that this would over-extend the introduction of the present concept.

Many different systems of chemical nomenclature have been peopoaed, some specifically designed for convenient handling of rather limited sets of very similar compounds, such as the cholestane derivatives, whereas others are defined to serve as a universal nomenclature. Some of these proposed nomenclatures have found general acceptance, while others were never mentioned again, quite often undeservedly.

The present permutational nomenclature differs considerably in some essential features from any previous attempt to create a universal chemical nomenclature which does not break down in "pathological cases", *i.e.* for molecules with complicated skeletons and involved stereochemistry. In contrast to other systems, the permutation nomenclature deals with the molecule as an entity, and dissects it only in exceptional cases, which are described separately, as is done with the (*R*),(*S*)-nomenclature of molecules with more than one element of chirality. In contrast to the systems of nomenclature in current use, the descriptor does not tell "what a molecule looks like", but it is an instruction on how to draw or let a computer draw the steric formula of the molecule, or (which is often more easily done) how to construct a steric model of the molecule, *e.g.* a Dreiding model. The descriptors of molecules are based upon the representation of the molecule by an algebraic formalism, which in fact, is a general principle of order in chemistry and provides a framework of thought which helps to understand the steric aspects of chemistry.

There are many cases in which the conventional nomenclatures are fully adequate and more convenient to use than this descriptor system. For open chain chiral compounds (of *class* ***a***) with only a few elements of chirality (*e.g.* "asymmetric carbons") the (*R*),(*S*)-nomenclature works well and is easier to use than the descriptors. On the other hand, the (*R*),(*S*)-nomenclature is very cumbersome to use or fails completely with compounds like *(3)*, for which, to our knowledge, there is no other adequate system of nomenclature than the present. The metal complexes with a coordination number higher than four are compounds for which the permutational nomenclature seems to be the only acceptable solution to the nomenclature problem [45].

For molecules with a polycyclic skeleton and complicated stereochemistry the permutational nomenclature is superior and often the only satisfactory description of the molecule, with the exception of some classes of very similar compounds which have their own specific reference system and nomenclature, like the steroids.

[45] Cf. *K. A. Jensen*, Inorg. Chem. *9*, 1 (1970).

Some of the computer-oriented nomenclature systems [46] which have been developed recently are called topological nomenclature systems. These systems do not use the concept of topological spaces for the representation of steric features, but represent the chemical constitution of molecules in terms of graph theory.

Since the treatment of enantiotopicity [47], diastereotopicity [47], and prochirality [48] according to the present formalism follows in a straightforward manner from the principles presented, in addition to the definitions and procedures included herein, no chapter on these subjects will be found.

Within the framework of thought, as presented here, chirality appears only as a secondary aspect of permutational isomerism. Chirality is, however, a phenomenon which is relevant to chemistry, and a test for any theoretical treatment of the steric aspects of chemistry. A formalism which fails to deal adequately with chirality is severely limited in its application to stereochemistry.

The present formalism does not represent the mirror image of a chiral object as the mirror image "as reflected by a plane mirror"; it does, however, represent molecules in such a manner that the algebraic representations of mirror images differ, and it deals with chiroids of both *classes*, ***a*** and ***b***, adequately.

The discussion of an alternate mechanism for pentacoordinate isomerization was introduced in an effort to show how the extension of the algebraic formalisms led to the reinvestigation of a reaction. The mechanism proposed for the Wittig reaction on the basis of the turnstile discussions illustrates the use of the formalism further.

The utility of topological concepts for the discussion of reaction mechanisms has already been recognized by several authors. *Evans* [39] and *Dewar* [40] applied the topological concept of isoconjugation to transition complexes, a particularly important contribution in this context.

The present authors will discuss the relation of mathematical structures and chemical reactions in greater detail in the near future. A promising field of application is biochemistry. Hydrophobic interactions, quaternary structures of proteins, the nucleic acid structures, and enzymatic processes are some of the problems to which the present concept could be applied.

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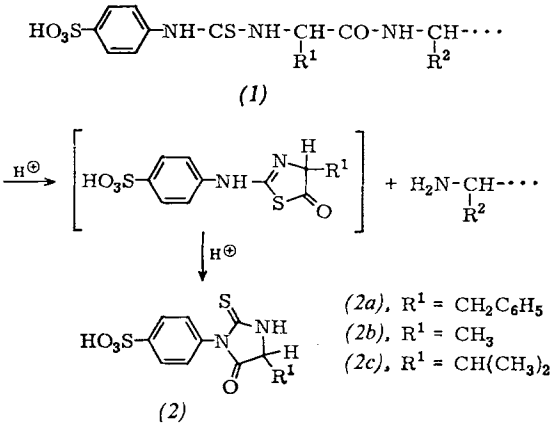
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4-Isothiocyanatobenzenesulfonic Acid as Reagent for Edman Peptide Degradation

By *Christian Birr*, *Christian Reitel*, and *Theodor Wieland*[*]

The method developed by *Edman*[1] for the sequential analysis of peptides — in which the N-terminal amino acid of a protein is made to react with phenyl isothiocyanate, cleaved off as 5-thiazolinone, and subsequently detected after rearrangement to the thiohydantoin derivative — has been modified in many ways. All variants of the degradation, however, suffer from a common failing: Incompletely degraded portions of peptide are present in the next degradation cycle; hence, from step to step in the degradation reaction there appear more and more thiohydantoins so that after a few cycles it becomes more difficult and finally impossible to identify the main product of degradation. This is particularly true in the case of monotonous peptide sequences.

We have now found that the use of 4-isothiocyanatobenzenesulfonic acid, as suggested by *Just*[2], affords a simple means of identifying the degradation products of a peptide sequence. The sulfonated phenylthiocarbamoyl peptide *(1)* occurring in this Edman degradation can be separated quite easily from unreacted peptides by ion-exchange chromatography on DEAE Sephadex (Cl^- form, diameter 1.5 cm, length 20 cm) using 0.1 N HCl as eluent. On evaporating the acid eluate the N-terminal amino acid derivative is cleaved from the peptide and immediately rearranges to the 4-sulfophenylthiohydantoin *(2)*. The peptide, which is now shorter by one amino acid is separated from the cleaved amino acid derivative by further chromatography on the DEAE Sephadex column before carrying out the next degradation step. The compound *(2)* eluted from the column can be unequivocally identified as the pure substance by thin-layer chromatography using an authentic sample for comparison.



We tested the new variant of the degradation on the tripeptide Phe-Ala-Val which we had treated according to the procedure given by *Edman*[1]. The peptide (2 mmole, 670.8 mg) was dissolved in pyridine/water (1:1; 25 ml); the pH of the solution was adjusted to 8.7 by addition of 1 N NaOH. The addition of sodium 4-isothiocyanatobenzenesulfonate (4 mmoles, 950 mg) dissolved in pyridine/water (1:1) was carried out at this pH and 40 °C. Reaction was complete after 25 minutes. The reaction mixture was then extracted twice with benzene and the aqueous phase neutralized and evaporated at 30 °C under vacuum. The resulting residue was dissolved in water and transferred to the above mentioned DEAE Sephadex column; this was eluted with 0.1 N HCl. The unreacted peptide (<10 %) passed through the column along with the neutral front and was collected after *ca.* 2 minutes at a high throughput rate; the sulfonated thiocarbonyl peptide *(1)*, on the other hand, was contained in the acid eluate collected after about 30 minutes. On evaporation at 30 °C under vacuum, the dipeptide was cleaved and the substituted phenylalanine simultaneously cyclized to the 4-sulfophenylaminothiohydantoin derivative *(2a)*. The separation of the components was, once again, achieved by ion-exchange chromatography. The second and third degradation step was carried out in the same way using 0.26 mmole (50 mg) of Ala-Val and 25 mg of valine and gave the alanine derivative *(2b)* and valine derivative *(2c)* respectively. The authentic amino acid derivatives *(2a)—(2c)* (S-PTH derivatives) were characterized by elemental analysis, IR spectroscopy (carbonyl absorption 1755—1760 cm^{-1}), UV spectroscopy (λ_{max} = 273 nm), and thin-layer chromatography [2-butanone/glacial acetic acid/water (20:1:4); *(2a)*: R_f = 0.55; *(2b)*: R_f = 0.40; *(2c)*: R_f = 0.50].

If the degradation steps are not carried out in the absence of oxygen, then small amounts of hydantoin amino acid derivatives are formed from the thiohydantoin during the chromatographic separation; however, the sequence analysis remains unimpaired. This type of degradation can be readily mechanized.

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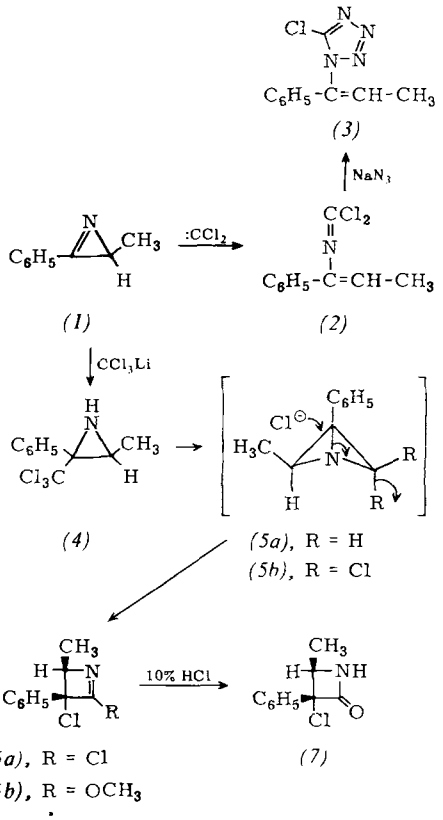
Reactions of Azirines. Synthesis and Properties of a 1-Azetine[**]

By *Alfred Hassner*, *J. O. Currie, Jr.*, *A. S. Steinfeld*, and *R. F. Atkinson*[*]

In connection with our studies on azirines[1] we found that addition of dichlorocarbene to 3-methyl-2-phenylazirine *(1)* does not lead to substituted azabicyclobutanes but to the open ring products *(2)*. Stepwise nucleophilic addition of trichloromethyllithium to *(1)* followed by treatment with base gave 2,3-dichloro-*cis*-4-methyl-3-phenyl-1-azetine *(6a)*, presumably *via* the azabicyclobutane *(5b)* as intermediate. Azetines represent a rare class of heterocycles of which only few 2-alkoxy or thioalkyl derivatives have been reported[2,3].

Azirine *(1)*[4] on refluxing with $C_6H_5HgCCl_3$ (a source of dichlorocarbene[6]) led in 60 % conversion to the dichloromethyleneamine *(2)*, which is converted by sodium azide to tetrazole *(3)* and by aqueous acid to propiophenone. On the other hand, treatment of *(1)* with trichloromethyllithium at −100 °C gave after distillation (80 °C/0.5 torr) *cis*-3-methyl-2-phenyl-2-trichloromethylaziridine *(4)* in 75 % yield [IR (neat): ν = 3290 cm^{-1} (NH); NMR (CCl_4): τ = 2.3—2.8 (5-phenyl-H/m), 7.10 (1 C—H/q), J = 5.7 Hz, 8.1 (1 N—H/br. s), 9.07 (3-methyl-H/d), J = 5.7 Hz].

Slow addition of potassium *tert*-butoxide to a solution of *(4)* in DMSO gave a product which on preparative thin layer chromatography (PF_{254} silica gel) with chloroform furnished 2,3-dichloro-*cis*-4-methyl-3-phenyl-1-azetine *(6a)* in 51 % yield. The ^{1}H-NMR spectrum of *(6a)* in carbon tetrachloride shows τ = 2.62 (5 phenyl-H/s), 5.58 (1 C—H/q), J = 6.7 Hz, and 9.07 (3 methyl-H/d), J = 6.7 Hz. The isomeric azabicyclobutane structure *(5b)* was discarded on the basis of



(6a), R = Cl
(6b), R = OCH_3

the ^{13}C-NMR spectrum and since the ^1H-NMR spectrum of *(5a)*, prepared by dimethylsulfonium methylide addition[7] to *(1)*, shows its *endo* ring proton absorption at $\tau = 8.6$. The mass spectrum and elemental analysis also support the structure *(6a)*. The strong IR band at 1580 cm^{-1} is consistent with the C=N in four-membered rings.

The reactivity of azetine *(6a)* was significantly different from that of azabicyclobutanes which are very acid sensitive. Although mild sensitivity to air was observed, *(6a)* was recovered unchanged (80 % yield) on stirring in anhydrous ether saturated with HCl for 40 h at 25 °C. In 10 % aqueous HCl, 3-chloro-*cis*-4-methyl-3-phenyl-2-azetidinone *(7)* was obtained [IR (CCl_4), 1770 cm^{-1} (C=O); NMR ($CDCl_3$): τ = 2.6 (5 phenyl-H and 1 N—H/m), 5.81 (1 C—H/q), J = 6.4 Hz, 9.11 (3-methyl-H/d), J = 6.4 Hz]. An isomeric 3-azetidinone structure was excluded by the exact mass spectrum of *(7)*. Chloroazetine *(6a)* is slowly converted to the ether *(6b)* with $NaOCH_3$.

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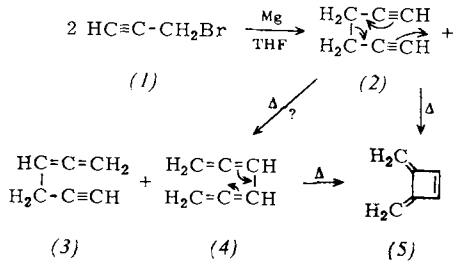
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1,2,4,5-Hexatetraene (Biallenyl)

By *Henning Hopf*[*]

When propargyl bromide *(1)* is treated with magnesium in tetrahydrofuran, 1,5-hexadiyne *(2)*, 1,2-hexadien-5-yne *(3)*, and 1,2,4,5-hexatetraene (biallenyl) *(4)* are formed[1]. Of these products, only *(2)* has so far been characterized in detail.

By adopting *Groizeleau-Miginiac*'s procedure[1d], we have now succeeded in isolating 1,2,4,5-hexatetraene *(4)*, which on heating is isomerized to 3,4-dimethylenecyclobutene *(5)*.



Gas-chromatographic analysis of the mixture of C_6H_6 isomers obtained from *(1)* shows that it consists of 60 % of *(2)*, 25 % of *(3)*, and 15 % of *(4)*. Pure biallenyl may be obtained by preparative-scale gas chromatography on either a DBP column at 30 °C or a carbowax column at 60 °C. The compound (n_D^{20} = 1.5356) crystallizes as needles (m.p. −36 °C) at −78 °C and is stable for a few hours at this temperature. At room temperature it discolors and a brownish-yellow polymeric material is precipitated. Solutions in tetrahydrofuran, diethyl ether, or pentane are stable for months at −35 °C.

The spectra exhibit features that are typical for allenes: NMR (δ, ppm): 4.92 (4 H/m), 5.63 (2 H/m). IR (CCl_4): 1951 and 851 cm^{-1} (no bands at 3300 and 2100 cm^{-1}). UV (*n*-hexane): shoulder at 225 nm (ε = 15000). Mass spectrum: *m/e* 78 (M), 63, 51, 39[2].

1,2,4,5-Hexatetraene *(4)* has been suggested as an intermediate in the thermal isomerization of 1,5-hexadiyne *(2)* to 3,4-dimethylenecyclobutene[3–5]. We have found that *(4)* is pyrolyzed quantitatively to *(5)* (200 ± 1 °C/35–65 torr, 15 min). A number of substituted 1,2,4,5-hexatetraenes are known to behave analogously[3,6]. The gas chromatogram of the fresh pyrolyzate shows a single peak whose retention time and mass spectrum are identical with those of an authentic sample of *(5)*[2].

The half-life for the conversion of *(4)* into *(5)* at 151 ± 1 °C is about 10 min. Using the kinetic data of *Huntsman* and *Wristers*[4], a half-life of 16 days is calculated for the isomerization of *(2)* to *(5)* at 151 °C. Provided that *(4)* is an intermediate in this process, the conversion of *(2)* into *(4)*, which may be formulated as a Cope-type rearrangement, is the rate-determining step in the cyclization of *(2)* to *(5)*.

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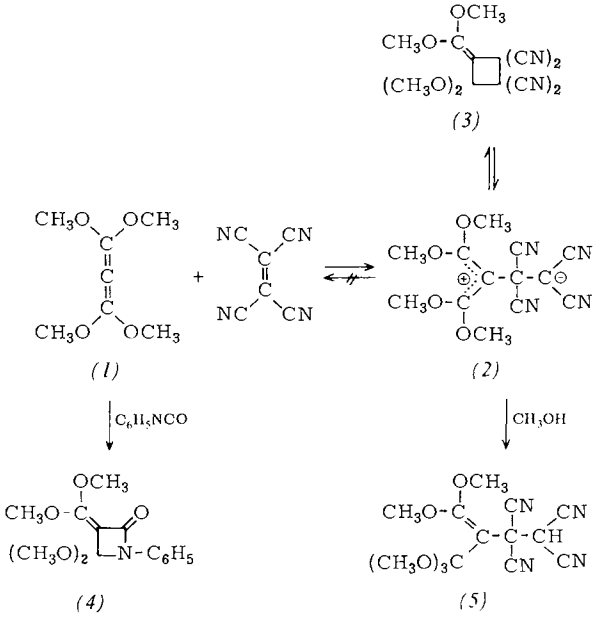
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The Adduct of Tetramethoxyallene and Tetracyanoethylene

By *R. W. Hoffmann* and *W. Schäfer* [*]

We report here on a two-step (2 + 2) cycloaddition, in which the second step is reversible at room temperature [1]: On mixing toluene solutions of tetramethoxyallene *(1)* [2] and tetracyanoethylene the color of the toluene-tetracyanoethylene CT complex immediately disappeared. Colorless crystals of an unstable 1:1 adduct (decomp. pt. 105–110 °C) gradually separated (yield 93 %) whose NMR spectrum ($CDCl_3$) exhibits only one singlet at $\tau = 6.23$. This is *prima facie* hardly consistent with structure *(3)*, which corresponds *e.g.* to that of the (2 + 2) cycloadduct *(4)* of *(1)* and phenyl isocyanate [3]. On the other hand, one can equally well discount the presence of the 1,4-dipole *(2)*, since the tetramethoxyallyl cation shows a resonance signal at $\tau = 5.75$ [4].



That a dynamic phenomenon is involved here was shown by recording the NMR spectra during cooling of a CD_2Cl_2 solution: below −50 °C a broadening of the signal at $\tau = 6.23$ was observed; at lower temperatures the signals expected for *(3)* at $\tau = 5.75$, 5.90, and 6.30 (1:1:2, half-width at −95 °C still 4 Hz) became recognizable. Accordingly, at −65 °C there is a rapid exchange process ($k > 60$ s^{-1}) of all methoxy groups in *(3)*. This is not due to complete reversibility of the cycloaddition, for no tetramethoxyallene *(1)* can be trapped from solutions of *(3)*: On addition of phenyl isocyanate to a solution of *(3)* the adduct *(3)* was recovered unchanged, whereas treatment of *(1)* under the same conditions led to the ready formation of *(4)*. Compound *(4)* did not react with tetracyanoethylene. Moreover, treatment of a solution of *(3)* with methanol did not yield hexamethyl orthomalonate [2]; instead the 1,4-dipole *(2)* underwent methanolysis to *(5)* [1] — as the NMR spectra of the solution after treatment with CH_3OH [s at $\tau = 4.83$, 6.11, 6.13, and 6.67 (1:3:3:9)] or CD_3OD [s at $\tau = 6.11$, 6.13, 6.67 (3:3:6)] suggest. Hence, at room temperature *(2)* and *(3)* are fully equilibrated while decomposition of *(2)* into its components could not be detected.

The equilibrium between *(2)* and *(3)* lies predominantly on the side of *(2)*. This follows from a comparison of the chemical shifts of the methoxy signals of the equilibrating mixture in CD_2Cl_2 ($\tau = 6.16$) with the average value of the signals of *(3)* at −95 °C ($\tau = 6.06$) and with the signal of the tetramethoxyallyl cation ($\tau = 5.75$, $CHCl_3$).

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[4] From *(1)* and fluorosulfonic acid in chloroform.

Simple Synthesis of Phosphorofluoridous Acid, $H[PHO_2F]$ [**]

By *Hans Falius* [*]

While the fluoro acids $H_2[PO_3F]$ and $H[PO_2F_2]$ derived from orthophosphoric acid have been known for a long time, phosphorofluoridous acid $H[PHO_2F]$ *(1)* has so far defied all attempts at isolation in pure form. The formation of *(1)* in the hydrolysis product of PF_3 and in an aqueous solution of $H_2[PHO_3]$ and HF has been established by *Blaser* and *Worms* [1] on the basis of the reaction behavior. *Centofanti* and *Parry* [2] obtained milligram quantities of the acid, contaminated with PF_3, on dismutation of liquid $PHOF_2$. The product obtained by *Heinz* and *Röhner* [3] from P_4O_6 and HF, however, appears to be the adduct $HF \cdot H_2[PHO_3]$ instead of $H[PHO_2F] \cdot H_2O$ [4].

The hexatomic compound *(1)* is the first to contain just one H atom and one F atom bound to the same atom of phosphorus. It is formed rapidly according to the equation:

$$PCl_3 + 2\,H_2O + HF \rightarrow \underset{(1)}{H[PHO_2F]} + 3\,HCl$$

Formation of $H_2[PHO_3]$ *(2)* and $H_2[P_2H_2O_5]$ *(3)* as by-products of the reaction cannot be suppressed. On use of DF and D_2O the reaction yields the deuterated acid $D[PDO_2F]$ *(4)*.

The acid *(1)* is a liquid at room temperature ($d_4^{20} = 1.587$ g cm^{-3}; $n_D^{20} = 1.3682$). On heating it decomposes above about 70 °C with foaming (phosphine formation); when cooled it solidifies to a glass at about −100 °C. Extrapolation of a few vapor-pressure measurements between 0 and 30 °C gave b.p. 209 °C. The heat of vaporization is $\Delta H_{298} = 8300$ cal $mole^{-1}$, and the entropy of vaporization is $\Delta S_{298} = 17.2$ e.u. Thus association occurs in the vapor state.

Since *(1)* is hydrolyzed in aqueous solution, salts cannot be prepared in that medium. The acid is insoluble in apolar solvents. The first salts to be prepared, *i.e.* $Li[PHO_2F]$ *(5)* and $Li[PDO_2F]$ *(6)*, were obtained smoothly by reaction of ethereal solutions of *(1)* and *(4)*, respectively, with LiBr.

In each of the ^1H-, ^{19}F-, and ^{31}P-NMR spectra (external standards: $(CH_3)_4Si$; CF_3COOH, 85 % H_3PO_4) of *(1)* (cf. ref. [2]), a doublet of doublets is observed, as expected for an AMX system; the ^1H-NMR spectrum contains an additional singlet for the OH proton.

^1H-NMR: $\delta_{HP} = -7.89$, $\delta_{HO} = -14.2$ ppm; $J_{HP} = 779$, $J_{HF} = 113$ Hz.

^{19}F-NMR: $\delta = -15.5$ ppm; $J_{FP} = 1032$, $J_{FH} = 115$ Hz.

^{31}P-NMR: $\delta = -2.97$ ppm; $J_{PH} = 785$, $J_{PF} = 1032$ Hz.

The spectra of *(4)* each contain a doublet of triplets having

^{19}F-NMR: $\delta = -14.6$ ppm; $J_{FP} = 1030$, $J_{FD} = 17.3$ Hz and

^{31}P-NMR: $\delta = +2.1$ ppm; $J_{PD} = 119$, $J_{PF} = 1027$ Hz.

The frequency of νPH in *(1)* is remarkably high; $PHOF_2$ also gives a similarly high value of 2503 cm^{-1} [2].

IR and Raman spectra:

H[PHO$_2$F] *(1)* Raman	D[PDO$_2$F] *(4)* Raman	Li[PHO$_2$F] *(5)* IR	Li[PDO$_2$F] *(6)* IR
2510s (p) νPH	1828s (p) νPD	2462vs νPH	1747s νPD
1020s νPO	1040s (p) νPO	1247vs $\nu_{as}PO_2$	1241vs $\nu_{as}PO_2$
996s δHP	947m(p)νP-OD	1137vs ν_sPO_2	1140vs ν_sPO_2
952m(p)νP-OH	890s (p)νPF	1053s δHP	855vs νPF
884vs (p) νPF	743s δDP	1010vs δ HP	776s δDP
524s	645w	857vs νPF	742s δDP
427s	583w	565s	560s
412s	505s (p)	479s δ	478s δ
	408s	372s	381s

Experimental:

A solution of 40 % HF (10.0 g, 0.2 mole) in ether (80 ml) is added dropwise with ice-cooling to a stirred solution of PCl_3 (27.5 g, 0.2 mole) in anhydrous ether (30 ml). The ether must be dry in order that a check may be kept on the amount of water present. After removal of ether and HCl at reduced pressure, the oily residue, consisting of *(1)*, *(2)*, and *(3)*, is fractionated in a high vacuum below 50 °C: *(1)* is collected in a cold trap at −23 °C (CCl_4 solid/liquid). After two more distillations under the same conditions, most conveniently into traps connected in series, the yield is about 5 g (30 %).

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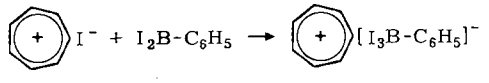
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Tropylium Triiodophenylborate[1]

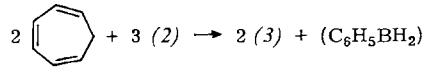
By *Walter Siebert*[*]

Although the iodide ion is a rather weak Lewis base, it reacts with triiodoborane in the presence of the stabilizing trityl cation to form the tetraiodoborate ion[2]. We have now been able to synthesize the first example of the monosubstituted complex ion $[R-BI_3]^{\ominus}$ by allowing tropylium iodide *(1)* to react with diiodophenylborane, a weaker Lewis acid than BI_3.

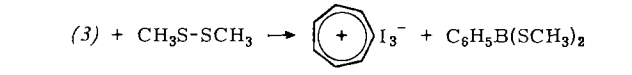


(1) *(2)* *(3)*

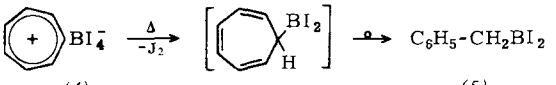
Tropylium triiodophenylborate *(3)* can be obtained in a 71 % yield in a more refined method from cycloheptatriene and *(2)* by hydride transfer from carbon to boron; the non-isolable phenylborane is thought to be formed in the reaction.



Like tropylium tetraiodoborate *(4)*[2], which is prepared from C_7H_8 and BI_3, the compound *(3)* has a brilliant yellow color which rapidly turns brown in moist air. Ether cleavage, a characteristic reaction for B—I compounds, leads in the case of *(3)* to the formation of *(1)*, ethyl iodide, and di(ethoxy)phenylborane. Both *(3)* and *(4)* undergo a redox reaction with dimethyldisulfane — the former yielding tropylium triiodide and di(methylthio)phenylborane and the latter yielding tropylium triiodide, tri(methylthio)-borane, and iodine.



We assume that the disulfane does not attack the sp^3-hybridized boron atom in *(3)* or *(4)* but rather the sp^2-hybridized starting compounds *(2)* and BI_3 which are in equilibrium with *(3)* and *(4)*, respectively. No formation of methylthioborates was observed in the reaction. Thermal decomposition of *(3)* leads mainly to *(1)* and *(2)*; however, an intramolecular redox reaction with formation of iodine also takes place. An analogous elimination of halogen is observed on heating of tropylium tetrachloroborate which leads to the formation of benzyldichloroborane in 31 % yield[3]. Although iodine ought to be a much more favorable leaving group than chlorine, the cleavage of iodine from *(4)* followed by ring contraction has not yet been used for the preparation of benzyldiiodoborane *(5)*, first synthesized by *Paetzold*[4], since the yields are only about 10 %.



(4) *(5)*

The presence of the triiodophenylborate is confirmed by elemental analysis, the redox reaction, and the ether cleavage, as well as from the IR spectrum[5] which shows a broad νBI band at 534 cm^{-1} that is slightly shifted to higher frequency in contrast to the νBI band at 517 cm^{-1} of $NH_4^+BI_4^-$[6].

Experimental procedure:

Since the reactants and products are sensitive to hydrolysis and oxidation, the reactions must be carried out in presence of an inert gas (N_2).

a) Compound *(2)* (1.4 g, 4.1 mmoles) is added dropwise with vigorous stirring to a solution of *(1)* (0.51 g, 3.2 mmoles) in methylene dichloride (100 ml). The suspension brightens as the red compound *(1)* goes completely into solution. The yellow crystals of *(3)* which separate after a few minutes are isolated, washed with CH_2Cl_2, and dried *in vacuo*: yield 0.8 g [62 % w.r.t *(1)*]; m.p. 121 °C (dec).

b) C_7H_8 (7.38 g, 80.2 mmoles) is added dropwise to a solution of *(2)* (8.87 g, 26.0 mmoles) in methylene dichloride (100 ml). A yellow precipitate forms immediately; this is isolated after 12 hours: yield 6.9 g (71.1 % w.r.t. *(2)*).

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Azido Metal Complexes as N_3 Generators

By *Wolfgang Beck* and *Karl Schorpp* [*]

The deep red solutions of tetraphenylarsonium salts with the complex anions $[Au(N_3)_4]^-$ and $[Pb(N_3)_6]^{2-}$ [1] in tetrahydrofuran (THF) or methylene dichloride are rapidly decolorized by the action of diffuse daylight, the central metal ion being reduced to form gold(I) and lead(II) complexes, respectively, and nitrogen being formed as oxidation product of the azide ligand:

$$\overset{+3}{[Au(N_3)_4]^-} \rightarrow \overset{+1}{[Au(N_3)_2]^-} + 3\ N_2$$

The color of these Au^{III} and Pb^{IV} complexes arises from CT transitions, which can be regarded as electron transfer from the azide ligand to the metal [1]. Formation of nitrogen is preceded by the following primary process [2]:

$$[M^{z+}(N_3^-)_n]^{(n-z)-} \xrightarrow{h\nu} [M^{(z-1)+}(N_3^0)\,(N_3^-)_{n-1}]^{(n-z)-}$$

In accordance with this scheme, it was possible to detect a one-electron reduction proceeding *via* Au^{II} for tetrachloroaurate(III) [3].

We attempted to detect the expected species N_3^0 by interception with olefins. Thus $AsPh_4[Au(N_3)_4]$ was dissolved in acrylonitrile, ethyl acrylate, or acrolein and the course of reaction followed by IR and NMR spectroscopy. When the solutions are exposed to daylight, the $\nu_{as}N_3$ bands of the complex $[Au(N_3)_4]^-$ become less intense and the characteristic absorptions of organic azides appear (Table 1).

Table 1. $\nu_{as}N_3$ bands of organic azides formed from azido complexes and olefins.

olefin	$\nu_{as}N_3$ (cm^{-1}) [a]
acrylonitrile	2112
ethyl acrylate	2132, 2107
acrolein	2157, 2110
cyclohexene	2141, 2114

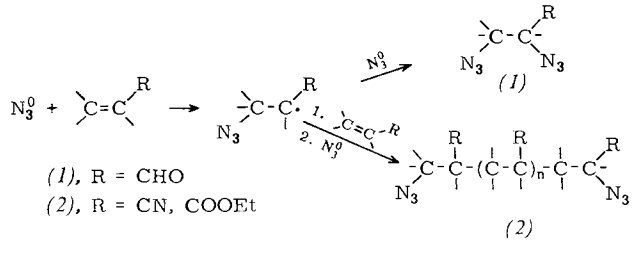
[a] The $\nu_{as}N_3$ bands of the azido complexes ($\approx$ 2030 cm^{-1}) differ appreciably from those of the organic azides.

In the ^1H-NMR spectrum, the effect of exposure to light is to reduce the intensity of the olefinic proton signals while simultaneously giving rise to new aliphatic proton signals.

Reaction of $(AsPh_4)_2[Pb(N_3)_6]$ with acrylonitrile or acrolein gives the same products.

On prolonged action of light on solutions of $AsPh_4[Au(N_3)_4]$ in the olefins mentioned above, the Au^{III} present is reduced to the metal; with acrolein in particular a coherent film of gold appears on the wall of the reaction vessel within a few hours at room temperature.

Photochemical reaction of the azido complexes with ethyl acrylate or acrylonitrile leads to polymerization [4]. The stability of the solutions in the dark and the observation that polymerization starts at the side of the reaction vessel that is turned to the light suggest a free-radical chain mechanism in which N_3^0 acts as chain initiator. The following reaction course is consistent with the experimental data [5]:



The reaction of $AsPh_4[Au(N_3)_4]$ with cyclohexene in THF, however, probably leads, by analogy with the reaction of cyclohexene with *N*-bromosuccinimide or highly dilute bromine, not to addition to the double bond but to substitution in the allylic position: the mass spectrum of the reaction solution was shown to contain the molecular ion of diazidocyclohexene.

N_3 transfer also occurs in the reaction of $Pt^0(PPh_3)_n$ (n = 3,4) with $AsPh_4[Au(N_3)_4]$ in THF/benzene. In these reactions N_3 behaves formally as a pseudohalogen in an oxidative addition, as in the reactions of halogens [6] or cyanogen [7] with $Pt(PPh_3)_n$. However, the reaction probably follows a bridge mechanism [8].

$$Pt(PPh_3)_n \rightleftharpoons Pt(PPh_3)_2 + (n-2)PPh_3$$

$$\overset{+3}{[Au(N_3)_4]^-} + \overset{0}{Pt(PPh_3)_2} \rightarrow \left(\begin{array}{c} N_3 \quad N_3 \quad PPh_3 \\ N_3 - Au - Pt \\ N_3 \quad N_3 \quad PPh_3 \end{array}\right)^{\ominus}$$

$$\rightarrow \overset{+1}{[Au(N_3)_2]^-} + \begin{array}{c} N_3 \quad PPh_3 \\ \overset{+2}{Pt} \\ N_3 \quad PPh_3 \end{array}$$

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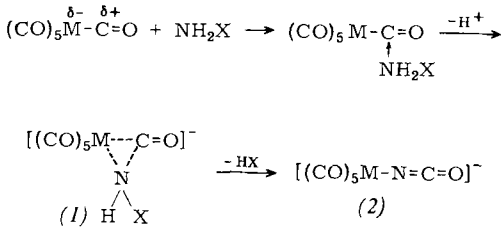
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Hofmann- and Lossen-Rearrangements of Metal Carbonyl Complexes

By *Wolfgang Beck* and *Boris Lindenberg* [*]

Reactions of metal carbonyl complexes in which a nucleophile attacks the positively charged C atom of a CO ligand include those with alkyl- and aryllithium compounds [1], hydroxide and alkoxide ions [2], ammonia [3] and amines [4], hydrazine [5], and the azide ion [6]. The latter reactions, *i.e.* of N_2H_4 or N_3^- with metal hexacarbonyls of chromium, molybdenum, and tungsten, lead to isocyanato complexes as stable end products.

We have now found that isocyanatopentacarbonylmetalates(0) $[M(CO)_5NCO]^-$ (M = Cr, Mo, W) are also formed under mild conditions in the reaction of $M(CO)_6$ with hydroxylamine or chloramine, presumably in accordance with the following reaction mechanism:



X = OH, Cl

The intermediates *(1)*, which can be formulated as the hydroxamic acid R—C(O)-NHOH or *N*-halogeno acid amide R—C(O)—NHCl (R = $M(CO)_5$), form stable isocyanato complexes by loss of H_2O or HCl respectively: this corresponds to the rearrangement in the Lossen degradation of hydroxamic acids and in the Hofmann degradation of carboxylic amides, in the same way that the reaction of $M(CO)_6$ with N_3^- [6] corresponds to the Curtius degradation of carboxylic azides. In contrast to organic isocyanates, which give primary amines and urethanes respectively on reaction with water or alcohol, the isocyanato complexes are stable toward solvolysis.

In reactions of longer duration both chloramine and hydroxylamine react oxidatively toward hexacarbonyls with formation of CO_2 and metal oxides. Furthermore, $W(CO)_5NH_3$ was detected as secondary product; in this case ammonia is present as a result of reduction or disproportionation of hydroxylamine. Other metal carbonyl compounds, *e.g.* $Mn(CO)_5Br$, react with NH_2OH to give isocyanato complexes.

Experimental procedure:

On uniting a suspension of the hexacarbonylmetal complex in ethanol with an ethanolic solution of hydroxylamine or chloramine (molar ratio $M(CO)_6:NH_2X$ = 1:4) the mixture immediately turns yellow. After a few minutes the tetraphenylarsonium salt of *(2)* [6] can be precipitated from the filtered solution with $[As(C_6H_5)_4]Cl$ by addition of water.

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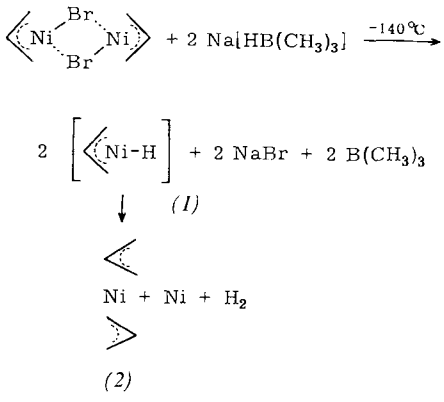
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π-Allylhydridonickel Compounds[1]

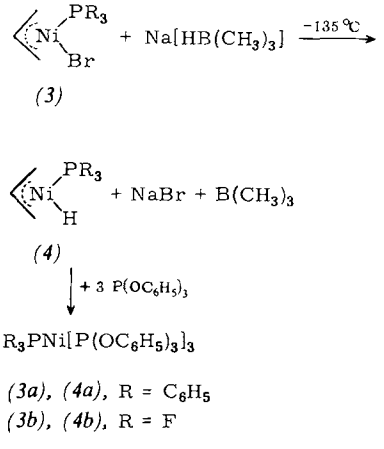
By *Helmut Bönnemann*[*]

The thermally labile compound π-allylmethylnickel [2] decomposes at temperatures above —80 °C with ligand exchange to give predominantly the *trans* isomer of bis(π-allyl)nickel [3].

The corresponding π-allylhydrido complex of nickel, which is not stabilized by further ligands, undergoes such a disproportionation even at extremely low temperatures. Thus, reaction of π-allylbromonickel with $Na[HB(CH_3)_3]$ [4] at —140 °C yields bis(π-allyl)nickel, which, according to the ^{1}H-NMR spectrum [5], is mainly present as the *trans* isomer *(2)* (94 %).

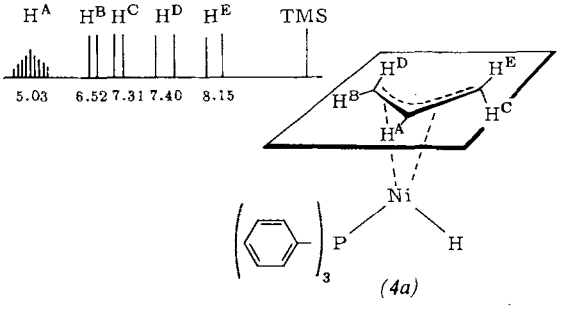


If, however, the 1:1 adducts *(3)* of phosphines and π-allylbromonickel are used as starting material then reaction with $Na[HB(CH_3)_3]$ at —130 °C gives the red-brown crystalline π-allylhydridonickel compound *(4)*, which reacts with an excess of triphenyl phosphite with transfer of the hydrogen bound to nickel to the π-allyl group and loss of propene.



(3a), *(4a)*, R = C_6H_5
(3b), *(4b)*, R = F

The triphenylphosphine addition compound *(4a)* is stable up to —30 °C. It can be seen from the ^{1}H-NMR spectrum [5] that the *syn*- and *anti* protons are not equivalent so far as pairing is concerned, thus suggesting a tetragonal-planar arrangement of ligands. The H atom attached to the nickel does not give a resonance signal in the region up to τ = 15.

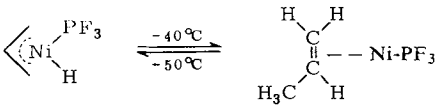


(4a)

The ^{1}H-NMR spectrum [5] of the trifluorophosphine adduct *(4b)* is remarkably dependent upon temperature. At —75 °C the characteristic signals of a symmetrically arranged π-allyl group appear at τ = 5.30 (*meso*), 7.27 (*syn*), and 8.50 (*anti*). If the sample is allowed to warm over a few hours to —40 °C the spectrum shows three further signals (multiplet, τ = 4.15; double doublet, centered at τ = 4.85; doublet at τ = 8.43) in the intensity ratio 1:2:3, which can

be assigned to a metal-bonded propene molecule. On recooling to −50 °C this process proved to be reversible.

Accordingly, a temperature-dependent equilibrium exists between the π-allylhydridonickel compound *(4b)* and a propene-Ni^0 complex *(5)*.



(4b) *(5)*

This is the first direct indication for the so-called "π-allyl mechanism" of olefin isomerization at a transition metal[6], which is believed to proceed *via* a 1,3-H shift: At −40 °C the hydrogen attached to the nickel transfers to the π-allyl group while at lower temperatures allylic C—H bonds of the olefin are cleaved from the nickel-ligand system with regeneration of the π-allyl group. If *(4b)* is replaced by the corresponding π-allyldeuterionickel compound it can be shown by ^{1}H-NMR spectroscopy that exclusively the C-1 and C-3 atoms of the propene in *(5)* are deuterated.

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The Si-Si Group as a Structural Unit in Open-Chain and Cyclic Phosphorus Ylides[1]

By *Hubert Schmidbaur* and *Wolfgang Vornberger*[*]

It is known that various ylide functions are considerably stabilized by silyl groups, and various possible explanations have been offered for this "silicon effect"[1,2]. Since a transition from the simple silyl group to structural units containing a chain of silicon atoms generally leads to far-reaching changes in bonding, which could arise from the formation of a (d-d)π system[3], we have now also studied alkyldisilanyl-substituted ylides.

Introduction of one pentamethyldisilanyl group proceeds readily:Pentamethyldisilanylmethylenetrimethylphosphorane *(2)* is obtained smoothly, both by dehydrohalogenation of the corresponding phosphonium salt *(1)* by butyllithium and by direct transylidation *in situ*.

$$(CH_3)_3PCH_2 + (CH_3)_3SiSi(CH_3)_2Cl \longrightarrow [(CH_3)_3\overset{\oplus}{P}\text{-}CH_2\text{-}Si(CH_3)_2Si(CH_3)_3]\,Cl^{\ominus} \quad (1)$$

$$(1) \xrightarrow{C_4H_9Li} (CH_3)_3P{=}CH\text{-}Si(CH_3)_2Si(CH_3)_3 \quad (2)$$

$$2\,(CH_3)_3PCH_2 + (CH_3)_3SiSi(CH_3)_2Cl \xrightarrow[-[(CH_3)_4P]Cl]{} (2)$$

The occurrence of deprotonation at the methylene bridge of the phosphonium salt affords a proof of the stabilizing effect that the $(CH_3)_5Si_2$ group exerts on the ylidic function; the effect is comparable with that of a $(CH_3)_3Si$ group. However, whereas a second silylation of the ylidic C atom occurs in the case of the $(CH_3)_3Si$ group, thus leading to an additional stabilization, the second disilanyl group always takes up a position in a side chain of the ylide to yield a product of type *(3)*.

$$3\,(CH_3)_3PCH_2 + 2\,(CH_3)_5Si_2Cl \xrightarrow[-2\,[(CH_3)_4P]Cl]{}$$

$$(CH_3)_2P(=CH\text{-}Si(CH_3)_2Si(CH_3)_3)(CH_2\text{-}Si(CH_3)_2Si(CH_3)_3) \quad (3)$$

$$\downarrow$$

$$(CH_3)_3P{=}C(Si(CH_3)_2Si(CH_3)_3)_2 \quad (4)$$

Compounds *(3)* undergo neither thermal nor catalytic rearrangement to the isomer *(4)*[4], a fact which we attribute to a steric effect of the β-silyl groups.

Confirmatory evidence is provided primarily by the ease with which cyclic ylides are formed in which the repulsive interaction of the substituents is eliminated by direct linkages:

$$(CH_3)_3P{=}CH\text{-}Si(CH_3)_3 \xrightarrow[2.\ C_4H_9Li]{1.\ (CH_3)_4Si_2Cl_2} (CH_3)_2P(=CH_2)(C(Si(CH_3)_2)_2Si(CH_3)_3) \quad (5)$$

$$6\,(CH_3)_3PCH_2 + 2\,(CH_3)_4Si_2Cl_2 \xrightarrow[-4\,[(CH_3)_4P]Cl]{} (CH_3)_2Si(C(P(CH_3)_3)Si(CH_3)_2)_2 \quad (6)$$

$$2\,(CH_3)_3P{=}C(Si(CH_3)_2Cl)_2 \xrightarrow{Li\ in\ THF} (6)$$

The stabilization of ylidic centers by Si—Si chains can be explained in terms of a delocalization of the carbanionic charge into the vacant orbitals of the silicon atoms of the p→(d-d)π type. The increased shielding of the β-methylsilyl protons in *(2)*, which even exceeds that of the α-methylsilyl protons, further supports this assumption:

$$R_3\overset{\oplus}{P}\text{-}\underset{H}{C}\text{-}SiR_2\text{-}\overset{\ominus}{SiR_3}$$

Experimental:

Preparation from 10 mmole amounts of starting materials afforded *(1)* in 80% yield: m.p. > 300 °C; ^{1}H—NMR ($CHCl_3$): δ CH_3P—134 Hz, d, $J(H_3CP)$ 13.9; δ CH_2—119 Hz, d, $J(H_2CP)$ 19.0; δ CH_3Si_α—23 Hz, s; δ CH_3Si_β—13 Hz, s; intensity ratio 9:2:6:9. — Reaction of *(1)* with C_4H_9Li affords the ylide *(2)*, yield greater than 50% (as in the trans-

ylidation also); m.p. −10 °C, b.p. 35 °C/0.1 torr; ^{1}H—NMR (without solvent): δ CH_3P −75 Hz, d, $J(H_3CP)$ 12.1; δ CH + 57.5 Hz, d, J(HCP) 6.5; δ CH_3Si_α + 6 Hz, s; δ CH_3Si_β + 8 Hz, s; intensity ratio 9:1:6:9.

(3) is formed from $(CH_3)_3PCH_2$ (52 mmoles) and $(CH_3)_5Si_2Cl$ (35 mmoles) as a colorless nondistillable liquid (yield 61 %); ^{1}H—NMR: δ CH_3P −34 Hz, d, $J(H_3CP)$ 12.0; δ CH_2 −17 Hz, d, $J(H_2CP)$ 15.5; δ CH + 65 Hz, d, J(HCP) 6.5; δ $CH_3Si_2CH_2$ + 15 Hz, s; δ CH_3SiCH_2 + 11 Hz, s; δ CH_3Si_2CH + 26 Hz, s; δ CH_3SiCH + 20.5 Hz, s; intensity ratio 6:2:1:9:6:9:6.

Treatment of the salt formed from $(CH_3)_3PCHSi(CH_3)_3$ (77 mmoles) and $(CH_3)_4Si_2Cl_2$ (39 mmoles) with C_4H_9Li (65 mmoles) gives a 20 % yield of *(5)*: b.p. 65 °C/0.1 torr; ^{1}H—NMR (without solvent): δ CH_3P −75 Hz, d, $J(H_3CP)$ 11.5; δ CH_2 −54 Hz, d, $J(H_2CP)$ 12.5; δ$(CH_3)_3Si$ + 1.5, s; δ $(CH_3)_2SiCH_2$ −5.5 Hz, s; δ $(CH_3)_2SiC$ −2 Hz, s; intensity ratio 6:2:9:6:6. Reaction of $(CH_3)_3PCH_2$ (55 mmoles) with $(CH_3)_4Si_2Cl_2$ (14 mmoles) in ether followed by filtration, distillation, and resublimation affords 17 % of *(6)*: m.p. 126–128 °C, sublimes at 138 °C/0.1 torr. Compound *(6)* is also formed in 30 % yield on reaction of $(CH_3)_3PC[Si(CH_3)_2Cl]_2$ [5] (20 mmoles) and finely divided lithium (300 mmoles) in THF (40 h, reflux); ^{1}H—NMR (benzene): δ CH_3P −25.5 Hz, d, J(HCP) 11.5; δ CH_3Si + 9 Hz, s; intensity ratio 3:4 [6].

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MINDO/2 Treatment of Species Present in Carbon Vapor[1]

By *Michael J. S. Dewar*, *Edwin Haselbach*, and *Muthanna Shanshal* [*]

The nature and properties of the species present in carbon vapor have aroused much interest in recent years; we have accordingly studied three of these, *i.e.* C_2, C_3, and C_5, using a recently developed semiempirical SCF MO method (MINDO/2 [3]), which has been shown to give good estimates of geometries and heats of formation for a wide range of carbon compounds. In its current form, the treatment cannot be applied satisfactorily to triplet states; C_4 had therefore to be excluded.

Calculations were carried out for various possible geometries of the various species and the equilibrium geometries were then estimated by parabolic interpolation.

Both C_3 and C_5 are predicted to be linear; CC stretching force constants were calculated from the variation in total energy with bond length. The results are compared with experimental values, where available, in the Table; while the geometry of C_5 has not yet been studied, that of C_3 is linear, as predicted.

The agreement between the calculated and observed heats of formation is reasonably good in view of the uncertainties in the experimental values (cf. [8]).

Species	Heat of formation (kcal/mole)		Bond length (Å)		Force constant (dyne/cm × 10^{-5})	
	calc.	obs.	calc.	obs.	calc.	obs.
C_2	167.5	183 ± 10 [4]	1.160	1.24 [5]	15.2	12.17 [5]
C_3	226.5	200 ± 10 [4]	1.275	1.280 [6]	9.54	10.3 [6]
C_5	273.0	240.5 ± 58 [7]	1.260	(terminal)	9.72	—
			1.305	(central)	10.55	—

The calculated CC bond length and stretching force constant for C_3 are in excellent agreement with experiment. In the case of C_2, the discrepancy between theory and experiment is greater, though still not excessive; the differences are consistent in that too short a bond length should correspond to too large a force constant.

The species discussed here are "electron deficient" in that their valence shell orbitals are not completely utilized; apparently the MINDO/2 method can be extended satisfactorily to such systems and it should therefore be equally applicable to a study of their reactions [9].

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Cleavage of a Carbon-Sulfur Bond by Organodihaloboranes

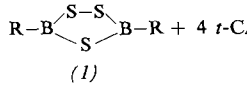
By *Max Schmidt* and *Falk R. Rittig* [*]

Reaction of iodoboranes with disulfanes results in liberation of iodine and cleavage of the sulfur-sulfur bond in a redox reaction to give the corresponding thioboranes [1], *e.g.*:

$$RBI_2 + R'SSR' \rightarrow RB(SR')_2 + I_2 \qquad (1)$$

We have now found that di-*tert*-butyldisulfane reacts differently with organodiiodoboranes: Substitution occurs with C—S cleavage to give 3,5-diorgano-1,2,4,3,5-trithiadiborolanes *(1)*, *tert*-butyl iodide, and sulfur.

$$2\ RBI_2 + 2(t\text{-}C_4H_9)_2S_2 \rightarrow$$



$$+\ 4\ t\text{-}C_4H_9I + 1/8\ S_8 \qquad (2)$$

(1)

In this new synthesis of the five-membered boron-sulfur ring the reactants are mixed together at room temperature, *e.g.*, in hexane; after several hours' stirring the volatile components are removed under reduced pressure and the crystalline residue is recrystallized.

In these reactions, which in contrast to the other redox reactions of organoboranes are not particularly exothermic, liberation of iodine is observed, especially on dropwise addition of disulfane to the iodoborane, thus indicating a redox reaction of the sulfur formed with unused iodoborane[2]:

$$2\ RBI_2 + 3/8\ S_8 \rightarrow (1) + 2\ I_2 \qquad (3)$$

An analogous reaction is basically also possible with the weaker Lewis acid phenyldichloroborane, albeit only at higher temperatures.

Experimental data for reactions of organodihaloboranes with di-*tert*-butyldisulfane.

RBX_2	Reaction time (h)	Product *(1)*	Yield (%)	B.p. (°C/torr)	M.p. (°C)
n-$C_4H_9BI_2$	24	$(n\text{-}C_4H_9B)_2S_3$ [a]	77.6	73–75/0.1	
$C_6H_5BI_2$	24 [b]	$(C_6H_5B)_2S_3$	90.4		115–117
p-CH_3-$C_6H_4BI_2$	24 [b]	$(p\text{-}CH_3\text{-}C_6H_4B)_2S_3$	86.8		124–126
$C_6H_5BCl_2$	16 [c]	$(C_6H_5B)_2S_3$	44.1		114–115

[a] Formation of polymer as by-product; [b] in n-hexane; [c] reflux (bath temperature 160–170 °C).

All operations were carried out under nitrogen in carefully dried solvents, and the products were identified by elemental analysis and by their IR and NMR spectra.

As in the cleavage of di-*tert*-butylsulfanes by haloboranes *via* the 1:1 adducts as intermediates[3] and in the scission of unsymmetrical ethers by haloboranes[4], the substitution in the reaction formulated in (2) should be promoted by the intermediacy of an energetically favorable carbonium ion; similar cleavages of di-*tert*-butyl peroxide are currently being studied.

C–S cleavages in di-*tert*-butyldisulfane are also known in the case of the reactions with dichlorocarbene[5] and hexacarbonylmolybdenum.

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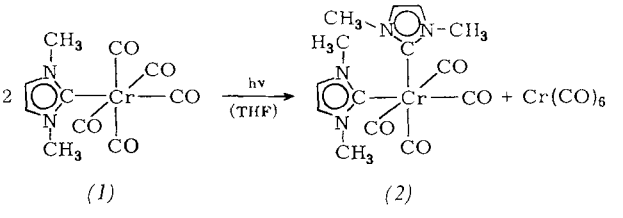
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Tetracarbonylbis(1,3-dimethyl-4-imidazolin-2-ylidene)chromium(0)[1]

By *Karl Öfele* and *Max Herberhold*[*]

The synthesis of transition metal-carbene compounds by transformation of a carbonyl[2] or isocyanide group[3] that is already coordinated to the central metal into a carbene ligand has hitherto afforded only neutral complexes having just one carbene ligand. The reactions of heteroaromatic cations with the hydrogencarbonylmetalate ions $[HCr(CO)_5]^-$ [4,5] and $[HFe(CO)_4]^-$ [5], and of 3,3-dichlorocyclopropene derivatives with either $Na_2Cr(CO)_5$ [6] or palladium metal[7] also result in the introduction of only one carbene ligand into the complex. The only compounds so far known to contain two carbene groups per metal atom are mercury complexes of the type $[Hg(carbene)_2]^{2+}$ [8]; it is, however, uncertain to what extent the mercury-carbon bond in these cations is comparable with the metal-carbene coordinative bond in the above neutral complexes.

We have now been able to show that a second carbene ligand can be introduced into pentacarbonyl(1,3-dimethyl-4-imidazolin-2-ylidene)chromium(0) *(1) via* photoinduced substitution of a carbonyl group. On irradiation of a solution of *(1)* in boiling tetrahydrofuran (THF) a small amount of the yellow complex *cis*-[tetracarbonylbis(1,3-dimethyl-4-imidazolin-2-ylidene)chromium(0)] *(2)* is formed which is readily separable from *(1)* owing to its insolubility in diethyl ether. The reaction can be interpreted as a "dismutation":



(1) *(2)*

The slight decomposition observed in THF solution can be almost completely suppressed by addition of a small amount of pyridine or acetonitrile to the reaction mixture. We assume that these donor ligands play a role in the stabilization of coordinatively unsaturated carbonylmetal fragments. Transfer of a carbene ligand onto complex fragments such as $[Fe(CO)_4]$ has recently been exploited by *E. O. Fischer et al.* in the synthesis of tetracarbonyl(methoxyphenylcarbene)iron(0) [9].

The yellow, air-stable crystals of *(2)*, m.p. 227–230 °C (decomp.), sublime at 120 °/$\approx 10^{-3}$ torr with partial decomposition; they are sparingly soluble in most organic solvents except THF. The composition $Cr(CO)_4(C_5H_8N_2)_2$ was established by elemental analysis and molecular-weight determination (osmometry in benzene) as well as by the mass spectrum[10]: The molecular ion $Cr(CO)_4L_2^+$ (*m/e* 356) is accompanied *inter alia* by fragments of the type CrL_2^+ (244), CrL^+ (148), and L^+ (96) (L = $C_5H_8N_2$).

The *cis* relationship of the two carbene ligands in the octahedral complex *(2)* is revealed by the number of IR-active C≡O stretching vibrations; in agreement with the local symmetry C_{2v}, four absorptions are observed (1986, 1870, 1847, and 1825 sh cm^{-1}; in $CHCl_3$). Further support for this structure comes from the dipole moment of $\mu = 9.66 \pm 0.1$ D (in benzene), which is considerably higher than that of *(1)* ($\mu = 7.0 \pm 0.1$ D). Simple vector addition of two *cis* partial moments of 7.00 D enclosing an angle of 90 ° would give an overall moment of 9.90 D.

Apart from the C≡O stretching region, the IR spectra of the carbene complexes *(1)* and *(2)* are almost identical. The UV absorption spectrum of *(2)* in ethanol contains two broad maxima at 365 (log ε = 3.35) and 258 nm (log

$\varepsilon = 4.39$); the absorption curve of *(2)* is shifted somewhat toward longer wavelengths compared with that of *(1)* [350 (log $\varepsilon = 3.48$) and 253 nm (log $\varepsilon = 4.60$); in ethanol].

The ^{1}H-NMR spectrum of *(2)* ([D$_6$]acetone; 25 °C) consists of two sharp singlets at $\tau = 6.48$ and 2.93 (intensity ratio 3:1) for the *N*-methyl and ring protons, respectively. The corresponding signals of *(1)* occur at $\tau = 6.13$ and 3.12[4].

Experimental:

$Cr(CO)_5C_5H_8N_2$ *(1)* is prepared in 90 % yield by heating bis(1,3-dimethyl-4-imidazolium)decacarbonyldichromate-(-I) $(C_5H_9N_2)_2[Cr_2(CO)_{10}]$ to 120 °C in a high vacuum[11], in a modification of a previous method[4].

A solution of *(1)* (1.0 g, 3.47 mmoles) and acetonitrile (0.16 g, 4 mmoles) in dry, degassed THF (75 ml) in a Duran glass Schlenk tube fitted with reflux condenser is exposed to the light emitted by a high-pressure mercury vapor lamp (Hanovia, type L, 450 W); the lamp is enclosed in a water-cooled quartz jacket during irradiation. The reaction solution rapidly comes to boiling. After 4 h, the solution is filtered under suction through a G 4 frit covered with filtration aid and the filtrate is evaporated to dryness *in vacuo*. Unreacted *(1)* can be dissolved out of the pale yellow residue with diethyl ether. The remaining yellow crystals of *(2)* are recrystallized from THF/*n*-hexane; yield 50 mg (≈ 8 %).

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[1] This work was supported by the Deutsche Forschungsgemeinschaft.

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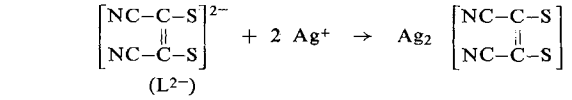
[10] Atlas CH 4; ion source TO 4; 50 eV. Measurements by Dr. *J. Müller*, München.

[11] Carried out by Dipl.-Chem. *W. Golla*.

The "Silver Salt" of *cis*-1,2-Dicyano-1,2-ethylenedithiol

By *Hermann Wernet*[*] and *Gerhard Bähr* (deceased)

The reaction of *cis*-1,2-dicyano-1,2-ethylenedithiolate (L^{2-}) with silver ions in aqueous solution was initially described as simple salt formation[1,2].



A complex anion $[AgL_2]^{3-}$ was later also considered as a possible product[3].

On the basis of further studies we have now been able to show that this reaction actually leads to the complex $Ag_2[Ag_2L_2]$ containing two sets of differently bonded silver atoms. Sulfide ions react successively with the microcrystalline salt disilver bis(*cis*-1,2-dicyano-1,2-ethylenedithio)diargentate(I), which is practically insoluble in water, according to the equations

$$Ag_2[Ag_2L_2] + S^{2-} \rightarrow [Ag_2L_2]^{2-} + Ag_2S \quad (1)$$

$$[Ag_2L_2]^{2-} + S^{2-} \rightarrow 2\,L^{2-} + Ag_2S \quad (2)$$

The reaction steps (1) and (2) overlap; however, (1) is much faster. Iodide coordinates only with the cationic silver. In contrast, cyanide is able to displace the dithiolate ligand when present in excess.

$$Ag_2[Ag_2L_2] + 4\,I^- \rightarrow [Ag_2L_2]^{2-} + 2\,[AgI_2]^-$$

$$Ag_2[Ag_2L_2] + 4\,CN^- \rightarrow [Ag_2L_2]^{2-} + 2\,[Ag(CN)_2]^-$$

$$Ag_2[Ag_2L_2] + 8\,CN^- \rightarrow 2\,L^{2-} + 4\,[Ag(CN)_2]^-$$

The anion $[Ag_2L_2]^{2-}$ reacts with tetraethylammonium ions to give a salt that is sparingly soluble in water. The yellow crystals have a sharp melting- and decomposition point of 219 °C; they dissolve most readily in acetone and are sensitive to light, especially when moist.

We have also succeeded in preparing addition compounds of the silver salt and in determining their composition by elemental analysis; *e.g.* $Ag_2[Ag_2L_2]\cdot 2\,KCN$, $Ag_2[Ag_2L_2]\cdot 2[N(C_2H_5)_4]CN$, $Ag_2[Ag_2L_2]\cdot 2\,AgNO_3$, $Ag_2[Ag_2L_2]\cdot 2(en)$.

Reaction of L^{2-} with Ag^+ always leads first to the soluble anionic complex,

$$2\,L^{2-} + 2\,Ag^+ \rightarrow [Ag_2L_2]^{2-}$$

which is precipitated by an excess of silver ions.

$$[Ag_2L_2]^{2-} + 2\,Ag^+ \rightarrow Ag_2[Ag_2L_2]$$

On further addition of ligand the cationic silver is eventually also coordinated.

$$Ag_2[Ag_2L_2] + 2\,L^{2-} \rightarrow 2\,[Ag_2L_2]^{2-}$$

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Is There an Energy Difference between Enantiomorphic Structures?

By *Wolfram Thiemann* and *Klaus Wagener*[*]

Sodium ammonium DL-tartrate consists of enantiomeric, optically active molecules (ratio of configurations 1:1) which are precipitated as a racemic mixture of pure, enantiomorphic crystals (containing only D or only L molecules) from its saturated aqueous solution below 27 °C[1]. We used this salt in the following experiment: A saturated solution of about 30 g of racemate was allowed to reach equilibrium with precipitated material at 25.5 °C. After removal of the precipitate, the solution was diluted with pure solvent (water) until the solubility limit was about

0 °C. When the temperature of the solution was allowed to fall slightly below the new solubility limit only a small precipitate was formed (about 50 mg). After equilibration under carefully controlled conditions, the precipitate and solution were separated, the precipitate was dissolved in water, and its optical activity was measured with respect to the solution as standard. After many preliminary experiments, ten measurements performed under very strict conditions all gave the same negative optical rotation[2] of the precipitate, namely $\alpha \approx 10^{-3}$ °.

In our search for an explanation of this remarkable phenomenon we considered the following possible causes: 1. Systematic errors in the measuring technique; they could be ruled out by switching the cells, repeated measurements, *etc.* — 2. Optically active impurities; this could be discounted on the basis of fractional (chromatographic) purification processes. — 3. Bacterial contamination of the solution, which would result in preferential degradation of the dextrorotatory[2] (natural) tartrate. We devoted the most attention to this last possible source of error and found: a) Concentrated solutions in open vessels are not infected at all within a week. b) If the observed activity were nevertheless due to an attack by bacteria then any variation in the time between precipitations would alter the magnitude of the effect. This was not the case. c) Addition of the bactericide toluene to the solution had no influence on the effect. — 4. The thought that external fields (such as the earth's magnetic field) could lead to D/L discrimination is untenable.

At the present time, the only remaining interpretation of our findings involves the assumption of different heats of solution for D and L crystals of sodium ammonium tartrate. And this means effectively that the lattice energies of the enantiomorphic crystals must differ, which in turn can only result from an asymmetric contribution to the interaction. Our measurements would indicate a relative difference in the heats of solution (or lattice energies) of a few 10^{-5}. We are currently examining the consequences of this phenomenon by other techniques and for other systems.

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[2] Sign and magnitude of the optical rotation of a compound depend upon the wavelength of the polarized light. We used a Cary 60 spectropolarimeter, produced by Cary Instruments/Varian, and worked at $\lambda = 280$ nm.

Errata

In the communication "Aminoazimines by Addition of Aminonitrenes to α-Carbonylazo Compounds" by *K. H. Koch* and *E. Fahr*, Volume 9, August 1970, the following corrections should be made:

On page 634, right-hand column, line 30 "alcohol-free glacial acetic acid" should read "alcohol-free ethyl acetate".

On page 635, left-hand column, line 1 "*(1a)–(1f)*" should read "*(1d)–(1f)*".

CONFERENCE REPORTS

Homolytic Reactions of the Alkyl-Metal Bond

By *Alwyn G. Davies*[*]

Bimolecular homolytic substitution (S_H2) reactions are normally recognized to occur at peripheral hydrogen atoms [eq. (1)] or, less commonly, at halogen, oxygen, or sulfur atoms.

$$X^{\bullet} + H{-}R \xrightarrow{k_1} H{-}X + R^{\bullet} \qquad (1)$$

Recent stereochemical, kinetic, and ESR studies have shown that this process will also take place, often much more rapidly, at a multivalent metallic center [eq. (2); M = *e.g.* Mg, Zn, Cd, B, Al, Sn, P, As, Sb, Bi], and provides the key to the interpretation of many organometallic reactions.

$$X^{\bullet} + MR_n \xrightarrow{k_2} X{-}MR_{n-1} + R^{\bullet} \qquad (2)$$

Reaction (2) can be studied as a step in a non-chain process if the radical $X^{\bullet}$ (*e.g.* $(CH_3)_3CO^{\bullet}$ [1], $(CH_3)_3CS^{\bullet}$ [2], or $(CH_3)_2N^{\bullet}$ [3]) is generated photolytically (from $(CH_3)_3C{-}O{-}O{-}C(CH_3)_3$, $(CH_3)_3C{-}S{-}S{-}C(CH_3)_3$, or $(CH_3)_2N{-}N{=}N{-}N(CH_3)_2$, respectively) in the cavity of an ESR spectrometer, when the spectrum of the displaced radical $R^{\bullet}$ can be observed.

Reaction (2) can also occur as a propagation step in a chain process if a reagent XY is chosen so that the chain carrier $X^{\bullet}$ is rapidly regenerated by the reaction (3).

$$R^{\bullet} + XY \longrightarrow RY + X^{\bullet} \qquad (3)$$

The overall reaction is that shown in eq. (4).

$$XY + MR_n \longrightarrow X{-}MR_{n-1} + RY \qquad (4)$$

Chain reactions of this type have been established for the radicals $R'C(CH_3)_2O^{\bullet}$ [4], $C_6H_5S^{\bullet}$ [5], $(CH_3)_2N^{\bullet}$ [6], and succinimidyl[7] where the reagent XY is $R'C(CH_3)_2OCl$, C_6H_5SH, $(CH_3)_2NCl$, and bromosuccinimide respectively.

The reaction which has been studied most thoroughly, however, is the autoxidation of an organometallic compound, where the overall addition process (5) involves the propagation steps (6) and (7)[8,9].

$$O_2 + MR_n \longrightarrow ROOMR_{n-1} \qquad (5)$$

$$ROO^{\bullet} + MR_n \longrightarrow ROOMR_{n-1} + R^{\bullet} \qquad (6)$$

$$R^{\bullet} + O_2 \longrightarrow ROO^{\bullet} \qquad (7)$$

The absolute rate constants, k_2, for a number of these S_H2 replacements at metal centers have been determined by a variety of techniques. Some of the values obtained, compared

Table. Rate constants k_1 and k_2 ($mole^{-1}s^{-1}$) for a few S_H2 reactions (Bu = butyl).

X·	HR	k_1	MR_n	k_2	T (°C)
ROO· [9]	$CH_3C_6H_5$	0.24	BBu_3	2×10^6	30
t-BuO· [4]	$(CH_2)_5$	5×10^4	BBu_3	7×10^6	40
$(CH_2CO)_2N$· [7]	—	—	$SnBu_4$	8×10^3	35

with the corresponding values, k_1, for reaction at hydrogen centers, are given in the Table [eq. (1)].

Lecture at Dortmund on June 16, 1970 [VB 244 IE]
German version: Angew. Chem. 82, 704 (1970)

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[1] *A. G. Davies* and *B. P. Roberts*, Chem. Commun. *1969*, 699; J. organometallic Chem. *19*, P 17 (1969); *P. J. Krusic* and *J. K. Kochi*, J. Amer. chem. Soc. *91*, 3942, 3944 (1969).

[2] *B. P. Roberts*, unpublished.

[3] *A. G. Davies*, *S. C. W. Hook*, and *B. P. Roberts*, J. organometallic Chem. *22*, C 37 (1970).

[4] *A. G. Davies*, *D. Griller*, *B. P. Roberts*, and *R. Tudor*, Chem. Commun. *1970*, 640.

[5] *A. G. Davies* and *S. C. W. Hook*, J. chem. Soc. (London) *B 1970*, 736.

[6] *A. G. Davies*, *S. C. W. Hook*, and *B. P. Roberts*, J. organometallic Chem. *23*, C 11 (1970).

[7] *A. G. Davies*, *B. P. Roberts*, and *J. M. Smith*, Chem. Commun. *1970*, 557.

[8] *A. G. Davies* and *B. P. Roberts*, J. chem. Soc. (London) *B 1967*, 17; *1968*, 1074; *1969*, 311, 317; *P. G. Allies* and *P. B. Brindley*, *ibid. 1969*, 1126.

[9] *K. U. Ingold*, Chem. Commun. *1969*, 911; *A. G. Davies*, *K. U. Ingold*, *B. P. Roberts*, and *R. Tudor*, unpublished.

Biogenesis of Steroids in Higher Plants

By *Herwig Hulpke*[*]

A great variety of steroids is encountered as natural products in the animal and plant kingdoms. For this reason an early interest was shown in elucidation of the biogenetic pathways leading to steroids. Tracer studies with acetic and mevalonic acids labeled specifically with radiocarbon revealed a characteristic incorporation of radioactivity into the steroid formed (labeling pattern). *Bloch* and *Lynen* have used this technique to determine the biogenesis of animal steroids.

The following simplified account may now be regarded as valid: Three molecules of acetyl-coenzyme A unite to give mevalonic acid which is converted into "biological isoprene" by dehydration and decarboxylation. Squalene is formed *via* farnesyl phosphate as intermediate and then undergoes a concerted reaction to give lanosterol, from which the steroids are formed.

This pathway was first established for the animal cell, but there is strong evidence suggesting that a similar route is followed in plants. The first cyclization product formed from squalene is cycloartenol, a triterpene common to many plants.

Among the phytosterols, the cardenolides are known as highly cardioactive substances. They differ from most other steroids in a number of characteristic features: Rings A and B are *cis*-linked; C-14 bears a β-OH group; and an α,β-unsaturated lactone ring (butenolide ring) is found at C-17. In biogenesis studies with specifically labeled mevalonic acid in *Digitalis* species, it is seen from the degradation of the butenolide ring that it contains more than one and less than three carbon atoms from the side chain of an "original steroid". Thus the cardenolides are possibly formed from a steroid containing 21 C atoms. Additional support for this concept comes from the observation that steroids containing 21 C atoms — termed digitenols by *R. Tschesche* — can be isolated from plants known to contain particularly large amounts of cardenolides. If [21-^{14}C]hydroxypregnenone[**] is administered to *Digitalis lanata* in the form of the glucoside, the plant is found to produce the cardenolides digitoxigenin, xysmalogenin, digoxigenin, and gitoxigenin.

Further elucidation of the biogenetic pathway has shown that this route leads from hydroxypregnenone to progesterone, then to a C_{21} steroid having a 14β-OH group, and finally to the cardenolides. Steroids having a butenolide ring on C-17 but no 14β-OH group are not converted into cardenolides.

Hydroxypregnenone also plays a significant role in the biogenesis of other plant steroids.

For instance, the formation of hellebrigenin (a cardioactive bufadienolide from the Christmas rose) and conessin (a steroidal alkaloid) from radioactive hydroxypregnenone has been established. As in animals, this precursor can also be formed from cholesterol in plants. Indeed, cholesterol is very important in the biogenesis of plant steroids containing 27 carbon atoms. Steroid saponins such as spirostanols, tigogenin, diosgenin, and gitogenin are formed from administered radioactive cholesterol. Alkaloids having a steroid structure, tomatidin and solanidin, are also formed from cholesterol.

The relatively good yields observed in these incorporations rule out the possibility of the products being formed in side reactions. The metabolic utilization of hydroxypregnenone and of cholesterol in plant tissues and the formation of phytosterols from these typical zoosterols shows that cholesterol and hydroxypregnenone play an important role in the biogenetic processes of higher plants.

Lecture at Mainz on June 18, 1970 [VB 245 IE]
German version: Angew. Chem. 82, 704 (1970)

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[**] Formerly known as pregnenolone.

Carcinogenic Alkylating Substances, Chemical Constitution and Action[**]

By *Hermann Druckrey*[*]

The prevention of cancer calls for an elucidation of the potential causes and their modes of action. At the same time it is important to produce in experimental animals the various types of tumor which are required as "models" for morphogenetic, biochemical, immunological, and chemotherapeutic studies. In order to achieve specific effects, the "transport principle", which has previously proved useful in cancer chemotherapy, (Honvan, Endoxan) has been used, *i.e.* the use of substances from which the actual "active form" occurs only after metabolic activation. Three groups of substances have been systematically investigated: *N*-nitroso compounds; hydrazo-, azo-, and azoxyalkanes; and 1-aryl-3,3-dialkyltriazenes. The first and decisive step in the activation of these groups of compounds is an enzymatic α-C hydroxylation of an alkyl residue, which is then cleaved off as the corresponding aldehyde. Thus, probably an alkyl diazohydroxide or an alkyldiazonium ion occurs as an alkylating intermediate. The alkylation of nucleic acids, particularly at N-7 in guanine, has been observed and the resulting change of the genetic code in the cells is looked upon as the initiation of their carcinogenic transformation.

These investigations revealed highly specific effects. *Symmetrical* dialkylnitrosamines, for instance, induce predominantly liver cancer, whereas the *asymmetrical* compounds produce carcinoma of the esophagus. Methylbutylnitrosamine proved to be carcinogenic when inhaled even at concentrations as low as 0.05 ppm. However, acylalkylnitrosamides, which undergo easy heterolysis, have a local effect and produce cancer of the forestomach when administered orally; *acetyl*-methylnitrosourea, on the other hand, specifically causes cancer of the glandular stomach. In contrast, the stable and chemically important *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide proved to be comparatively harmless. Striking differences were observed when injecting the compounds intra-

venously: Methylnitroso*urethane* led to lung cancer, methylnitroso*urea* to cancer of the brain.

In the series of hydrazo-, azo-, and azoxyalkanes the methyl compounds selectively produced cancer of the colon and rectum, whereas the ethyl homologs did not; the latter, however, produced malignant tumors of the brain, the olfactory bulbs, cancer of the breast, and leukemias. 1-Methyl-2-benzylhydrazine had an intermediate effect. Azoisobutyronitrile, which is important as an initiator of radical reactions, was not carcinogenic, nor were aliphatic hydrazides azines, and hydrazones; *N*-methyl-benzaldehyde- and -nicotinealdehyde-hydrazone, however, were carcinogenic.

1-Aryl-3,3-dialkyltriazenes proved to be potent *neurotropic* carcinogens. The potency increases in the order: phenyl, 3-pyridyl, pyridyl-*N*-oxide, and methyl, ethyl, respectively. The monoalkyl compounds which, according to *O. Dimroth* (1905) are "stabilized diazoalkanes" and act as alkylating agents, produce local tumors. Methylation of guanine at N-7 could be demonstrated *in vitro* and *in vivo*.

In *transplacental* experiments, a single small dose of an *ethyl* compound from any one of the three classes of substances, when administered to pregnant rats, led to malignant tumors in the brain and nervous system of practically all the progeny, azoethane even after inhalation. The *methyl* homologs, however, were either completely inactive or only slightly carcinogenic to the fetus, as were dialkylnitrosamines.

Since the "active forms" in all three groups of substances are the same *i.e.* alkyldiazonium compounds, the specificity of the effects must be attributed to the whole molecule of the "transport forms" or to their enzymatic activation. The detection of carcinogenic properties in diazomethane and diazoacetate as well as in directly acting alkylating agents such as alkyl halides, aziridines, dialkyl sulfates, and 1,3-propane sultone gives considerable support to the alkylation theory. The potential risk of contact with direct or indirect alkylating agents is emphatically pointed out.

Lecture at Erlangen, June 26, 1970 [VB 246 IE]
German version: Angew. Chem. *82*, 777 (1970)

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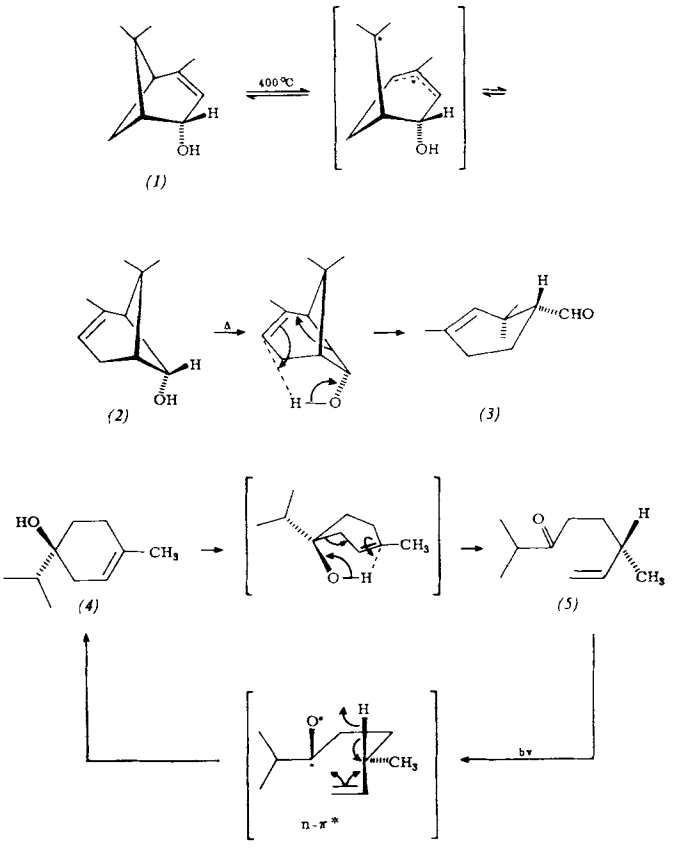
[**] In collaboration with *R. Preussmann*, *S. Ivankovic*, *Ch. Landschütz*, and *H. Kruse*.

The Significance of Monoterpene Chemistry Today

By *Gunther Ohloff*[*]

Their great structural variety, known stereochemistry, and easy accessibility make the monoterpenes ideal model compounds for the elucidation of many problems in modern organic chemistry. This has been demonstrated in the case of the following two topics: 1. Thermally induced reactions. 2. Chirality of α-ionone and its relation to that of corresponding carotinoids.

The common mechanistic character of the thermal isomerization of the diastereomers of pinane, 2-pinanol, verbenol, as well as of α- and β-pinene, and verbenene, is the stepwise homolysis of the cyclobutane ring. Several series of sigmatropic 1,5-H-shifts take place as secondary reactions, which, in the case of the unsaturated monoterpenes, are accompanied by electrocyclic processes. Thus, *e.g.* (+)-*trans*-verbenol *(1)* is in homolytic equilibrium with *trans*-chrysanthenol *(2)* which subsequently decomposes to (+)-2,2,4-trimethyl-3-cyclohexene-1-carbaldehyde *(3)*.



(+)-Terpin-1-en-4-ol *(4)* is thermally converted, with induction of the center of chirality, into (+)-6*S*-2,6-dimethyl-7-octen-3-one *(5)* [1]. This concerted process is photochemically reversible [2]. The thermal cyclization of linalool (intramolecular ene reaction), the formation of isopulegol from β-citronellal (intramolecular thermal Prins reaction), and the deconjugation of α,β-unsaturated carbonyl compounds are concerted reactions of the sigmatropic 1,5-H-shift type.

The symmetry-permitted process of a sigmatropic homo-1,5-H shift was first reported for 4-carene and related compounds [3].

The configurational relation of α-ionone with degradation products of farnesiferol B and manool led to the establishment of the center of chirality on C-6 of all known carotinoids [4].

These examples illustrate the present significance of monoterpene chemistry for the solution of reaction mechanism and stereochemical problems. Monoterpenes are indispensible as precursors for the industrial preparation of odoriferous substances.

Lecture at Tübingen, July 3, 1970 [VB 248 IE]
German version: Angew. Chem. *82*, 777 (1970)

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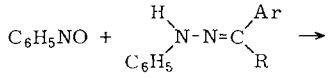
[1] *G. Ohloff* and *K. H. Schulte-Elte*, unpublished.

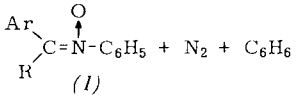
[2] *K. H. Schulte-Elte* and *G. Ohloff*, Tetrahedron Letters *1964*, 1143.

[3] *G. Ohloff*, Chem. Ber. *93*, 2673 (1960); Tetrahedron Letters *1965*, 3795.

[4] *C. H. Eugster*, *R. Buchecker*, *Ch. Tscharner*, *G. Uhde*, and *G. Ohloff*, Helv. chim. Acta *52*, 1729 (1969).

Phenyl nitrones *(1)* have been obtained from nitrosobenzene and phenylhydrazones by *D. W. Berry, R. W. Bryant, J. K. Smith,* and *R. G. Landolt.* The reactions are carried out in absence of solvent or in one of the common solvents at room temperature and preferably under nitrogen.

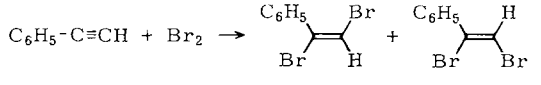




(1)

Of the many compounds suitable as starting materials are the phenylhydrazones of benzaldehyde, substituted benzaldehydes, and fluorenones. The yields are good. / J. org. Chemistry *35*, 845 (1970) / —Kr. [Rd 219 IE]

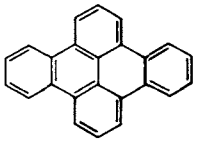
Pure *cis-* and *trans*-α,β-dibromostyrene have been synthesized and characterized by *J. König* and *V. Wolf.* Reaction of phenylacetylene with one equivalent of bromine at 10 °C in glacial acetic acid or chloroform gave *trans-* and *cis-(1)* in the ratio 70 : 30 or 82 : 18 resp. In glacial acetic acid the ratio increases to 97 : 3 on addition of 0.5 equivalent of LiBr;



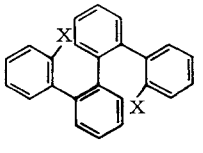
trans-(1) *cis-(2)*

trans-(1) was distilled off at 49 °C/0.02 torr. Pure *cis-(1)* can be readily isolated since *trans-(1)* is preferentially debrominated when a mixture of *cis-* and *trans-(1)* is treated with Zn dust and $ZnCl_2$ in ethanol at 25 °C. The structures were determined spectroscopically. / Tetrahedron Letters *1970*, 1629 / —Kr. [Rd 221 IE]

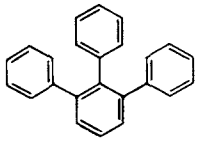
The photo-aryl coupling reaction opens up a new route to the synthesis of polycondensed aromatics. *T. Sato, S. Shimada,* and *K. Hata* obtained dibenzo [*fg,op*]naphthacene *(1)* by irradiation of the following compounds in benzene with a mercury vapor lamp (20—22 hours): *(2)* in presence of an



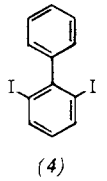
(1)



(2), X = H; *(5)*, X = Cl



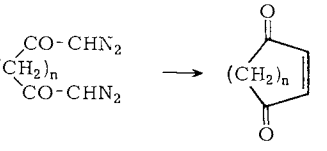
(3)



(4)

equimolar amount of iodine gave *(1)* in 57 % yield; *(3)* + I_2 → 21 % *(1)*; *(4)* → small amount of *(1)* + 42 % triphenylene + 24 % *(3)*; *(5)* → 67 % *(1)*. The dehydrohalogenative cyclization reaction was successfully used for the synthesis of triphenylene. Irradiation of 2-chloro- and 2-bromo-2′-iodobiphenyl in benzene gave triphenylene in 37 and 25 % yields respectively. / Chem. Commun. *1970*, 766 / —Ma. [Rd 223 IE]

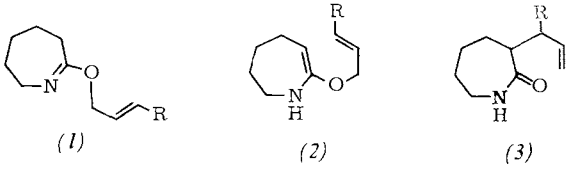
The intramolecular cyclization of bis(α-diazoketones) to cycloalk-2-ene-1,4-diones *(1)* has been achieved by *J. Font, F. Serratosa,* and *J. Valls* by catalytic decomposition in inert solvents using the high dilution principle. For example, the intramolecular cyclization of 1,7-bis(diazo)heptane-2,6-dione in boiling toluene with copper-bronze catalyst affords cyclohept-2-ene-1,4-dione in 20 % yield; by using soluble copper



(1)

chelates as catalyst the yield is increased to 32 %. Decomposition of 1,7-bis(diazo)-4-chloroheptane-2,6-dione with copper pentanedionate leads to 6-chlorocyclohept-2-ene-1,4-dione (15 %) from which 4-hydroxytropone (γ-tropolone) can be prepared in 70–75 % yield by promoted loss of HCl on treatment with weak bases. / Chem. Commun. *1970*, 721 / —Ma. [Rd 222 IE]

An extension of the Claisen rearrangement is reported by *D. St. C. Black* and *A. M. Wade.* Caprolactim *O*-allyl ether *(1a)* and *O*-cinnamyl ether *(1b)* undergo rearrangement to 3-allyl- *(3a)*, m.p. 87 °C, 60 %, and 3-cinnamylcaprolactam *(3b)*, m.p. 116—117 °C, respectively, on heating for several



(1) *(2)* *(3)*

a, R = H; *b*, R = C_6H_5

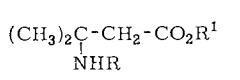
hours in a sealed tube at about 210 °C. Small amounts of *N*-allyl- and *N*-(1-phenyl-1-propenyl)caprolactam are formed as by-products. At higher temperatures compounds *(1)* afford products that are formed by migration of groups to the nitrogen. The isomerization product *(2)* is an intermediate in the formation of *(3)*. / Chem. Commun. *1970*, 871 / —Ma. [Rd 224 IE]

A new contribution to the chemistry of the halogen incandescent lamp is given by *E. G. Zubler.* The kinetics of the tungsten-oxygen-bromine reaction has been investigated. The weight loss of a tungsten sample was monitored in a flow system with 10^{-4}—10^{-2} torr O_2 and 0.3—2.7 torr Br_2 at 600—950 °C (carrier gas, N_2). The reaction was zero order with respect to bromine and first order with respect to oxygen. The function of the bromine is to remove the oxidation product by formation of volatile WO_2Br_2, presumably by the reaction

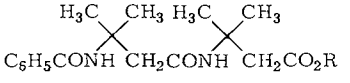
$$WO_2 \text{ (surface)} + Br_2 = WO_2Br_2.$$

This reaction is independent of the dissociative state of the gaseous bromine and permits the oxidation to proceed as it would at higher temperatures where the oxide is volatile. An empirical rate equation with an apparent activation energy of 31.0 kcal mole^{-1} was established; this activation energy is in good agreement with data for tungsten oxidation at similar pressure, but higher temperatures. / J. physic. Chem. *74*, 2479 (1970) / —Hz. [Rd 228 IE]

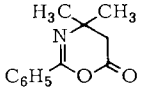
Synthesis of peptides from β-amino acids *via* oxazinone intermediates has been accomplished by *J. Lowbridge* and *C. N. C. Drey*. While preparation of peptides from 3-amino-3-methylbutyric acid is very difficult with the usual coupling agents, aminolysis of the intermediate oxazinone proceeds readily to yield the desired product. Thus compound *(1)* gives the oxazinone *(2)* from the dipeptide *(4)* which is formed on aminolysis with the ester *(3)*. Treatment of *(4)* with acetic



(1), R = COC_6H_5, R^1 = H
(3), R = H, R^1 = CH_3



(4)



(2)

anhydride (after hydrolysis) affords the "dipeptide-oxazinone", which gives the tripeptide on reaction with the ester *(3)*. / Chem. Commun. *1970*, 791 / —Ma. [Rd 225 IE]

A nuclear magnetic resonance study of the 2,6-lutidine/water system in the critical region is reported by *Y. Arata* and *T. Fukumi*. In this system, a lower critical point of mixing occurs at 33.93 °C and 29.94 % (w/w) lutidine. Below the critical temperature, the water proton chemical shift moves upfield almost linearly with increasing temperature, but shifts downfield abruptly by about 2 Hz at the critical point. This is interpreted as due to an anomalous increase in the ratio of the hydrogen-bonded to free water molecules. With about 0.2 % tris(1,3-pentanedionato)chromium(III) added, the linewidth of the water proton resonance goes through a sharp maximum at the same temperature (33.02 °C) where the sample exhibits critical opalescence (the critical temperature is lowered by the presence of the chromium "impurity"). These results show that NMR measurements can be useful in investigations of critical phenomena in binary liquid mixtures. / Molecular Physics *19*, 135 (1970) / —Hz. [Rd 229 IE]

The Hall effect and electrical conductivity of lithium-ammonia solutions were measured by *R. D. Nasby* and *J. C. Thompson* at concentrations of 1.2 to 14 mole-% lithium and 200 to 240 °K, except in the miscibility gap (consolute temperature about 210 °K). Above 9 mole-% Li, the Hall coefficients are those expected for free electrons; below this concentration, they increase to about twice the free-electron value. Below 8 mole-% Li, the mobility of the conduction electrons seems to be thermally activated, with a maximum of the activation energy (0.15 eV) at about 3 mole-% Li. These results show that the solutions behave as liquid metals above 9 mole-% Li; at lower concentrations, metallic conduction behavior gradually recedes, and the characteristics of solvated electrons emerge. At 3 mole-% Li the influence of free electrons can no longer be detected. / J. chem. Physics *53*, 109 (1970) / —Hz. [Rd 230 IE]

Oligomeric molecules in acetone, methanol, and formic acid vapors were detected by *H. Knof* and *D. Krafft* in a specially designed mass spectrometer *via* their negative ions. In this mass spectrometer electron source and collision chamber are separated by a tube cooled with liquid air. With electrons of *ca.* 200 eV entering the collision chamber and a vapor pressure of some 10^{-4} torr the yield of negative ions without fragmentation was an optimum. The pressure dependence of the corresponding mass peaks indicates that the negative ions are formed preferentially by electron attachment and not by ion molecule reactions. Appearance of the dimers of acetone and formic acid and of trimeric methanol was verified. With benzene, however, only the monomeric molecule ion was found, and only fragments with cyclohexane, under the same conditions. From intensity ratios it is concluded that a permanent dipole moment is essential for the formation of the oligomers whereas polarizabilities do not seem to play an important role. / Z. Naturforsch. *25a*, 849 (1970) / —Hz. [Rd 231 IE]

The specific heat of [2.2]paracyclophane was measured by *J. T. S. Andrews* and *E. F. Westrum jr.* with the aid of a quasi-adiabatic calorimeter at 10—350 °K. Near 50 °K the temperature dependence of the heat capacity is characteristic of a second-order phase transition. The thermodynamic data of this transition are T_{max} = 55.5 °K, ΔS = 1 ± 0.5 cal mol^{-1}deg^{-1}, and ΔH = 51 cal mol^{-1}. The uncertainty of the transition entropy is due to uncertainties in the extrapolation of the lattice heat capacity. The following explanation for this transition is advanced as most plausible: the strain of the molecule is partly due to the eclipsed conformation of the hydrogen atoms in the bridges. This strain can be reduced by a small twist of the CH_2 links. At low temperatures, the mutual conversion of the two possible conformations is frozen; at temperatures higher than the transition region, the two conformers are interconverted by a torsional vibration. The room temperature X-ray structure of the molecule is the time average of this torsional vibration. / J. physic. Chem. *74*, 2170 (1970) / —Hz. [Rd 232 IE]

Relaxation of sulfur hexafluoride after excitation with 10.6 μ radiation from a pulsed CO_2 laser was studied by *J. I. Steinfeld*, *I. Burak*, *D. G. Sutton*, and *A. V. Nowak*. The time dependence of infrared absorption was followed by means of a second continuous CO_2 laser tunable through several lines in the range 931—954 cm^{-1}. The laser pulse effects overpopulation of some vibration-rotation levels of SF_6 located in the available energy range, thereby causing the corresponding absorption lines to disappear for a short time. Rotational energy transfer fills in this "hole" in the absorption spectrum in not more than two collisions (some 100 nanoseconds). Vibrational energy is dissipated at essentially the same time over all excited vibrational states. The rate-controlling step on returning to thermal equilibrium is vibration-translation relaxation of the lowest excited vibrational level at 363 cm^{-1} with a time constant of 122 ± 8 μsec·torr in pure SF_6. / J. chem. Physics *52*, 5421 (1970) / —Hz. [Rd 233 IE]

The Virial Coefficients of Gases. A Critical Compilation. By *J. H. Dymond* and *E. B. Smith* (Oxford Science Research Papers No. 2) Clarendon Press: Oxford University Press, London, 1969. 1st Edit., xv + 231 pp., bound, 45 s.

Knowledge of the virial coefficients of a gas is very important both from the point of view of industrial applications and for theoretical investigations. This compilation of virial coefficients available up to the beginning of 1968 is therefore most welcome.

The authors begin with a clear and concise introduction to the power expansion of the equation of state for gases, and explain the relationship between the virial coefficients and intermolecular potential. In addition, they give formulas for the calculation of the thermodynamic properties of gases from virial coefficients (fugacity, internal energy, enthalpy, molar heat, entropy, and Joule-Thomson coefficients).

The tables of the virial coefficients of gases stem from earlier work by *McGlashan* dating back to 1955. The substances are arranged according to the Chemical Abstracts system. The search for a given gas is also facilitated by a list of contents arranged according to chemical formulas, as well as an alphabetical one arranged according to the common names.

The publications from which virial coefficients can be determined are given in chronological order for each substance. In most cases there is a brief note stating the method of measurement, the number of coefficients in the power expansion of the equation of state, the maximum pressure and temperature region, and remarks on the accuracy of the measurements and on the agreement between the latter and the data published by other authors. This is followed by tables of values for the second and, where possible, third virial coefficient as a function of temperature, taken from the original literature. The temperatures are always quoted in K. The virial coefficients were always converted to the usual dimensions of $cm^3/mole$ and $cm^6/mole^2$ (for the second and third virial coefficients). Whenever results showing satisfactory agreement were available from several authors, a smooth curve was drawn through all the measurements. The literature data are preceded by the resulting virial coefficients or "best values", for which the estimated error is also stated. This inclusion of "best" values together with the limits of error, the critical remarks on individual literature data, and, not least, the conversion of the data cited to the same dimensions, make *Dymond* and *Smith*'s book a valuable tool for everyone engaged in the study of real gases and intermolecular forces.

Klaus Schäfer [NB 890 IE]

An Introduction to Physical Organic Chemistry. By *E. M. Kosower*. Wiley and Sons, Inc., New York-London-Sydney 1968. 1st Edit., xvi, 503 pp., numerous figures and tables, 115 s.

Once more an American author presents a book on a topic that, since the appearance of *Hammett*'s "Physical Organic Chemistry", should be represented in the library of every chemistry student. The successful textbooks on this subject so far concentrate either on a comprehensive discussion of reaction mechanisms (*Hine*, *Gould*) or on the detailed description of methods (*Wiberg*, *Streitwieser*).

E. M. Kosower includes his introduction in the first group and divides it into three parts: 1. Substituent effects (250 pp.), 2. Solvent effects (120 pp.), and 3. Intermediates and unusual molecules (70 pp.).

In the first part, the acidity of organic compounds and the substituent constants are dealt with first under the heading "Polar Transition States" (130 pp.). Reaction mechanisms follow in the sections on nucleophilic substitution and carbonium ions. The reactions with free-radical and apolar (isopolar) transition states are then given 50 and 60 pages respectively.

The treatment of the various fields is right up to date if one considers the year of publication of the book (the references extend up to 1967). Thus cycloadditions and rearrangements are discussed in the light of the Woodward-Hoffmann rules. Considerable space is also devoted to the discussion of carbonium ion chemistry and of free-radical reactions. However, the text is incomplete in other respects. Reactions of the carbonyl group are practically ignored. Thus one will search in vain for the aldol condensation and the Wittig reaction to name only two examples. As for aromatic substitutions, only the nucleophilic variant is mentioned to illustrate solvent effects. No mention is made of elimination reactions, electrophilic substitutions, or a large number of rearrangements that do not proceed concertedly.

The best rounded-off part of the book is undoubtedly the chapter on solvent effects. The reader is familiarized here with the significance and the problems of this field, which is very important to our deeper understanding of chemical reactions.

Finally, the third part of the book is not satisfactory. Here we again find more or less detailed discussions of carbonium ions, carbanions, and free radicals, which should really have been included in the first part. Thus the temperature-dependent NMR spectrum of the norbornyl cation appears on p. 410, whereas it is discussed on p. 137. Carbene chemistry, which is sought in vain in Part 1, is dealt with here in 15 pages. A few "unusual" molecules are shown in a diagram, but are not discussed further.

In the reviewer's opinion, the book is unsuitable as an introduction, since it omits many important reactions. On the other hand, it offers stimulating reading for the advanced reader. The detailed discussion of solvent effects is very welcome, and the introduction of a new nomenclature for substitution reactions that takes into account the reaction mechanism (with or without intermediate) deserves discussion. The use of the term "methylenoid" instead of "carbenoid", on the other hand, seems less successful. Results of spectroscopic studies are mentioned in gratifying numbers. In view of the large volume of material, it has not always been possible to describe the methods mentioned in detail, so that references to relevant monographs were essential. A detailed grounding of the Woodward-Hoffmann rules would however have been welcome (the non-crossing rule is not mentioned). The book is excellently presented, and 184 examples for practice provide an opportunity reinforcing what has been read. The figures are also clear throughout. In the graphical representation of qualitative Hückel-molecular orbitals (pp. 204, 206), however, the electrons should not have been added as dots at discrete points of the wave function.

Harald Günther [NB 879 IE]

Grundzüge der anorganischen Kristallchemie. Mit einer Einführung in die Theorie der chemischen Bindung (Fundamentals of Inorganic Crystal Chemistry. With an Introduction to the Theory of the Chemical Bond). By *H. Krebs*. Ferdinand Enke Verlag, Stuttgart 1968. 1st Edit., xii + 376 pp., 254 figures, 41 tables, bound DM 45.—.

A wide readership should derive benefit from this excellent introduction to the problems of crystal chemistry. The subtitle gives an indication of the broad area which the author sees as relevant to crystal chemistry (one third of the book). Such a framework does, of course, mean that much appears in unconventional presentation, but the logical application of quantum-chemical theory to a few types of structure is extremely valuable to those interested in this subject. The

material has been subjected to highly judicious pruning so as to preserve clarity and facilitate understanding of the seemingly boundless data. The form and arrangement of the individual sections (atomic structure; bond systems and their utilization; description and explanation of the structures of elements, binary and ternary compounds, alloys and glasses) are novel and are completely subordinated to the chemical problems involved in structural geometry, stoichiometry, and bonding.

A drawback of the book is the scant treatment given to metals and intermetallic phases. One also notes the total absence of complex compounds in the narrower sense. This despite the fact that, in view of the selected framework, the structures of these substances would have been of considerable importance. Furthermore, to the quantum chemist the facts may appear to be clear and understandable – but is this in fact the case?

H.-G. v. Schnering [NB 891 IE]

Enamines. Synthesis, Structure, and Reactions. Edited by *A. G. Cook*. Marcel Dekker Inc., New York-London 1969. 1st ed., xi, 515 pp., numerous formulas and tables, $ 35.75.

The first review of enamines (113 pp.) was written in 1963 in "Advances in Organic Chemistry" by a single author, *J. Szmuszkovicz*. The present second review, which is also the first book on enamines, has eight authors, each of whom contributed a self-contained chapter.

In the first chapter, "Structure and physical properties of enamines" (54 pp.), *S. K. Malhotra* discusses the influence of steric and electronic factors, taking the cyclanone enamines as examples. Only a little information is found on the other enamines in the short sections on IR-, UV-, mass-, and particularly NMR-spectroscopy. No coupling constants or chemical shifts of R_2N–CH=, vinylogous amides, dienamines, enediamines, ketene aminals, and immonium salts or comparisons with the values for other nucleophilic olefins are given here.

The second chapter (46 pp.), "Methods and mechanisms of enamine formation" by *L. W. Haynes*, is mainly confined to tertiary enamines with no functional groups. An excellent survey is presented, though the fundamental work by *Sauer* and *Prahl* on the *cis,trans* isomerism of the enamines deserves a more detailed (and more positive) discussion.

The third chapter (13 pp.), "Hydrolysis of enamines" by *E. J. Stamhuis*, presents a thorough discussion of the kinetics and mechanism of the hydrolysis as a function of the pH value and the structure of the enamine. It shows how the C-protonation, as the rate-determining step, is replaced with decreasing pH by the hydration of the immonium ion and then by the decomposition of the amino alcohol.

In the fourth chapter (54 pp.), "Electrophilic substitutions and additions to enamines", *G. H. Alt* discusses protonation, alkylation, acylation, and reactions with other electrophiles, all reactions that reappear in other chapters. This is only observed later; too late, many readers will think, as they bemoan the lack of coordination. Following the demonstration, by many examples, of the close relationship of electrophilic substitutions and additions with cycloadditions, it would perhaps have been better to consider these reactions together in one large chapter. Mention should be made of the improbable formulation of the reaction with acrolein (pp. 128/129) and to exceptions (ref. 22) to O-protonation and O-alkylation of the acetylacetone enamines.

J. V. Paukstelis gives a very good, concise review of "Nucleophilic addition to iminium salts" in the fifth chapter (41 pp.).

In the sixth chapter (42 pp.), "Cycloaddition reactions of enamines", *A. G. Cook* surprises the reader with his liberal interpretation of the term "cycloaddition" and by his failure to include orbital symmetry considerations. He assumes a two-step mechanism for all cycloadditions, and this is probably why he is rather sparing with formulated mechanisms and with formulas in general. The range of addends includes not only alkenes, alkynes, cumulenes, O_2, isobenzofuroxane, carbenes, carbenoids, and 1,3-dipoles, but also cyclopropanes, cyclopropenes, aziridines, quinones, cumulenes + S, and cumulenes + isocyanide.

In the lengthy seventh chapter (60 pp.), "Heterocyclic enamines" by *O. Červinka*, the preparation, structure, properties, and reactions are followed by a section on aldol reactions of heterocyclic enamines and their importance to the biosynthesis of alkaloids.

The eighth chapter (156 pp.), "Enamines in organic synthesis" by *M. E. Kuehne*, is an excellently written survey. It is characterized by equations in the short form without numbering, more formulas than text, and everything presented in an extremely concentrated manner, though even the most out-of-the-way literature is covered. This chapter is recommended to anyone who wishes a quick survey on enamines.

Rigorous dividing lines between the various chapters have been deliberately avoided, with the result that an unusual amount of overlap occurs. Repetitions, which are quite useful here and there in different contexts, become a problem when *e.g.* alkylation and acylation are discussed in four chapters, and cycloaddition in two chapters besides the chapter devoted to this topic. The number of authors and the number of pages reflect not only the rapid development of enamine chemistry, but also the individual plan of the book: "The objective of this book is to review and correlate in depth the synthetic, mechanistic, and physical properties of enamines. This has been done by surveying the field from eight different perspectives. Since these prespectives have certain common areas between them, and since it seemed desirable to allow each contributor to tell his story in its fullest scope and in his own style, there is some overlapping of material between the chapters. However, it is hoped that the difference of viewpoints and context in which this material appears in these chapters will provide the reader with fresh insights and stimulate further research".

This has led to a very comprehensive but readily readable book. Variety is provided by the different styles of the authors. However, what is an advantage for reading is a disadvantage for reference. Though searches are facilitated by detailed author and subject indexes, it is usually necessary to refer to several chapters (in some cases with the same examples, different nomenclature, and relatively many printing errors and inaccuracies). Apart from the unnecessary overlapping, however, the shortcomings are unimportant against the abundance of information that is provided without verbosity.

The monograph is the most comprehensive review so far of the preparation, structure, physical properties, and reactions of the enamines, mainly the simple enamines with no functional groups on the double bond. The book is generously provided with formulas. Reaction mechanisms are given in varying depths of detail. The literature is covered up to 1968. There is no comparable book on the market, and it is hoped that the price will not prove an excessively severe obstacle to its wide use.

Günter Opitz [NB 883 IE]

Fuel Cells and Fuel Batteries. By *H. A. Liebhafsky* and *E. J. Cairns*. J. Wiley and Sons, Inc., New York-London-Sydney-Toronto 1968. 1st ed., x, 692 pp., 190 figures, 3 tables, bound 258 s.

The book is subtitled "A Guide to Their Research and Development". This points out the main purpose of the authors. They are not concerned predominantly with describing the present position of research and technology in the field on fuel cells, but with showing the reader *how*, *i.e.* by what paths (and detours) this position has been reached, where the main problems lie, and in what direction further investigation seems necessary and worthwhile. This has led to a sort of textbook on battery research, and in fact a textbook of electrochemistry. The first nine chapters (about half of the book) deal with fundamental electrochemical

problems, which are important to electrochemists in general. The special applications to fuel cells are certainly kept in the foreground, but only as a continuous theme that allows these general facts to be illustrated for a particular example.

A brief introduction (Chapter 1) is followed by a historical survey, beginning in 1839 (*Grove*) and ending in 1933 (*Baur* and *Tobler*). This chapter is thus "historical", but not in the sense that we can nowadays pass over it with a tolerant smile. It is in fact here that we see clearly that though refined methods of investigation and advanced technology have led in the meantime to important progress, the fundamental problems have hardly changed, and in particular, the idea postulated by *Baur* is still surprisingly current.

The next few chapters (3—9) present what was described above as a textbook. The thermodynamics and the kinetics of electrode reactions are dealt with in detail; the concept of irreversibility, the types of overpotential, electrocatalysis, and the shape of the current-voltage curve are discussed. The authors attach special importance to the study of transport processes, which are often regarded as being of minor significance, and consequently go into great detail in this chapter (79 pages). The next sections lead us more toward the practice of fuel cells; these are the chapters on the electrode structure, experimental methods, and the oxygen and hydrogen electrodes.

This first, general part of the book has already presented all the theoretical and practical information about "normal" fuel cells (H_2/O_2 in aqueous electrolytes) that is worth knowing, so that only special types remain to be discussed separately in the succeeding chapters (10—13). These are systems that use liquid fuels, those that utilize hydrogen indirectly, *i.e.* after conversion of hydrocarbons, those that burn hydrocarbons directly, and those in which non-aqueous electrolytes, *i.e.* molten salts or solid electrolytes, are used. The discussion of ion exchangers as electrolytes (Chapter 14) leads over to the description of complete fuel batteries (Chapters 14 and 15). The authors confine themselves here to two types that have already proved themselves in practice, *i.e.* the batteries developed by General Electric for the Gemini space missions and the methanol batteries constructed by Brown-Boveri for the long-term supply of power to television translators. This limitation is justified on the grounds of the enormous amount of data, which cannot be covered in a single book. On the other hand, because of this very abundance of material, the reader would expect such a comprehensive work to contain a critical selection of fundamentally or technically interesting prototypes, even if these have not yet come into practical use, even at the risk of being proved wrong in the assessment of future prospects. Instead of this the last chapter, which deals with the decisive step from the fuel *cell* to the fuel *battery*, closes with a consideration of the main problems involved, though further information can be obtained from references. The surprising brevity of the discussion of the technique of battery construction is compensated for, however, by a more thorough account of the development and practical testing of the Gemini batteries, interesting details of which can be provided by the authors as former employees of General Electric.

The book on the whole is thorough, comprehensive, and flowingly written in the "dry" theoretical sections. Its main value probably lies in the fact that it is a valuable source of information for the expert, but is equally suitable for use by the non-expert as an understandable introduction to what is for him a new field. Despite the continuous theme, each chapter, and particularly those that are predominantly theoretical, is self-contained (some of them have already been published as independent articles), so that special sections may be skipped for a general picture. This is particularly worthy of mention in that in this age of space travel, which has provided the most spectacular demonstration so far of the value of fuel cells, even many who are not electrochemists may be expected to have an interest in these modern sources of current.

Helmut Schmidt [NB 877 IE]

The Use of Chemical Literature. Published by *R. T. Bottle*. In the series "Information Sources for Research and Development". Butterworth, London 1969. 2nd Edit., xii + 294 pp., numerous illustrations and tables, bound 65 s.

The present book is the first in the series "Information Sources for Research and Development" published by *D. J. Foskett* and *R. T. Bottle*. Since important changes have taken place in the field of information since the appearance of the first edition (1962)[*] the authors have revised and expanded almost every chapter. Thus, sections have been added on spectroscopic data, physical methods, literature on analytical chemistry, and sources relating to prices and manufacturers of chemicals. The original chapters on data collections, physicochemical literature, literature on inorganic chemistry, nuclear chemistry, organic chemistry with a special chapter on Beilstein, and patents have been supplemented by a chapter on polymer chemistry. New also is the chapter on less conventional sources of information like market reports, personalities (Who's Who?) *etc.*

Although the work is designed predominantly for scientists from the English-speaking world, as the publisher emphasizes at the beginning, and the directions for the use of the chemical literature were written from this standpoint, the book should be generally useful to all readers interested in this field. The chapters on the work of libraries, primary literature (journals, reports, dissertations), secondary literature, in which the well-known larger abstracting services are described in detail, and works of reference give a particularly good survey even though the German-language services, which of course are important for the German scientist, are given only incomplete coverage.

A special chapter is devoted to translations and translation journals. A reference section for Russian literature is also supplied. The list of acronyms used in the literature and their meanings (Appendix I) is extremely useful. Appendix II contains exercises (with answers) on problems broached in the book.

It is difficult to see why Dissertation Abstracts and information services are mentioned under primary sources, while there is no reference to patents in this section. Furthermore, the Signal Information from the All-Union Institute for Scientific and Technical Information, Moscow, is not included in the section on information services while the reference to Express Information is inappropriate at this point.

The index at the end of the book is valuable, like every aid to search, but unfortunately random checks showed that it is not complete (no entry under CA Condensates and Basic Journal Abstracts and no reference to the paragraph on ASLIB on p. 18).

Despite its minor shortcomings, however, this book can be recommended to those interested in the field of information.

Christian Weiske [NB 887 IE]

The Biochemistry of Folic Acid and Related Pteridines. Vol. 13 in the series "Frontiers of Biology". By *R. L. Blakley*. North Holland Publ. Co., Amsterdam-London 1969. 1st ed., xxi, 569 pp., Dfl. 90.—.

The chemist knows the pterins only as an unusual class of rather intractable heterocyclic natural pigments that lead a somewhat aloof existence in the wings of the brimstone butterfly or in the skin of frogs. The biochemist also knows that pteridines and pteridine derivatives occupy key positions in metabolism as cofactors of several reactions. They have recently attracted increasing attention from plant physiologists as primary photoelectron acceptors in green leaves, from which the best-known conjugated pteridine derivative, folic acid, takes its name. However, relatively simple unconjugated pterins are active here and in the hydroxylation of aromatic rings; the more complex folic acid, on the other

[*] See Angew. Chem. *75*, 740 (1963).

hand, must be reduced to the tetrahydrogenated cofactor before it acquires its coenzyme functions in the metabolism of the active C_1 units, their transfer, and their interconversion. This enables them to act in the degradation of histidine and serine, in the synthesis of purines and nucleic acids, in the biosynthesis of methionine, in the formation of methane, and finally as an induction cofactor for protein synthesis in bacteria and cell organelles. Vitamin B_{12} derivatives also take part in some reactions of the C_1 compounds, and this leads to a system of vitamin interrelations that has not yet been fully elucidated. The pteridines are biosynthesized from the purines (the cell synthesis of which is itself folate-dependent); the biosynthesis of the folate cofactors also requires *p*-aminobenzoic acid, and can be blocked by sulfonamides, as well as by folate antagonists that inhibit the folic acid reductases. This offers various possibilities of chemotherapeutic interventions in the metabolism, which have become very widely used, as is well known.

All these confusing facts are presented carefully and faultlessly by *R. L. Blakley*, a pioneer of several fields of the chemistry and biochemistry of folic acid coenzymes, in this fine volume. The subject matter ranges from the nomenclature of conjugated and unconjugated pteridines, their occurrence in nature, and their chemistry and biochemistry to the enzymatic reactions catalyzed by them and carried out with them (in some cases in conjunction with the corrin cofactors) for absorption, storage, and analysis. The extensive original literature up to 1967 has been almost completely sorted, ordered, and critically evaluated. This skill in the assessment of the arguments is seen in the analysis of the data and observations reported by various groups of workers, which are discussed fairly and never without a careful and reasonable judgement based on experience with the difficult material and the experimental traps that result from premature interpretations. This is an excellent book in every respect, in which the answers to all relevant questions can be found. The factual information and the comparison of hypotheses will provide the reader with welcome stimuli as well as warnings. The presentation of the book is also extremely good, free from errors, and an aesthetic pleasure, particularly in the clear formulas.

L. Jaenicke [NB 885 IE]

The Structure and Action of Proteins. By *R. E. Dickerson* and *I. Geis*. Harper and Row, Publishers, New York-Evanston-London 1969. 1st Edit., viii + 120 pp., numerous figures, paperback, DM 20.50.

In conjunction with the determination of amino-acid sequences, X-ray structural analysis of crystallized proteins has opened up completely new horizons for the understanding of enzymes. The importance of this development has not so far been adequately reflected in introductory biochemistry textbooks. One does of course find the obligatory illustration of the hemoglobin molecule, but the accompanying text is invariably so meager as to contribute very little to one's understanding of protein structure; at best it can merely highlight the current importance of this field.

In the circumstances it is gratifying to report that the beginner will find X-ray enzymology very clearly explained in the present book by *Dickerson*, of the California Institute of Technology, who has himself taken part in a number of X-ray structural investigations. Starting with amino acids, a description is given of the rules according to which a peptide chain can fold itself to the secondary structure, and of the stability conditions (using the Ramachandran diagram). This is followed by a lucid and detailed, though not overelaborate discussion of the form of structural proteins (silk fibers, α-keratin, collagen), molecular carrier proteins, (myoglobin, hemoglobin, cytochrome c), and enzymes (lysozyme, ribonuclease, chymotrypsin, papaine, carboxypeptidase).

The book ends with a chapter on electron-microscope studies of proteins, which are built up from a number of subunits. Just to whet the appetite, the author refers briefly, when considering future prospects, to the complement system from the standpoint of the enzymologist. Nowhere will the reader find himself bogged down in purely descriptive, morphological treatment, every effort being made to bridge the gap between structure and function. Proteins are regarded as machines on the molecular scale, with the atoms as moving parts. A decisive contribution to didactic clarity has been made by *Irving Geis*, who has already gained world-wide acclaim for his brilliantly executed illustrations in the Scientific American. Both text and the illustrations in this introductory textbook are exemplary. A supplement containing 55 stereo illustrations of nine of the proteins discussed in the book and accompanied by a simple viewer constitute another useful feature. The book may be warmly recommended to everyone interested in the development of modern biochemistry.

Guido Hartmann [NB 892 IE]

Methoden der organischen Chemie (Houben-Weyl). Bd. VII, Teil 4: Sauerstoffverbindungen II (Methods of Organic Chemistry (Houben-Weyl). Vol. VII, Part 4: Oxygen Compounds II). Edited by *Eugen Müller*. Georg Thieme Verlag, Stuttgart 1968. 4th Edit., ix, 508 pp., numerous formulas, bound DM 178.—.

The present volume describes the preparation and transformation of isatins, thionaphthenequinones, ketenes, carbon suboxide, and ketene derivatives.

The first two chapters, on isatins and thionaphthenequinones (including 3-hydroxythionaphthenes) (pp. 1—51) provide the dye chemists with a detailed survey of historically interesting and now apparently closed field of indigoid dyes.

Most of the volume (pp. 53—447) deals with the diversified field of ketenes and ketene derivatives, which is of great importance to the preparative organic chemist. In addition to the preparation methods which are already regarded as "classical", such as the pyrolysis of ketones and carboxylic acid derivatives, the modern photochemical methods (pp. 73—75) and the photofragmentation method (p. 106) for the preparation of ketenes are also described.

Considerable space (pp. 113—225) is devoted to the many applications of the extremely reactive ketenes. In addition to their use as acylating agents for compounds which contain active hydrogen, the addition reactions, which frequently proceed with cyclization (*e.g.* formation of β-lactams and dihydropyridines, 1,4-cycloadditions, additions of ketenes to enamines, vinyl ethers, and isocyanates), and which have led to a wide range of novel heterocyclic compounds, are also discussed. Reactions with carbonyl compounds, which lead to different products depending on the reaction (*e.g.* to β- or γ-lactones), are then dealt with. Separate chapters are finally devoted to reactions with halogens, inorganic acid halides, and organometallic and nonmetallic organoelement compounds.

The next section (pp. 226—285) deals with the preparation and transformation of diketenes and of oligomers and polymers of ketenes. One of the most important properties of diketene is its ability to act as an acetoacetylating agent (3-oxobutanoylating agent) for hydroxy and amino compounds. In suitable cases these compounds react further to give heterocyclic compounds, in the same way as acetoacetic ester. A subsection deals with the use of diketene for *C*-acetoacetylation in the presence of Lewis acids. The preparation and reactivity of alkylketene dimers, ketoketene dimers, ketene oligomers, and ketene polymers are then discussed. As in the other chapters, the material is presented clearly here with the aid of numerous tables.

Carbon suboxide is described in monograph (pp. 286—311) form. The preparative chemist is still very interested in this fourfold heterocumulene. It is therefore particularly pleasing to find that its many reactions have now been described in

detail. The sulfur analogs thioketene and carbon subsulfide are also mentioned briefly.

The last part of the volume (pp. 323–447) describes the preparation and transformation of ketene derivatives, *i.e.* ketenimines, ketene *O,O*- and *O,N*-acetals, and ketene mercaptals and aminals (*N,N*-acetals). The syntheses and properties of this class of compounds have only recently been investigated in detail. Owing to their relationship with the ketenes, the preparative organic chemist will find here reactive starting compounds for the preparation of many heterocyclic ring systems and other valuable intermediates, such as amidines, esters of carboxylic acids, ortho esters, acetoacetic ester derivatives, and cyclobutane derivatives.

Though more up-to-date formulations of the reaction mechanisms would appear desirable in some places (*e.g.* diazoketone rearrangement p. 87ff., 2-halogenocyclobutanone rearrangement p. 103, acyl-sulfonium ylide rearrangement p. 107, carboxylic acid imide formation p. 336), the present volume provides an excellent survey of the varied material. It is presented lucidly, and is well supplemented by many practical examples. The literature has been covered up to the end of 1967. The evaluation of many patents and BIOS and FIAT Reports makes this work an up-to-date, valuable aid for the preparative chemist, which fills a marked need.

Heinrich Wamhoff and *Friedhelm Korte* [NB 893 IE]

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Kinetic Evidence for Reactive Intermediates[**]

By Rolf Huisgen[*]

Spectroscopic methods have recently been developed that allow the direct detection of reactive intermediates under favorable circumstances. The most general and reliable method, however, is still the indirect one, which makes use of the principle of kinetic competition; this method is based on the freedom of the intermediate to choose between several reaction possibilities. The following discussion is addressed less to the specialist in reaction mechanisms than to the outsider who wishes to obtain some idea of the value and limitations of the kinetic method.

1. Fundamental Concepts

It is not true that chemists became interested in reaction mechanisms only about 40 years ago. The reaction event fascinated even the chemist of earlier periods, but the knowledge and methods required for the experimental testing of views on reaction mechanisms were lacking. These workers, consequently, often had to be satisfied with determining the stoichiometry of a reaction.

The methods that have been developed in the meantime have led to a rapid growth of our knowledge of reaction mechanisms. The term *reaction mechanism* leads us first to think of the *structural changes* in the components during the reaction event. Changes in the distance functions and bond lengths can be described, possibly supplemented by electron density and charge separation. The conceptual clarity of these pictures and models was enhanced by the introduction of *energy relations*. At the beginning of his course, the chemistry student of today is taught to look on the interplay of the molecules as an "energy landscape". Depending on their internal energy content, the molecules or collision complexes move up and down in their potential troughs. The reaction event is associated with escape from such a trough, *i.e.* with passage over its rim.

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The structural and energetic approaches are combined in the *energy profile*. The chemical potential of the reacting system is plotted on the ordinate, preferably as the free energy, and the abscissa is the *reaction coordinate*, a geometrical parameter symbolizing the interplay of successive breakage and formation of bonds. The energy profile may consist of a single barrier, the summit of which is referred to as the *transition state*; the *activation energy* $\Delta G^{\ddagger}$ must be supplied in order to reach this peak. This is followed by a descent into a trough with liberation of energy; the amount by which the energy set free exceeds the activation energy is known as the heat of reaction. The molecules or collision complexes usually leave their potential trough at the lowest point, even if this reaction path does not lead to the product with the maximum bond energy. The chemical reaction is controlled *kinetically*, *i.e.* by the height of the activation barrier, and not *thermodynamically* by the quality of the product, unless a series of forward and reverse reactions allows the thermodynamically favored outcome.

Many reactions that were described earlier by a simple activation peak (Fig. 1a) have turned out to be more complicated systems, frequently even involving several intermediates (Fig. 1b).

Transition states are not really "states" with finite lifetimes, but snapshots. On the other hand the dips in the energy profile, *i.e.* the intermediates, have definite lifetimes. Energy profiles can resemble a cross section through the Alps. A feature that they share with a mountain panorama is that only the *first* peak can usually be seen from the bottom, and one certainly

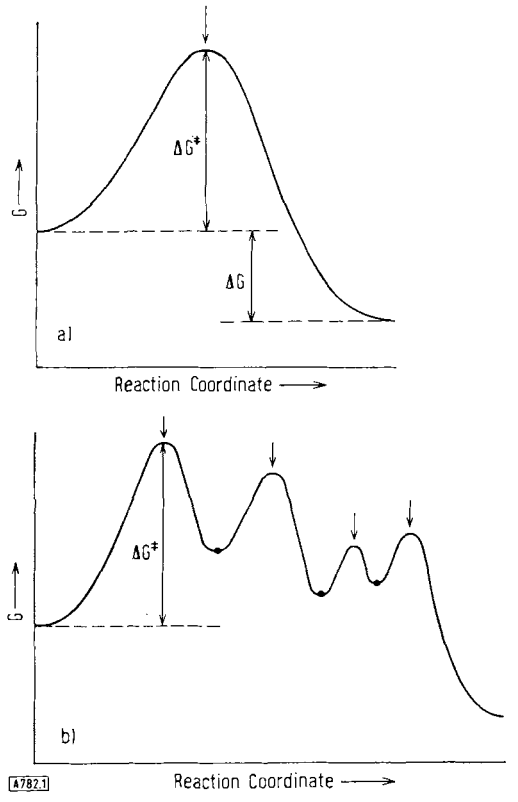


Fig. 1. Energy profiles of reactions (a) without and (b) with intermediates.
↓ : transition states; • : intermediates.

cannot see over the highest ridge. The rate-determining step of the system is the conquest of the highest peak. This is the only peak about which information is provided by the *overall kinetics* with the activation enthalpy and the activation entropy.

How does one obtain information about what happens behind the first high ridge? In other words, how does one detect *intermediates*? Only a few decades ago it was considered irresponsible to postulate intermediates that could not be isolated and stored in flasks. Nowadays scepticism is aroused by any claim to the isolation of a reactive intermediate as such. The substance in question is all too often a compound from a side-equilibrium of the kinetic system. The walls of the energy trough in which the reactive intermediate lies are often so low that the material cannot collect here, but flows away rapidly with formation of the products. To detect short-lived intermediates directly, it is necessary either to produce a sufficiently high stationary concentration, as occurs *e.g.* in flash photolysis, or to use an extremely sensitive method of analysis; ESR spectroscopy, for example, responds even to very small concentrations of free radicals. Though such spectroscopic methods provide valuable information on the nature of intermediates, they are not free from the above shortcoming in the distinction of main path and side-equilibria.

Elegant and reliable criteria for the detection of unisolable intermediates are based on *kinetic competition*. If there is only one energy peak between the reactants and the product, the product cannot contain anything that was not already present in the starting system, *i.e.* that did not enter into the rate-determining activation process; the energy profile is unambiguous. A dip in the energy profile, on the other hand, may be interpreted as a "breather" of the reacting system. The system comes to rest here, and can choose between several possible reactions. It can enter bonding interactions with molecules that were not involved in the first, rate-determining step, *i.e.* in the formation of the intermediate.

$$A \longrightarrow \underset{\text{Intermediate B}}{B} \longrightarrow C \qquad B \rightleftarrows A \longrightarrow C$$

in main path — in side-equilibrium

A well-chosen competition system gives reliable evidence for an intermediate, but not much more. Information about its nature is limited; such information may be available from the type of the reactions between which the intermediate chooses. As to the structure of the intermediate, analogies or the introduction of further experimental criteria, such as the steric course of the reaction, are necessary. Some role must also be given to chemical intuition here, though not to utter fantasy. Great caution should be exercised in the postulation of new elementary reaction steps or in the assumption of more intermediates than are verified experimentally and by convincing analogy. A principle that applies in all natural sciences, and which is known as *Occam*'s razor[1], enjoins the use of the simplest possible description: *Entia non sunt multiplicanda praeter necessitatem.*

What are reactive intermediates? It is not easy to add chemically to the above definition as a "dip in the energy profile". One usually thinks first of short-lived radicals, carbonium ions, carbanions, carbenes, azenes (nitrenes), and the like; some compounds of these classes can be intercepted and isolated. However, the range extends far beyond the electron-deficient and electron-rich compounds, as is shown by singlet oxygen[2], diimine[3], strained ring systems, unstable oxidation states, or energetically unfavored valence tautomers. Photo-excited states all belong to this group. Close relatives of classes of compounds that are known to be stable sometimes also defy isolation, and kinetic detection then becomes necessary, as illustrated later for diphenylnitrilimine.

If many of the examples described below are taken from our own work, this is not because we attach particular importance to it, but is rather intended to show that the kinetic detection of intermediates is a routine method for research on reaction mechanisms.

2. Reaction Order as Evidence for Intermediates

If the reaction product contains a structural unit that does not appear in the rate equation of the determining step, it is logical to conclude that an inter-

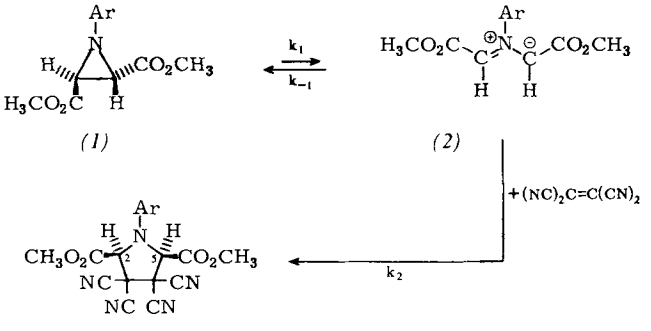
[1] *William of Occam*, born near London in 1285, died at Munich 1349.
[2] *C. S. Foote*, Accounts chem. Res. *1*, 104 (1968).
[3] For a review, see *S. Hünig, H. R. Müller*, and *W. Thier*, Angew. Chem. *77*, 368 (1965); Angew. Chem. internat. Edit. *4*, 271 (1965).

mediate is involved. The rate equation in this case does not reflect the stoichiometry of the process as a whole.

Aziridines of the type *(1)* can enter into cycloadditions in which the CC bond is broken [4, 5]. If we follow the adduct formation with tetracyanoethylene at 100 °C dilatometrically, we find that the rate equation does not contain the concentration of tetracyanoethylene, as long as it is present in an at least equimolar amount [6]. The equation is

$$d\,[\text{adduct}]/dt = k_1\,[\text{aziridine } (1)]$$

Experiments with 10, 20, and 30 equivalents of tetracyanoethylene gave the same dilatometric first order rate constant.



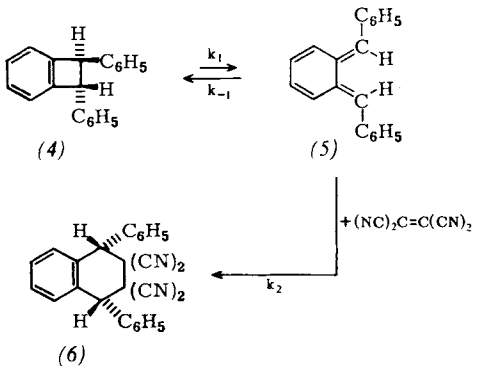
(1) *(2)* *(3)*

Ar = $C_6H_4OCH_3$-*p*

A step preceding the cycloaddition must therefore alone be rate-determining. It is not the aziridine *(1)*, but the azomethine ylide *(2)*, which is present in a low equilibrium concentration and combines as a 1,3-dipole with the olefinic dipolarophile. The reaction with tetracyanoethylene is so fast that the reverse reaction *(2)*→*(1)* is completely suppressed and the rate of the adduct formation is determined only by the ring cleavage *(1)*→*(2)*, *i.e.* by k_1.

The intermediate *(2)* can be detected stereochemically as well as kinetically. The aziridine-*trans*-2,3-dicarboxylic ester *(1)* gives a cycloadduct *(3)* with ester groups in the *cis*-2,5 positions. Such a steric course is inconceivable in a one-step process. A satisfactory explanation is provided by the *conrotatory* ring cleavage *(1)*→*(2)* [5].

Interrelations of benzocyclobutenes with *o*-quinodimethanes have been postulated, but the valence tautomerism *(4)*⇌*(5)* was demonstrated only by kinetic measurement of the adduct formation with tetracyanoethylene. As in the last example, the reaction rate depends only on the concentration of the 7,8-diphenylbenzocyclobutene. The constant k_2 is so large that the reverse reaction *(5)*→*(4)* is of no importance. The steric course also confirms the occurrence of the



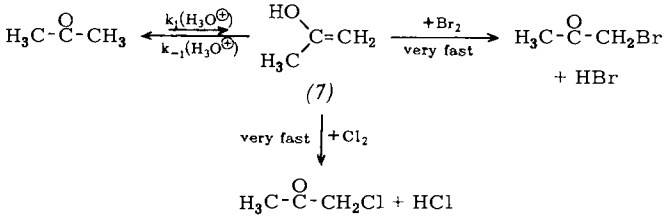
(4) *(5)* *(6)*

o-quinodimethane *(5)* as an intermediate, since the *trans*-diphenyl compound *(4)* gives a Diels-Alder adduct *(6)* with *cis*-phenyl residues [7].

A classic example of the discrepancy between stoichiometry and the rate equation is found in the halogenation of acetone in aqueous acid. *Lapworth* [8] discovered that bromine participates with "zero order" and that the rate is determined by the concentrations of acetone and of acid:

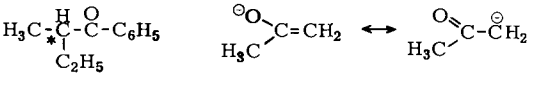
$$-\,d\,[\text{acetone}]/dt = k_2\,[H_3O^+]\,[\text{acetone}]$$

The chlorination proceeds with the same rate constant as bromination; in both cases an intermediate is intercepted by the halogen, the formation of this intermediate determining the overall rate of the reaction.



(7)

Regarding the nature of the intermediate, all we can learn from the kinetic investigation is its high rate of halogenation. Since the acid-catalyzed iodination and racemization of (+)-methylethylacetophenone *(8)* also show the same rate constant [9], it seems likely that the enol form *(7)* of acetone is involved. Kinetic measurements give equal rate constants for the base-catalyzed iodination and bromination of acetone, the reactions being of zero order with respect to NaOCl and NaOBr, respectively [10]. The decisive role of the enolate ion *(9)* was underlined by the observation that alkali-catalyzed racemization and H,D-exchange in the optically active ketone *(8)* proceed with equal rate constants [11].



(8) *(9)*

[4] *H. W. Heine, R. Peavy,* and *A. J. Durbetaki,* J. org. Chemistry *31*, 3924 (1965).

[5] *R. Huisgen, W. Scheer, G. Szeimies,* and *H. Huber,* Tetrahedron Letters *1966*, 397; *R. Huisgen, W. Scheer,* and *H. Huber,* J. Amer. chem. Soc. *89*, 1753 (1967).

[6] *R. Huisgen, W. Scheer,* and *H. Mäder,* Angew. Chem. *81*, 619 (1969); Angew. Chem. internat. Edit. *8*, 602 (1969).

[7] *R. Huisgen* and *H. Seidl,* Tetrahedron Letters *1964*, 3381.

[8] *A. Lapworth,* J. chem. Soc. (London) *85*, 30 (1904).

[9] *P. D. Bartlett* and *C. H. Stauffer,* J. Amer. chem. Soc. *57*, 2580 (1935).

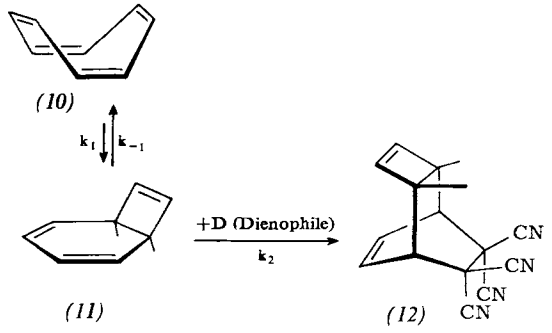
[10] *P. D. Bartlett,* J. Amer. chem. Soc. *56*, 967 (1934).

[11] *S. K. Hsü, C. K. Ingold,* and *C. L. Wilson,* J. chem. Soc. (London) *1938*, 78.

3. Competition of Forward and Reverse Reaction

In all the examples considered above, the rate-determining process was a tautomerization. In the absence of an intercepting reagent, the reactive tautomers occur in equilibrium concentrations so small that they cannot be detected directly. This means that the formation of the reactive tautomer (rate k_1) is much slower than its reverse reaction (k_{-1}). A reaction order of zero for the intercepting reagent indicates that the combination of this reagent with the intermediate is even much faster than the reverse reaction mentioned.

If k_{-1} and k_2 are of the same order of magnitude, this does not affect the reliability of detection of the intermediate. The rate equation becomes somewhat more complicated, and the intercepting reagent is now involved as a function of its concentration. The Diels-Alder reactions of cyclooctatetraene, which are accompanied by rearrangement, may be taken as an example. The addition of tetracyanoethylene is preceded by tautomerization to bicyclo[4.2.0]octatriene



(11); the equilibrium concentration of *(11)* found indirectly from kinetic data is only 0.01 % in dioxane at 100 °C [12].

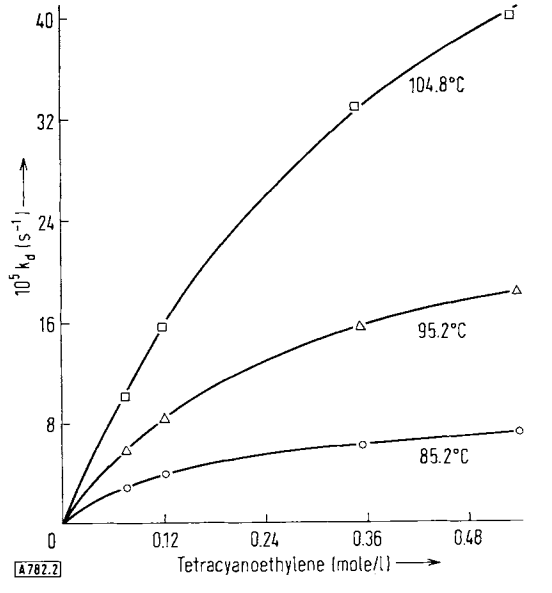


Fig. 2. Dilatometric rate constants k_d for the reaction of cyclooctatetraene (0.02 mole/l) with excess tetracyanoethylene in dioxane at various temperatures.

[12] *R. Huisgen* and *F. Mietzsch*, Angew. Chem. *76*, 36 (1964); Angew. Chem. internat. Edit. *3*, 85 (1964).

The formation of *(12)* is followed dilatometrically, evaluation as a first or pseudo-first order reaction being allowed by the use of a sufficiently large excess of dienophile. Figure 2 shows dilatometric constants (k_d) of this type as a function of the excess of dienophile and of the temperature. If the bimolecular combination with the dienophile alone were rate-determining, the results should be straight lines passing through the origin; $k_d = k_{1\psi}$ should be proportional to [D] (dienophile concentration).

The quantitative evaluation of the competition of reverse and forward reactions makes use of the *steady state* approximation (Bodenstein theorem) [13,14]. The change in the concentration of the intermediate *(11)* is negligible compared with those of *(10)* and *(12)*, and is equated to zero.

$$\frac{d\,[(11)]}{dt} = 0 = k_1\,[(10)] - k_{-1}\,[(11)] - k_2\,[D]\,[(11)]$$

$$[(11)] = \frac{k_1\,[(10)]}{k_{-1} + k_2\,[D]}$$

$[(11)]$ can be substituted in the rate equation for the adduct formation:

$$\frac{d\,[(12)]}{dt} = k_2\,[D]\,[(11)] = \frac{k_1 k_2\,[(10)]\,[D]}{k_{-1} + k_2\,[D]}$$

Comparison with the overall equation for the dilatometric measurement

$$d\,[(12)]/dt = k_d\,[(10)]$$

yields k_d as a function of [D]:

$$k_d = \frac{k_1 k_2\,[D]}{k_{-1} + k_2\,[D]}$$

Simple transformation gives the equation of a straight line for a plot of k_d against $k_d/[D]$; k_1 is the intercept on the ordinate and $-k_{-1}/k_2$ is the slope.

$$k_d = k_1 - \frac{k_{-1}}{k_2}\,\frac{k_d}{[D]}$$

In the extreme case $k_2/[D] \gg k_{-1}$, which was dealt with in Section 2, this expression becomes $k_d = k_1$. Since the k_d values in Figure 2 give straight lines in this new type of plot (Fig. 3), the kinetic system must be correct. The competition of a first order reverse reaction with a second order cycloaddition proves the occurrence of an intermediate in this case. At an infinitely high dienophile concentration, *i.e.* for $k_d/[D] = 0$, we obtain $k_d = k_1$. From the temperature dependence of the extrapolated k_1 values, the following values result for the activation process of the valence tautomerization: $\Delta H^{\ddagger} = 28.1$ kcal/mole; $\Delta S^{\ddagger} = +1$ e.u. [15].

[13] *M. Bodenstein*, Z. physik. Chem. *85*, 329 (1913).

[14] *A. A. Frost* and *R. G. Pearson*: Kinetics and Mechanism. Wiley, New York 1961, 2nd Edit.; Kinetik und Mechanismus homogener chemischer Reaktionen. Verlag Chemie, Weinheim 1964, p. 159.

[15] *F. Mietzsch*, Dissertation, Universität München 1965.

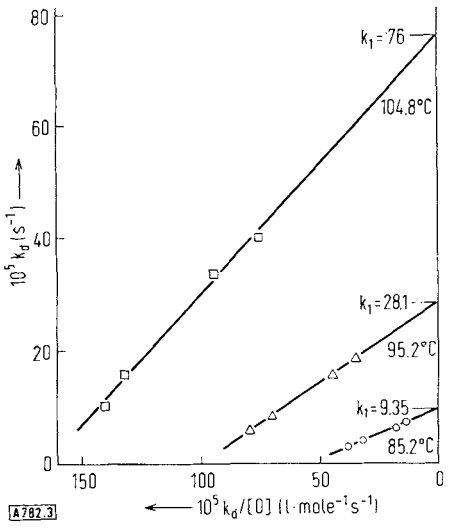


Fig. 3. Dilatometric constants of Fig. 2 plotted against $k_d/[D]$.

This tells us nothing about the nature of the intermediate. Bicyclooctatriene *(11)* has the quasi-planar diene system required for the Diels-Alder reaction, while *(10)* has not. In the equilibrium *(13)*⇌*(14)*, in which both tautomers can be isolated, only *(14)* again adds dienophiles[16]. The extrapolated k_1 values should be independent of the nature of the dienophile, as has in fact been shown for *(10)* and its phenyl derivative[13]. *Vogel, Kiefer,* and *Roth*[17] were able to confirm the existence of *(11)* by its preparation at −78 °C; *(11)* changes into *(10)* even below 0 °C.



(13) *(14)*



(15) *(16)*

The Diels-Alder adducts of cycloheptatriene *(15)* are structurally derived from norcaradiene *(16)*[18]. Kinetic measurements on the reaction with tetracyanoethylene gave k_d values that were proportional to the dienophile concentration over the entire range measured[19]. This means that the establishment of the equilibrium *(15)*⇌*(16)* is fast in comparison with the Diels-Alder reaction. The intermediate cannot be detected kinetically in this case. If it is assumed that the diene activity of *(16)* can be equated to that of *(14)* (equal k_2 values for the addition of tetracyanoethylene to the cyclohexadiene portion of the two molecules), a 0.1 % equilibrium concentration of *(16)* at 20 °C would lead to k_d values of the order found.

The classification of nucleophilic aliphatic substitutions as S_N1 and S_N2 by *Hughes* and *Ingold* is based on the kinetic criterion[20]. An ionization was postulated as the rate determining step for the first order substitution. It is interesting to note that kinetic evidence for the carbonium intermediate comes only from the deviations from the first order.

$$R{-}Cl \underset{k_2}{\overset{k_1}{\rightleftarrows}} R^{\oplus} + Cl^{\ominus} \xrightarrow[k_\psi]{+\,2H_2O} R{-}OH + H_3O^{\oplus} + Cl^{\ominus}$$

The ionization of 4,4′-dimethylbenzhydryl chloride *(17)* in aqueous acetone leads to a rather selective carbonium ion, which can not only react with water to give benzhydrol *(19)* but can also combine with chloride ion formed to regenerate the starting material. The kinetic situation, a combination of a reversible and a consecutive system, is similar to that described above, except that a second order reverse reaction (k_2) now competes with a pseudo-first order forward reaction (k_ψ) (since water is a component of the solvent, its concentration remains practically constant) for the intermediate. As above, the Bodenstein theorem is applied.

$$d[R^{\oplus}]/dt = k_1[RCl] - k_2[R^{\oplus}][Cl^{\ominus}] - k_\psi[R^{\oplus}] = 0$$

$$-\frac{d[RX]}{dt} = \frac{k_1[RCl]}{(k_2[Cl^{\ominus}]/k_\psi) + 1} \approx k_{overall}[RCl]$$

The ratio $k_2[Cl^{\ominus}]/k_\psi$ in the denominator is the competition constant of the reverse reaction and the carbinol formation. The hydrolysis of dimethylbenzhydryl chloride thus begins with the rate constant k_1 as long as no chloride ions are present. As the reaction proceeds, the liberated chloride ions cause a decrease in the overall hydrolysis constant. $k_{overall}$ is thus no longer really a "constant", and the treatment as a first order reaction is no longer a permissible approximation. In the special case, $k_{overall}$ falls to 72% of the initial value after 90% conversion when a 0.04 M solution of *(17)* in 85% aqueous acetone is used[21]. If the chloride ion is present in the solution from the outset, *e.g.* as 0.06 M LiCl, the hydrolysis begins with only 54% of the $k_{overall}$ value found without the addition of the salt. The hydrolysis constant of triphenylmethyl chloride in 85% acetone is decreased by a factor of 4 on addition of 0.02 M NaCl[22].

The influence of the chloride ion on the hydrolysis constant is even greater than appears from the above data. The kinetic scheme is further complicated by the

[16] *R. Huisgen, F. Mietzsch, G. Boche,* and *H. Seidl*: Organic Reaction Mechanisms. Chem. Soc. (London), Spec. Publ. *19*, 3 (1965).

[17] *E. Vogel, H. Kiefer,* and *W. R. Roth*, Angew. Chem. *76*, 432 (1964); Angew. Chem. internat. Edit. *3*, 442 (1964).

[18] For a review of the cycloheptatriene/norcaradiene problem see *G. Maier*, Angew. Chem. *79*, 446 (1967); Angew. Chem. internat. Edit. *6*, 402 (1967).

[19] *R. Huisgen* and *W. D. Wirth*, experiments performed in 1960/61.

[20] For reviews, see *C. K. Ingold*: Structure and Mechanism in Organic Chemistry. G. Bell and Sons, London 1953, p. 306; *A. Streitwieser*, Chem. Reviews *56*, 571 (1956).

[21] *L. C. Bateman, E. D. Hughes,* and *C. K. Ingold*, J. chem. Soc. (London) *1940*, 974.

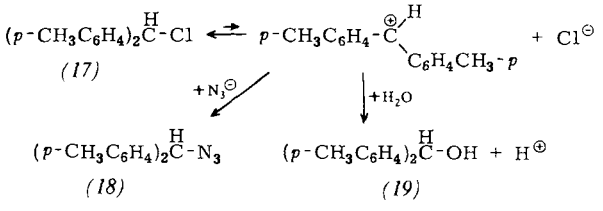
[22] *C. G. Swain, C. B. Scott,* and *K. H. Lohmann*, J. Amer chem. Soc. *75*, 136 (1953).

fact that salts in general cause an increase in the ionization rate by increasing the ionic strength of the solvent [23]. This acceleration by the salt effect is overcompensated in the case of the chloride ion by the regeneration of the organic chloride.

4. Rate-Product Discrepancy

This term covers the evidence for intermediates on the basis of incompatibility of the rate equation with the stoichiometry (see Section 2). We shall use the term rate-product discrepancy primarily to denote the absence of *quantitative* agreement.

If 0.05 M sodium azide is added to a solution of 4,4'-dimethylbenzhydryl chloride *(17)* in 85% acetone, the rate constant of the solvolysis increases by 48%; the product contains 60% of the organic azide *(18)* and 40% of the carbinol *(19)* [23]. If the increase in rate were due to a direct reaction of the chloride *(17)* with the azide ion, only 32% of *(18)*



should be expected. The rate acceleration is in fact a salt effect, which occurs to an equal degree on addition of 0.05 M tetramethylammonium nitrate. The reaction with the azide ion thus takes place only at the carbonium stage, where azide and water are competing.

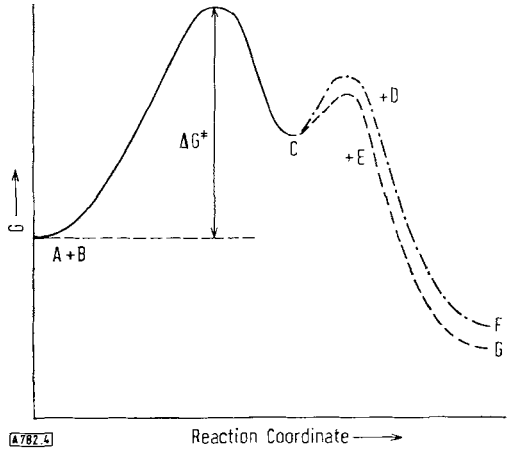


Fig. 4. Competition of two reaction components D and E for an intermediate C.

How does one define and determine competition constants? In Figure 4, the reactants D and E compete for the intermediate C with formation of the products F and G.

$$+ d[F]/dt = - d[D]/dt = k_D [C][D]$$
$$+ d[G]/dt = - d[E]/dt = k_E [C][E]$$

Division of the first differential equation by the second gives

$$\frac{d[D]}{d[E]} = \frac{k_D}{k_E} \frac{[D]}{[E]}$$

and furnishes, after transformation, the competition constant:

$$\varkappa = \frac{k_D}{k_E} = \frac{d[D]}{[D]} \frac{[E]}{d[E]} = \frac{d \ln [D]}{d \ln [E]}$$

The replacement of the differentials by finite differences is allowed. If $[D]_0$ and $[E]_0$ are the initial concentrations of the competing reactants and $[D]_e$ and $[E]_e$ their concentrations at the end of the reaction, we obtain an expression that contains only quantities that are experimentally accessible.

$$\varkappa = \frac{\log [D]_0 - \log [D]_e}{\log [E]_0 - \log [E]_e} = \frac{\log [D]_0 - \log ([D]_0 - [F]_e)}{\log [E]_0 - \log ([E]_0 - [G]_e)}$$

The validity of this equation is unrestricted. If D and E are present in a very large excess, there will be practically no change in their concentrations during the reaction. $[D]_0$ and $[E]_0$ are now constants, and integration leads to the even simpler expression:

$$\varkappa = \frac{k_D}{k_E} = \frac{d[D]}{d[E]} \frac{[E]_0}{[D]_0} = \frac{d[F]}{d[G]} \frac{[E]_0}{[D]_0} = \frac{[F]_e}{[G]_e} \frac{[E]_0}{[D]_0}$$

The experimental procedure is to allow D and E to compete for C in various ratios and to determine the concentrations of the products F and G. The reliability of the method is then shown by agreement in the competition constants $\varkappa$.

This can be illustrated by the detection of benzyne as an intermediate in the nucleophilic substitution of halobenzenes by phenyllithium or lithium piperidide. The substitution of unactivated aryl halides with strong nucleophiles proceeds with primary elimination, as is revealed by a characteristic change in the position of the substituent (cine substitution) [24].

The liberation of benzyne *(21)* from fluorobenzene in ether at 20 °C proceeds 25 times as rapidly with lithium

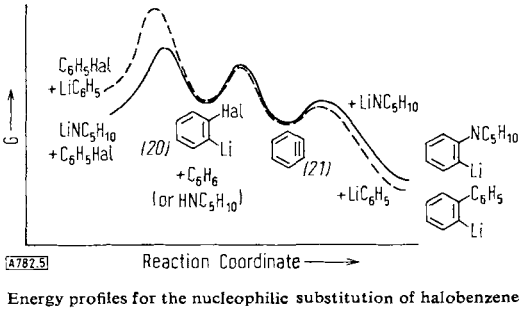


Fig. 5. Energy profiles for the nucleophilic substitution of halobenzene with phenyllithium and with lithium piperidide.

[23] *L. C. Bateman, M. G. Church, E. D. Hughes, C. K. Ingold,* and *N. A. Taher*, J. chem. Soc. (London) *1940*, 979.

[24] For reviews, see *R. Huisgen* and *J. Sauer*, Angew. Chem. *72*, 91 (1960); *R. W. Hoffmann*: Dehydrobenzene and Cycloalkynes. Verlag Chemie, Weinheim 1967.

piperidide as with phenyllithium[25]. The energy profile (Fig. 5) contains an additional dip; the first intermediate is the *o*-lithiohalobenzene *(20)*, which can also be intercepted. The slow, rate-determining formation of benzyne is followed by fast additions of nucleophilic agents to the short-lived intermediate. Competition tests with lithium piperidide and phenyllithium in various ratios give $\varkappa = 0.23$. Though slower by a factor of 25 in the liberation of benzyne, phenyllithium is 4.4 times as fast as lithium piperidide in the addition to *(21)*[26]. This discrepancy between the overall kinetics and the product composition makes the assumption of an intermediate *(20)* unavoidable.

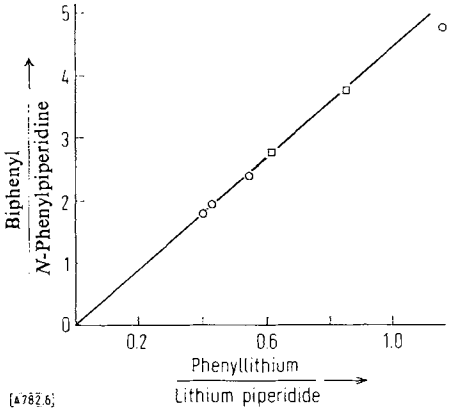


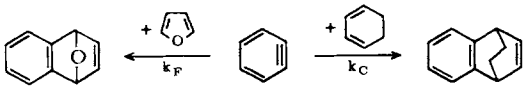
Fig. 6. Competition of phenyllithium and lithium piperidide in the addition to benzyne. Experiments with fluorobenzene (□) and chlorobenzene (○) in boiling ether [26].

Figure 6 shows a plot of the concentration ratio of the competing reactants against that of the products. The experimental data give a straight line passing through the origin. The agreement of the $\varkappa$ values for experiments with fluorobenzene and with chlorobenzene indicates that the intermediate responsible for the product formation is free from halogen. Can any other information be obtained?

5. Common Intermediate from Different Precursors

If one and the same intermediate is formed from different starting systems, the nature of the generating systems often provides evidence on the structure of the intermediate. The occurrence of a common intermediate should not be concluded merely from qualitative preparative findings. Rigid proof can be provided only by agreement of the competition constants in a quantitative competition test.

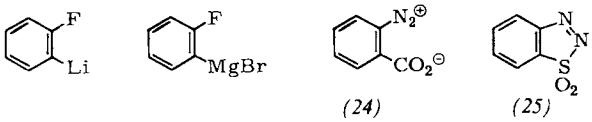
A pertinent example is again offered by the structure of benzyne; C_6H_4 was at first regarded with much suspicion. In addition to the above path *via* metalated halobenzenes, other precursors became known, in particular benzenediazonium *o*-carboxylate *(24)*[27] and benzo[*d*]thiadiazole 1,1-dioxide *(25)*[28]. The competing reactants for the detection of an identical intermediate in all these systems must be compounds that are neither electrophilic nor strongly nucleophilic, since reactions with the precursors of the benzyne must be avoided.



(22) *(21)* *(23)*

The cycloadditions to furan and cyclohexadiene to form *(22)* and *(23)* were found to be suitable. Under identical conditions, the benzyne from various sources adds to the two dienes with the same competition constant (Table 1) of 21.5 (average value)[29]. In view of the difference in the starting systems, it is difficult to imagine an intermediate other than C_6H_4 *(21)* as a "common denominator"; the only other possibility would be a complex of *(21)* with the solvent.

Table 1. Competitive addition of furan (k_F) and cyclohexadiene (k_C) to benzyne *(21)* from various precursors in tetrahydrofuran at 50 °C [29].



			(24)	*(25)*
k_F/k_C	20.8	21.2	21.4	22.4

A recent study made use of the competitive addition of benzyne to the 1,4- and 9,10-positions of 1,4-dimethoxyanthracene[30]. The competing reactants thus belong to one and the same molecule. The identity of the intermediate was confirmed and extended to two other starting systems. However, the competition constant was only 2.3.

One critical point is that the conclusion of a common intermediate is permissible only if the competition constant is sufficiently different from 1. Very "hot" intermediates react with the first partner encountered, *i.e.* randomly. Competition constants of 0.5 to 2 do not rule out the possibility of substantially *diffusion-controlled* processes. In such cases, independent experiments with different ratios of the competing reactants are particularly important.

Phenylations of aromatic compounds have been known for more than 70 years. They were ascribed to the free phenyl radical by *Wieland*[31] and by *Hey*[32].

Such phenylations have been observed *e.g.* in the homolysis of nitrosoacetanilide *(26)*, phenylazotri-

[25] *R. Huisgen* and *J. Sauer*, Chem. Ber. *92*, 192 (1959).

[26] *R. Huisgen, W. Mack*, and *L. Möbius*, Tetrahedron *9*, 29 (1960). Confirmation of the competition constant: *Th. Kauffmann, H. Fischer, R. Nürnberg, M. Vestweber*, and *R. Wirthwein*, Tetrahedron Letters *1967*, 2911.

[27] *M. Stiles* and *R. G. Miller*, J. Amer. chem. Soc. *82*, 3802 (1960).

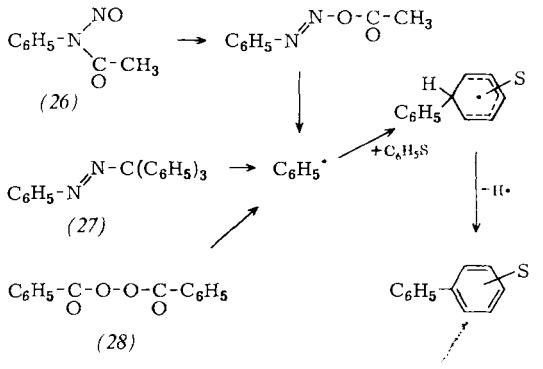
[28] *G. Wittig* and *R. W. Hoffmann*, Chem. Ber. *95*, 2718 (1962).

[29] *R. Huisgen* and *R. Knorr*, Tetrahedron Letters *1963*, 1017.

[30] *B. H. Klandermann* and *T. R. Criswell*, J. Amer. chem. Soc. *91*, 510 (1969).

[31] *H. Wieland* and *K. Heymann*, Liebigs Ann. Chem. *514*, 145, 154 (1934).

[32] *W. S. M. Grieve* and *D. H. Hey*, J. chem. Soc. (London) *1934*, 1797; *D. H. Hey, ibid. 1934*, 1966.



phenylmethane *(27)*, and dibenzoyl peroxide *(28)* in aromatic solvents C_6H_5S (S = substituent).

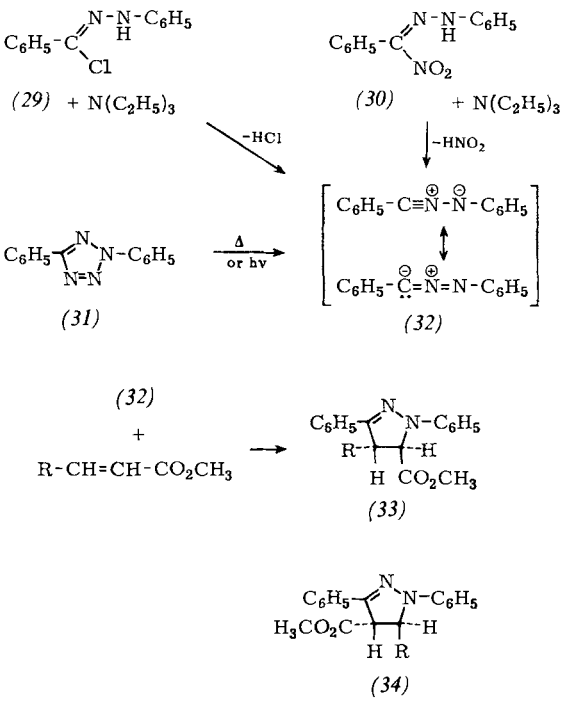
Competitive phenylations again confirm the identity of the intermediate responsible for the aromatic substitution in the decomposition of *(26)*–*(28)* (Table 2). The *o*-, *m*-, and *p*-positions of monosubstituted benzenes can compete *intramolecularly* for the phenyl radical, and this leads to a definite isomer ratio of the monosubstituted biphenyls. Mixtures of aromatic compounds allow the determination of *intermolecular* competition constants, as is shown in Table 2 for the example naphthalene/benzene.

Table 2. Isomer ratios in the free-radical substitution (phenylation) of aromatic compounds using nitrosoacetanilide *(26)*, phenylazotriphenylmethane *(27)*, or dibenzoyl peroxide *(28)* as phenyl generator.

Aromatic substrate	*(26)*	*(27)*	*(28)*
Chlorobenzene [33]			
% *o*-	56	58	57
% *m*-	28	28	27
% *p*-	16	14	16
Pyridine [34]			
% 2-	46	53	54
% 3-	43	31	32
% 4-	11	16	14
Naphthalene [33]			
% 1-	79	80	81
% 2-	21	20	19
(Naphthalene/benzene) [35]	13	14	11

Benzonitrile oxide is an isolable compound, but dimerizes rapidly in solution to give diphenylfuroxane. All efforts to isolate the related diphenylnitrilimine *(32)* have been unsuccessful because of its fast further reactions. However, cycloadditions can be readily carried out with *(32) in situ*, *i.e.* on liberation in the presence of suitable dipolarophiles, and this reaction has provided preparative routes to five-membered heterocycles.

Systems as different as the base-induced elimination of HX from (α-chlorobenzylidene)phenylhydrazine *(29)* and (α-nitrobenzylidene)phenylhydrazine *(30)* and photolysis or 160 °C-thermolysis of 2,5-diphenyltetrazole *(31)* produce the same cycloadducts with multiple bond systems. The occurrence of a common



intermediate is demonstrated conclusively by the numerical determination of competition constants. Hardly any intermediate other than *(32)* could conceivably be common to the above four systems [36].

Table 3. Cycloadditions of diphenylnitrilimine *(32)* to α,β-unsaturated carboxylic esters to form the pyrazolines *(33)* and *(34)*; intramolecular competition of the two addition directions [36].

Generator of *(32)*	Yield of *(33)* + *(34)* (%)	*(33)* : *(34)*
a) Methyl cinnamate (R = C_6H_5)		
(29) + $N(C_2H_5)_3$ at 80 °C in benzene	95	67 : 33
(30) + $N(C_2H_5)_3$ + NaI in acetonitrile	67	63 : 37
(29) + $N(C_4H_9)_3$ in anisole at 160 °C	79	57 : 43
(31) in anisole at 160 °C	65	59 : 41
b) Methyl crotonate (R = CH_3)		
(29) + $N(C_2H_5)_3$ in benzene at 20 °C	71	72 : 28
Photolysis of *(31)* in benzene at 20 °C	78	76 : 24

In the 1,3-dipolar cycloaddition of diphenylnitrilimine *(32)* to methyl cinnamate, the two addition paths leading to *(33)* and *(34)*, R = C_6H_5, compete with each other. The systems yielding *(32)* are compared in pairs in Table 3; care must be taken to ensure comparability of the reaction conditions with regard to temperature and solvent. The competition constant is independent of the temperature only if the competing reactions happen to have the same activation enthalpy.

In the case of methyl crotonate, the photolysis of diphenyltetrazole *(31)* was also examined. Though the ratios *(33)* : *(34)* agree satisfactorily within the series of experiments a or b, their values are only 1.3 : 1 and 3 : 1 respectively.

The *intermolecular* competition of two olefinic dipolarophiles for diphenylnitrilimine was therefore also

[33] *R. Huisgen* and *R. Grashey*, Liebigs Ann. Chem. *607*, 46 (1957).

[34] *D. H. Hey*, *C. J. M. Stirling*, and *G. H. Williams*, J. chem. Soc. (London) *1955*, 3963.

[35] *R. Huisgen*, *F. Jakob*, and *R. Grashey*, Chem. Ber. *92*, 2206 (1959).

[36] *J. S. Clovis*, *A. Eckell*, *R. Huisgen*, and *R. Sustmann*, Chem. Ber. *100*, 60 (1967).

measured (Table 4). The thermolysis of diphenyltetrazole *(31)* gives constants that agreed with that of the reaction *(29)* + tributylamine when tributylamine and tributylammonium chloride were added, *i.e.* when the medium is made identical. The magnitude of the competition constant, $\varkappa = 7.5$, makes the common intermediate convincing.

Table 4. Competition of ethyl cinnamate and indene for diphenylnitrilimine *(32)* in anisole at 160 °C [36].

Generator of *(32)*	Cinnamate adduct / Indene adduct
(29) + $N(C_4H_9)_3$	7.57, 7.36
(31) + $N(C_4H_9)_3$ + $\overset{\oplus}{H}N(C_4H_9)_3Cl^{\ominus}$	7.67, 7.36
(31) alone	9.50, 9.22

6. Selectivity of the Intermediate

If the intermediate lies in a relatively deep energy trough, it has sufficient time to choose carefully between the components D and E (Fig. 7). The size of the competition constant $\varkappa$ provides a measure of the *selectivity* of an intermediate. Highly selective intermediates are commonly referred to as "cold". These are contrasted with the "hot" intermediates, which react with the components D and E over very low activation barriers. The extreme case of a hot intermediate is one that reacts on the first collision with D or E, *i.e.* whose reaction is diffusion-controlled. The terms "hot" and "cold" should preferably be used in comparisons between several structurally related intermediates rather than in an absolute sense.

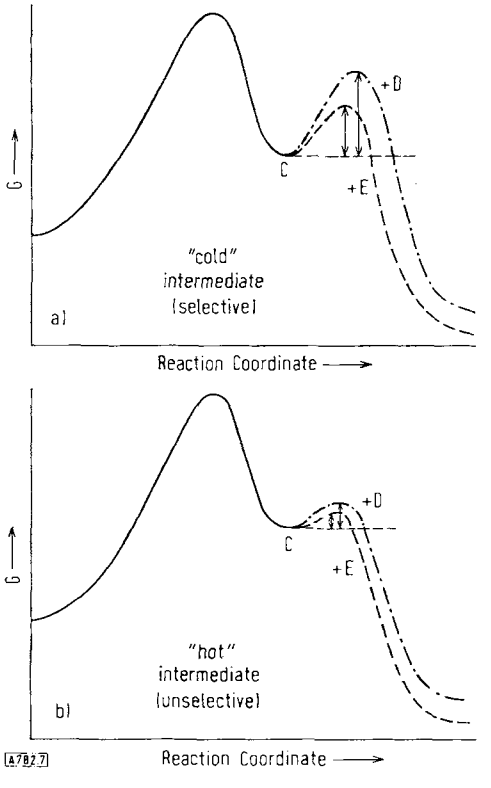


Fig. 7. Energy profiles (a) with a "cold" and (b) with a "hot" intermediate.

Substituents may stabilize or destabilize intermediates. A measure of this is provided by the selectivities as measured by the competition constants in a standard system D + E.

In the S_N1 hydrolysis of alkyl halides, the recombination of the ions competes with the reaction of the carbonium ion with water (Section 3). The quantitative evaluation gives $\varkappa = k_{Cl^{\ominus}}/k_{H_2O}$. Though the data in Table 5 are only approximate values, the decreasing selectivities clearly reflect the diminishing resonance stabilization of the carbonium intermediate.

Table 5. Competition constants for the reactions of carbonium ions with pairs of nucleophiles. $Cl^{\ominus}/H_2O$ (hydrolysis of RHal), and $N_3^{\ominus}/H_2O$ [21—23, 37].

R—Hal	$k_{Cl^{\ominus}}/k_{H_2O}$	$k_{N_3^{\ominus}}/k_{H_2O}$
Triphenylmethyl chloride	3100	280000
4,4'-Dimethylbenzhydryl chloride	600	240
4-Methylbenzhydryl chloride	320	
Benzhydryl chloride	120	170
tert-Butyl chloride	4	4

The selectivity of an intermediate may be influenced not only by substituents but also by the medium. The photochlorination of saturated hydrocarbons proceeds by a free-radical chain; the position of the substitution is determined by the abstraction of hydrogen from the alkane in the reaction with the chlorine atom. In the chlorination of 2,3-dimethylbutane *(35)* the hydrogen may be removed from a tertiary or from a primary carbon. Since the tertiary alkyl radical *(37)* is energetically favored over the primary one *(36)*, the tertiary hydrogen reacts preferentially. The competition con-

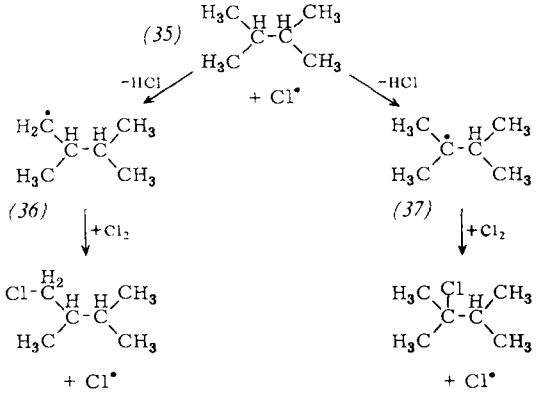


Table 6. Photochlorination of 2,3-dimethylbutane *(35)* at 55 °C; solvent dependence of the competition constant for the substitution on the tertiary and primary carbon atoms [38].

Solvent (concentration in moles/l)	$k_{tert.}/k_{prim.}$
None	3.7
Carbon tetrachloride (4.0)	3.5
Nitromethane (4.0)	3.3
Propionitrile (4.0)	4.0
Dioxane (4.0)	5.6
Chlorobenzene (4.0)	10
Benzene (2.0, 4.0, 8.0)	8.0, 15, 32
p-Xylene (4.0)	19
Mesitylene	25

[37] *A. G. Ogston, E. R. Holiday, J. S. L. Philpot,* and *L. A. Stocken,* Trans. Faraday Soc. *44*, 45 (1948).

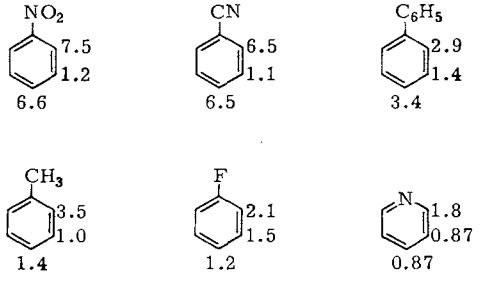
[38] *G. A. Russell,* J. Amer. chem. Soc. *80*, 4987 (1958).

stant can be determined from the ratio of the two substitution products (Table 6), taking into account the fact that *(35)* contains 12 primary and 2 tertiary hydrogens.

The preference for the tertiary H is relatively small, the competition constant being 3.7; the chlorine atom is a "hot" species. *Russell*[38] observed a striking increase in selectivity if the chlorination is carried out in aromatic solvents (Table 5). It must therefore be concluded that a stabilizing interaction occurs with the aromatic compound; the chlorine atom becomes "colder". A π-complex of the chlorine atom with the aromatic system is postulated as an intermediate.

The measurement of competition constants also allows the determination of the relative rates of many substrates with a given intermediate. This leads *e.g.* to the substitution rules for free-radical phenylation when *many* experiments of the type shown in Table 2 are carried out. After the determination of the $o : m : p$ ratio in the reaction of the phenyl radical with monosubstituted benzenes, it was necessary to determine the intermolecular competition constant of benzene with its monosubstituted derivatives. The combination of these data gives the "partial rate factors" of Table 7; these are relative values based on a value of 1.0 for H in benzene. The rate constants of the electrophilic bromination of monosubstituted benzenes extend over 24 powers of ten. In the free-radical substitution, the substituent effect is compressed to less than one power of ten; thus the phenyl radical is a less selective intermediate.

Table 7. Partial rate factors of the free-radical phenylation of aromatic compounds [39].

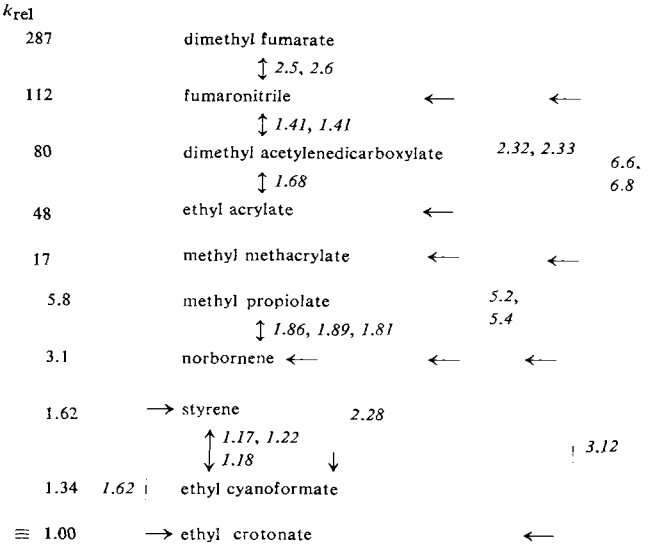


The detection of diphenylnitrilimine *(32)* as a common intermediate was described in Section 5. The same method was used for the stepwise construction of the characteristic scale of dipolarophile activities by competition of various pairs of dipolarophiles for the 1,3-dipole. Part of a larger volume of data is shown in Table 8[40]. Each double arrow denotes a pair competing for diphenylnitrilimine. To keep the experimental errors within limits, frequent additional pairings are recommended. The arbitrary assignment of a value of 1.0 to the addition constant k_2 (ethyl crotonate) leads to the relative rate constants (on left in Table 8).

[39] Data from *G. H. Williams*: Homolytic Aromatic Substitution. Pergamon Press, Oxford 1960, p. 72.

[40] *A. Eckell, R. Huisgen, R. Sustmann, G. Wallbillich, D. Grashey*, and *E. Spindler*, Chem. Ber. *100*, 2192 (1967).

Table 8. Competition of dipolarophile pairs for diphenylnitrilimine *(32)* in benzene at 80 °C; experimental x values in italics, the first column giving the relative addition constants.

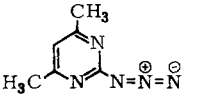


7. Kinetic Differentiation of Simultaneous Mechanisms

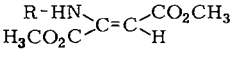
A multiplicity of products may be formed *via* a common intermediate or *via* energy profiles that are separated from the outset. It is not too rare to find that one and the same product is formed from the same precursor by different reaction paths.

Thus it is now known that in the chlorination of olefins in the liquid phase, both the addition to the double bond *and* the allylic substitution can proceed by a free-radical or by a cationic mechanism[40a]. The free-radical chain can be suppressed by operation under oxygen.

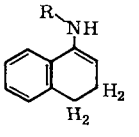
When the pyrimidyl azide *(38)* is heated to 150–160 °C with diethyl fumarate, 1,2-dihydronaphthalene, 1,3-dimethoxybenzene, or aniline, the substitution products



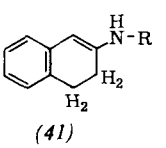
(38) = R-N_3



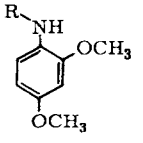
(39)



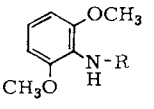
(40)



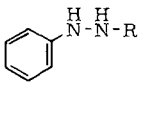
(41)



(42)



(43)



(44)

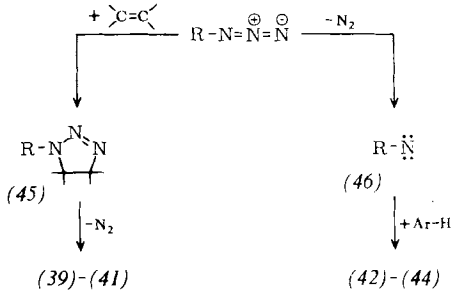
[40a] *M. L. Poutsma*, J. Amer. chem. Soc. *87*, 2161, 2172, **4285** (1965).

(39), or *(40)* plus *(41)*, or *(42)* plus *(43)*, or *(44)* are formed with elimination of nitrogen [41,42]. Do these formally similar reactions proceed by the same mechanism? The rate of nitrogen evolution from *(38)* was measured in chloronaphthalene with and without additives (Table 9). This experiment discloses a dichotomy of the reaction paths.

Table 9. Kinetics of nitrogen evolution from 2-azido-4,6-dimethylpyrimidine *(38)* (69 mmoles/l) in chloronaphthalene at 180 °C [41].

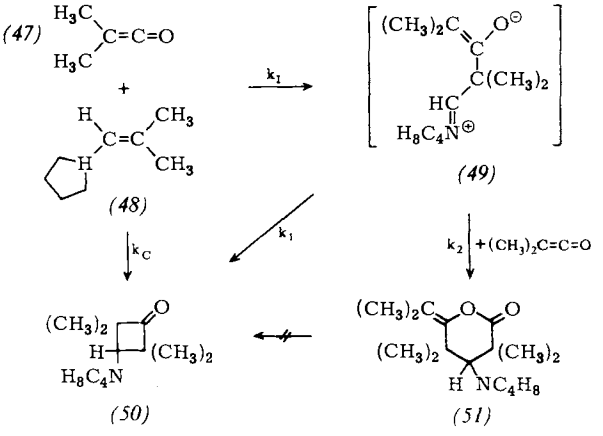
Additive (mmoles/l)	$10^5 k_1$ (s^{-1})	$10^5 k_2$ (l $mole^{-1}$ s^{-1})
Diethyl fumarate (948)	167	170
Diethyl fumarate (357)	63	168
Diethyl fumarate (231)	42	170
1,2-Dihydronaphthalene (948)	95	97
trans-Stilbene (911)	20	19
None	3.1	
1,3-Dimethoxybenzene (948)	3.0	
Aniline (948)	3.0	
Benzonitrile (948)	2.8	

Fumaric ester and olefins "induce" the liberation of nitrogen from the azide *(38)*; they enter into the rate equation. Division of the pseudo-first order constants, measured with excess fumaric ester, by the fumaric ester concentration gives constant k_2 values. This contrasts with the aromatic compounds, the addition of which does not increase the rate of the self-decomposition of *(38)*. k_1(self-decomposition) also varies only slightly in a large number of solvents. Despite the formal similarity of the products, therefore, two fundamentally different reaction paths are used. The CC double bond combines with the azide *before* the release of the nitrogen to form the Δ^2-triazoline *(45)*, which very rapidly loses nitrogen at the high reaction temperature. Enamines add azides particularly rapidly and allow the isolation of corresponding cycloadducts with *(38)* even at low temperatures [43].



On the other hand, the elimination of nitrogen from *(38)* to form the pyrimidylazene *(46)* precedes the interaction with phenol ethers or with aniline. It is therefore possible to distinguish between the azide cycloaddition and the azene reaction by a simple kinetic measurement. *(45)* and *(46)* are reactive intermediates; the olefinic component is involved only in the formation of *(45)*.

The last example will illustrate the simultaneous occurrence of two reaction paths in one and the same system producing the same product. The formation of cyclobutanones from ketenes and olefins has recently been the subject of mechanistic studies, in which most criteria point to a one-step multicenter addition, *i.e.* a simple activation peak (Fig. 1a), between the starting components and the product [44]. The second possible reaction path, which passes through a zwitterionic intermediate, occurs only in the addition of ketenes to enamines; in this case optimum stabilization of the intermediate is possible in accordance with *(49)*. Depending on whether 1-pyrrolidinoisobutene *(48)* or dimethylketene *(47)* is chosen in excess, the reaction yields more of the cyclobutanone *(50)* or of the 1 : 2 adduct *(51)* [45]. This points to a common intermediate *(49)*, which either undergoes ring closure to form *(50)* or enters into cycloaddition with a second molecule of dimethylketene to form *(51)*.



Kinetic measurements show that the rate is first order with respect to *(47)* and *(48)*. The dependence of the k value on the polarity of the solvent would be rather small for the formation of the zwitterion *(49)* in the rate-determining step: k(acetonitrile)/k(cyclohexane) = 78.

It was only the quantitative competition experiment that showed the simultaneous occurrence of the concerted formation (k_C) of the cycloadduct *(50)* and of the path involving the zwitterion (k_I) [46]. The enamine *(48)* was allowed to react with six equivalents of *(47)* in increasing dilution with the solvent. If the reaction proceeded entirely *via* the intermediate *(49)*, the yields of *(50)* and *(51)* should be related as follows:

$$\frac{[(50)]}{[(51)]} = \frac{k_1}{k_2}\,[(47)]$$

This simple mass law relation was not obeyed. Only after the subtraction of a quantity of the cyclobutanone *(50)* formed by the path with k_C which is

[41] *R. Huisgen, K. v. Fraunberg*, and *H. J. Sturm*, Tetrahedron Letters *1969*, 2589.

[42] *R. Huisgen* and *K. v. Fraunberg*, Tetrahedron Letters *1969*, 2595.

[43] *R. Fusco, S. Rossi*, and *S. Maiorana*, Tetrahedron Letters *1965*, 1965.

[44] *R. Huisgen, L. A. Feiler*, and *G. Binsch*, Chem. Ber. *102*, 3460 (1969).

[45] *P. Otto, L. A. Feiler*, and *R. Huisgen*, Angew. Chem. *80*, 759 (1968); Angew. Chem. internat. Edit. *9*, 737 (1968).

[46] *R. Huisgen* and *P. Otto*, J. Amer. chem. Soc. *91*, 5922 (1969).

characteristic for each solvent [43 % of the *(50)* formed in acetonitrile, 63 % in chloroform, 92 % in cyclohexane] was the above relation valid for the remainder of the material. The difference in the solvent dependence of the two branches of the overall reaction is typical:

	k(acetonitrile)/k(cyclohexane)
Overall reaction	78
Concerted addition (k_C)	36
Path *via* the zwitterion (k_I)	560

The formation of the zwitterion *(49)* is associated with strong charge separation, corresponding to an increase in solvation during the activation process, *i.e.* to strong promotion by the polarity of the solvent.

8. Closing Remarks

It is meaningless to ask which method is the most significant in the elucidation of reaction mechanisms and in the detection of reactive intermediates. Without chemical kinetics [47], our knowledge would be much poorer and more fragmentary. The kinetic method can often positively rule out postulated reaction paths; it can show with certainty the *occurrence* of an intermediate. Information on the *nature* of the intermediate is not provided with the same certainty, since several mechanisms sometimes follow the same kinetic scheme. However, the number of possible intermediates can be cut down by the methods described in Section 5, and it may also be possible to establish the structure of the intermediate *per exclusionem*.

Our knowledge of reaction mechanisms has swelled over the last 40 years into a broad stream fed from many tributaries. The work of *Hughes* and *Ingold* [20], who first made systematic use of the kinetic method in the elucidation of nucleophilic aliphatic substitution, played an important part in the early phase of this development.

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German version: Angew. Chem. *82*, 783 (1970)
Translated by Express Translation Service, London

[47] The following are recommended as introductions to chemical kinetics of increasing depth and detail: *R. Huisgen* in Houben-Weyl-Müller: Methoden der organischen Chemie. 4th Edit., Vol. III/1, p. 101, G. Thieme Verlag, Stuttgart 1955; *A. A. Frost* and *R. G. Pearson*: Kinetics and Mechanism. Wiley, New York 1961; Kinetik und Mechanismen homogener chemischer Reaktionen. Verlag Chemie, Weinheim 1964; *A. Weissberger*: Technique of Organic Chemistry. Vol. VIII (2 Volumes), 2nd Edit., Interscience Publ., New York 1961.

Recent Results in Carbanion Chemistry[**]

By Ulrich Schöllkopf[*]

The Wittig rearrangement of ethers metalated in the alpha position with alkali metals is a 1,2-shift to an atom with a lone pair of electrons. The alkyl shift proceeds with racemization (and partial retention) at the migrating carbon atom. The experimental observations suggest a cleavage-recombination mechanism involving a radical pair, as must also be assumed for the ylide rearrangements. In the allyl migration, the double bond is displaced within the migrating residue (allyl inversion). This is readily explained by a one-step S_Ni' mechanism, the transition state of which is allowed on symmetry grounds. In the case of benzyl 2-butynyl ether metalated on the butynyl residue, the ortho isomerization (corresponding to the Sommelet rearrangement) predominates. – α-Metalated alkyl isocyanides can react with carbonyl compounds to form olefins and metal cyanate (carbonyl olefination). Isocyanoacetic esters occupy a special place; they react with aldehydes and ketones to form β-substituted α-formylaminoacrylates (formylaminoalkoxycarbonylmethylenation), which can enter into a wide range of reactions. β-Hydroxyalkyl isocyanides or 2-oxazolines can be isolated as intermediates in the carbonyl olefination. α-Metalated isocyanides react with acylating agents to form β-ketoalkyl isocyanides, which cyclize to give oxazoles.

1. Introduction

Like all branches of our science, carbanion chemistry is currently in a state of rapid development [1–4]. The present article cannot, therefore, be a review, but can merely point out individual facets of research in this field.

The first part of the article deals with the mechanism of Wittig rearrangements, and will show that carbanion chemistry holds questions as intriguing as those in cation or free-radical chemistry to the chemist who is interested in reaction mechanisms. The second part deals with syntheses using alkyl isocyanides α-metalated with alkali metals. This part will show that research in carbanion chemistry, which has already provided the preparative organic chemist with an abundance of valuable processes, is still capable of yielding new synthetic methods.

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[**] Based on a lecture to the General Meeting of the Gesellschaft Deutscher Chemiker in Hamburg, September 15–20, 1969.

[1] Cf. *G. Wittig*, Angew. Chem. *66*, 10 (1954); Experimentia *14*, 389 (1958).

[2] *D. J. Cram*: Fundamentals of Carbanion Chemistry. Academic Press, New York 1965.

[3] *M. Szwarc*: Carbanions, Living Polymers and Electron-Transfer Processes. Interscience, New York 1968.

[4] *A. W. Johnson*: Ylid Chemistry. Academic Press, New York 1966; *R. W. Hoffmann*: Dehydrobenzene and Cycloalkynes. Verlag Chemie, Weinheim and Academic Press, New York 1967.

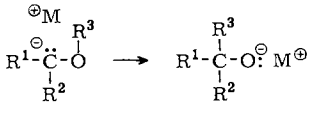
[5] *G. Wittig* and *L. Löhmann*, Liebigs Ann. Chem. *550*, 260 (1942).

[6] *G. Wittig* and *W. Happe*, Liebigs Ann. Chem. *557*, 205 (1947).

2. Mechanism of the Wittig Rearrangement

2.1. General

The Wittig rearrangement is the isomerization of ethers metalated in the α-position with alkali metals to form alkali metal alkoxides (cf. Scheme 1) [5–13].



Scheme 1. Reaction scheme of the Wittig rearrangement. Examples:

$R^1 = C_6H_5$, $R^2 = H$
$R^1 = R^2 = C_6H_5$
$R^1 + R^2$ = *o,o'*-biphenylylene
$R^1 = CH{=}CH_2$, $R^2 = H$

R^3 = alkyl, aryl, allyl
M = alkali metal

The metal atom is lithium or, less commonly, sodium or potassium. The migrating group (R^3 in Scheme 1) may be an alkyl, allyl, or aryl group (cf. below). The stationary metalated groups (R^1 and R^2 in Scheme 1) may be benzyl, benzhydryl, fluorenyl, phenacyl, or

[7] *G. Wittig*, *H. Döser*, and *I. Lorenz*, Liebigs Ann. Chem. *562*, 192 (1949).

[8] *G. Wittig* and *R. Clausnizer*, Liebigs Ann. Chem. *588*, 145 (1954).

[9] *G. Wittig* and *H.-H. Schlör*, Soumen Kemistilehti *31*, 2 (1958); Chem. Zbl. *130*, 12183 (1959).

[10] *G. Wittig* and *E. Stahnecker*, Liebigs Ann. Chem. *605*, 69 (1957).

[11] *C. R. Hauser* and *S. W. Kantor*, J. Amer. Chem. Soc. *73*, 1437 (1951).

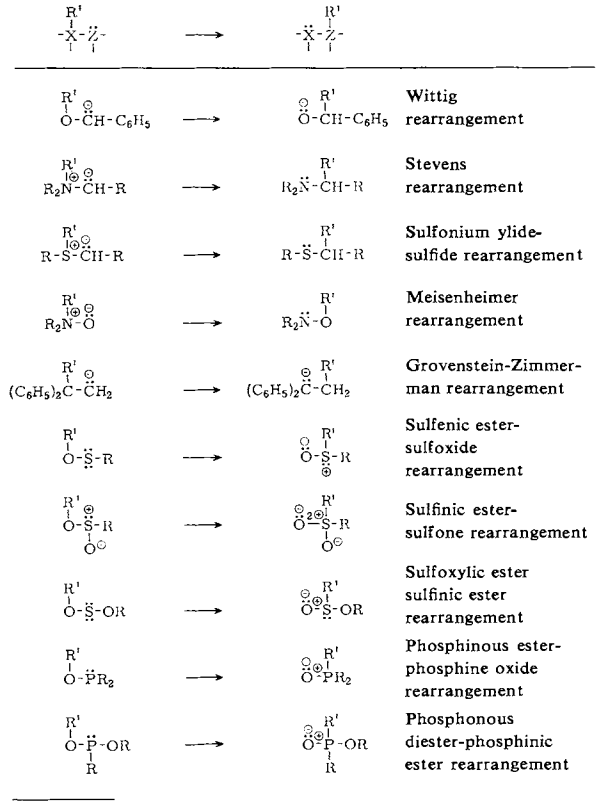
[12] *C. R. Hauser*, *S. W. Kantor*, and *W. R. Brasen*, J. Amer. Chem. Soc. *75*, 2660 (1953).

[13] *D. L. Dalrymple*, *T. L. Kruger*, and *W. N. White* in *S. Patai*: The Chemistry of the Ether Linkage. Interscience, London 1967, p. 617ff.

allyl groups. A characteristic shared by all these groups is that they can effectively delocalize a pair of electrons. These metalated ethers consequently possess an ionic carbon-metal bond [14–16], particularly in the ionization-promoting tetrahydrofuran that is normally used as the solvent. The cation and the anion are not, however, dissociated (or at least not to any appreciable extent), but form a contact or solvent-separated ion pair [3].

It has been shown conclusively in the rearrangement of metalated benzhydryl phenyl ethers to triphenylmethoxides [10] ($R^1 = R^2 = R^3 = C_6H_5$, M = Li, K, Na, in Scheme 1) that the Wittig rearrangement is in fact the isomerization of an anionic residue of the molecule and not of a covalent organometallic compound. The species that is capable of isomerizing is red, as is to be expected for an anionic benzhydryl derivative. The rates of the rearrangements are almost totally independent of the nature of the cation [17]. The same is true of the electronic spectra of the three compounds [17], which also obey the Beer-Lambert law (in dilute solution in tetrahydrofuran), an indication of complete ionization. The lithium compound reacts with zinc or magnesium chloride to form colorless organometallic compounds with covalent carbon-metal bonds, which can no longer rearrange. Lithiomethyl methyl ether ($R^1 = R^2 = H$, $R^3 = CH_3$ in Scheme 1), which probably has a covalent structure (even in tetrahydrofuran), does not isomerize [18].

Table 1. 1.2-Shift to an atom with a lone pair of electrons.



	Wittig rearrangement
	Stevens rearrangement
	Sulfonium ylide-sulfide rearrangement
	Meisenheimer rearrangement
	Grovenstein-Zimmerman rearrangement
	Sulfenic ester-sulfoxide rearrangement
	Sulfinic ester-sulfone rearrangement
	Sulfoxylic ester sulfinic ester rearrangement
	Phosphinous ester-phosphine oxide rearrangement
	Phosphonous diester-phosphinic ester rearrangement

[14] On the nature of benzyllithium, see *P. West* and *R. Waack*, J. Amer. Chem. Soc. *89*, 4395 (1967), earlier literature cited there.

[15] On the nature of fluorenyllithium, see *A. Streitwieser jr.* and *J. I. Braumann*, J. Amer. Chem. Soc. *85*, 2633 (1963); *T. E. Hogen-Esch* and *J. Smid*, *ibid. 88*, 307, 318 (1966); cf. also [3].

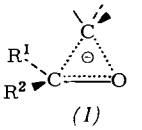
[16] On the nature of allyllithium, see *P. West*, *J. I. Purmort*, and *S. V. McKinley*, J. Amer. Chem. Soc. *90*, 797 (1968).

[17] Slight differences are to be expected, since the interaction between the cation and the carbanion should differ in the three metal cation-carbanion pairs, so that the energy levels of the ground states will also be different.

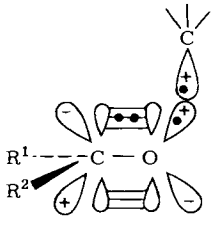
Broadly speaking, the Wittig rearrangement is a 1,2-shift to an atom with a lone pair of electrons (cf. Table 1). This is the formal counterpart of the sextet rearrangement, and corresponds to the scheme shown at the top of Table 1, where X and Z may be positively or negatively charged or electrically neutral atoms. The rearrangements could all proceed by the same mechanism, since the reacting systems are isoelectronic.

2.2. Mechanism of the Alkyl Migration

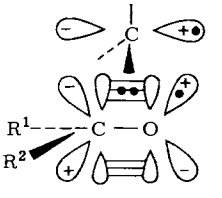
The migration of a saturated carbon atom in rearrangements of this type was initially formulated as an intramolecular nucleophilic substitution with a transition state involving a three-membered ring, as indicated in *(1)* [11, 12, 19]. This seemed plausible, since *Ingold* [20] had previously postulated a nucleophilic substitution with simultaneous ligand exchange "from the front side" (S_Ni) for the thermolysis of alkyl chlorosulfites and since approximately 98 % retention of the configuration at the migrating carbon atom, as is to be expected for a mechanism of this type, had been found for the migration of the α-phenylethyl residue in the Stevens rearrangement (cf. Table 1) [21].



(1)



(2)



(3)

It is now known that retention of configuration is not conclusive proof of an S_Ni mechanism (see below). The thermolysis of chlorosulfites, which was formulated by *Ingold* as a one-step reaction, really proceeds by way of a short-lived ion pair [22], in which the chloride ion remains at the "front side" of the carbon cation under certain conditions, so that the recombination yields an alkyl chloride with no change in the configuration [22]. The stereochemistry of the Stevens rearrangement can be explained in a similar manner, but with a short-lived radical pair as the intermediate [23].

[18] *P. Schmidt*, Diplomarbeit, Universität Göttingen 1967; *P. Hänssle*, Diplomarbeit, Universität Göttingen 1967; cf. Abstracts of the 3. Int. Sympos. on Organometallic Chemistry, München, Aug. 29–Sept. 1, 1967, p. 30.

[19] Cf. *Eu. Müller*: Neuere Anschauungen der Organischen Chemie. Springer-Verlag, Berlin 1957, 2nd Edit., p. 408; *C. K. Ingold*: Structure and Mechanism in Organic Chemistry. Cornell University Press, Ithaca, New York 1953, p. 528.

[20] *W. A. Cowdrey*, *E. D. Hughes*, *C. K. Ingold*, *S. Masterman*, and *A. D. Scott*, J. Chem. Soc. *1937*, 1252.

[21] *J. H. Brewster* and *M. W. Kline*, J. Amer. Chem. Soc. *74*, 5179 (1952); see also [11].

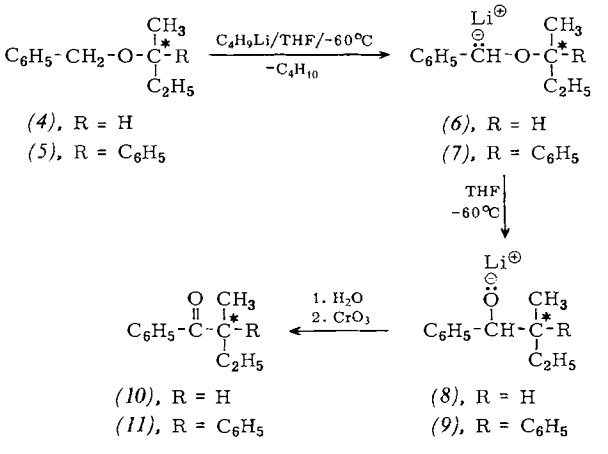
[22] *E. S. Lewis* and *C. E. Boozer*, J. Amer. Chem. Soc. *74*, 308 (1952); *D. J. Cram*, *ibid. 75*, 332 (1953).

[23] See also *U. Schöllkopf*, *U. Ludwig*, *G. Ostermann*, and *M. Patsch*, Tetrahedron Lett. *1969*, 3415.

If the 1,2-shift is regarded as a sigmatropic shift [24], the synchronous course with retention of configuration [corresponding to the S_Ni process *(1)*] is forbidden by symmetry [cf. *(2)*]. The migrating carbon atom cannot be involved simultaneously in a bonding interaction both with the oxygen and with the carbon of the stationary residue *via* its sp^3 orbital, since the π^* function of a carbonyl group is antisymmetric. On the other hand, the one-step reaction course with inversion of the configuration is allowed according to the Woodward-Hoffmann rules, since parts of orbitals with like signs come together in the (sterically unfavorable) transition state *(3)*, in which the migrating atom is in interaction with the stationary group *via* a p function.

If the reaction proceeded in one step, the carbon atom should migrate either with total retention or with total inversion. To check this question, we studied the stereochemistry of the rearrangement of optically active lithiobenzyl *sec*-butyl ether *(6)* into lithium 2-methyl-1-phenyl-1-butoxide *(8)* [25] and of the phenyl derivative *(7)* into *(9)* [26] (cf. Scheme 2).

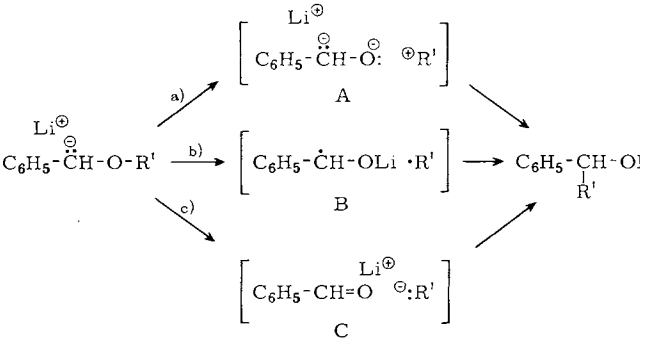
The metalated ethers *(6)* and *(7)* are obtained from the ethers *(4)* and *(5)* with butyllithium in tetrahydrofuran. The alkoxides *(8)* and *(9)* were hydrolyzed and oxidized to the ketones *(10)* and *(11)*, the rotation values of which were measured. The relative configurations of *(4)* and *(10)* and of *(5)* and *(11)* and the optical purities of these compounds could be readily determined or found from the literature [25, 26]. *(6)* and *(7)* as well as *(8)* and *(9)* were found to be configurationally stable under the reaction conditions.



Scheme 2. Reaction scheme for the determination of the stereochemistry of the Wittig rearrangement.

The isomerizations *(6)*→*(8)* and *(7)*→*(9)* (in tetrahydrofuran at about −60 °C) proceed with about 80 and about 20% racemization respectively, the configuration being retained in the unracemized portion. In other words, about 60% of the *sec*-butyl groups migrate with retention of configuration (and about 40% with inversion), while about 90% of the 2-phenylbutyl groups migrate with retention (and about 10% with inversion).

The stereochemical findings opposed a one-step course for the rearrangement (cf. above) and pointed to a two-step cleavage-recombination mechanism. This offers three possibilities (cf. Scheme 3): (a) the alkyl residue migrates as a cation *via* an ion pair of the type A, (b) it migrates as a radical *via* a radical pair B, or (c) it migrates anionically *via* the intermediate C.



Scheme 3. Possibilities for the two-step course of the Wittig rearrangement.

It was possible to rule out path (a), since alkyl groups giving unstable cations migrate without rearrangement of the skeleton. Thus lithiobenzyl cyclobutyl ether *(12)* isomerizes to lithium cyclobutylphenylmethoxide *(13)*, whereas the isomers *(14)* and *(15)* cannot be detected [27]. On the other hand lithiobenzyl cyclopropylmethyl ether *(16)* gives small quantities of *(15)* together with the alkoxide *(14)*, but not *(13)* [27, 28]. No conclusions can be drawn from the formation of small quantities of *(15)* from *(16)*, since cyclopropylmethyl anions and cyclopropylmethyl radicals can both rearrange to form homoallyl anions and radicals respectively [29, 30]. Lithiobenzyl 2,2-dimethylcyclopropyl ether *(17)* gives lithium (2,2-dimethylcyclopropyl)phenylmethoxide *(18)* (though only in yields of about 30%, together with high-boiling resins), but neither of the allyl derivatives *(19)* and *(20)* [31, 32].

[24] *R. B. Woodward* and *R. Hoffmann*, J. Amer. Chem. Soc. *87*, 2511 (1965). Reviews: *R. Hoffmann* and *R. B. Woodward*, Accounts Chem. Res. *1*, 17 (1968); *J. A. Berson*, *ibid. 1*, 152 (1968); *D. Seebach*, Fortschr. Chem. Forsch. *11*, 177 (1969); *S. I. Miller*: Advan. Phys. Org. Chem. *6*, 235 (1968).

[25] *U. Schöllkopf* and *W. Fabian*, Liebigs Ann. Chem. *642*, 1 (1961).

[26] *U. Schöllkopf* and *H. Schäfer*, Liebigs Ann. Chem. *663*, 22 (1963).

[27] *P. T. Lansbury* and *V. A. Pattison*, J. Amer. Chem. Soc. *84*, 4295 (1962).

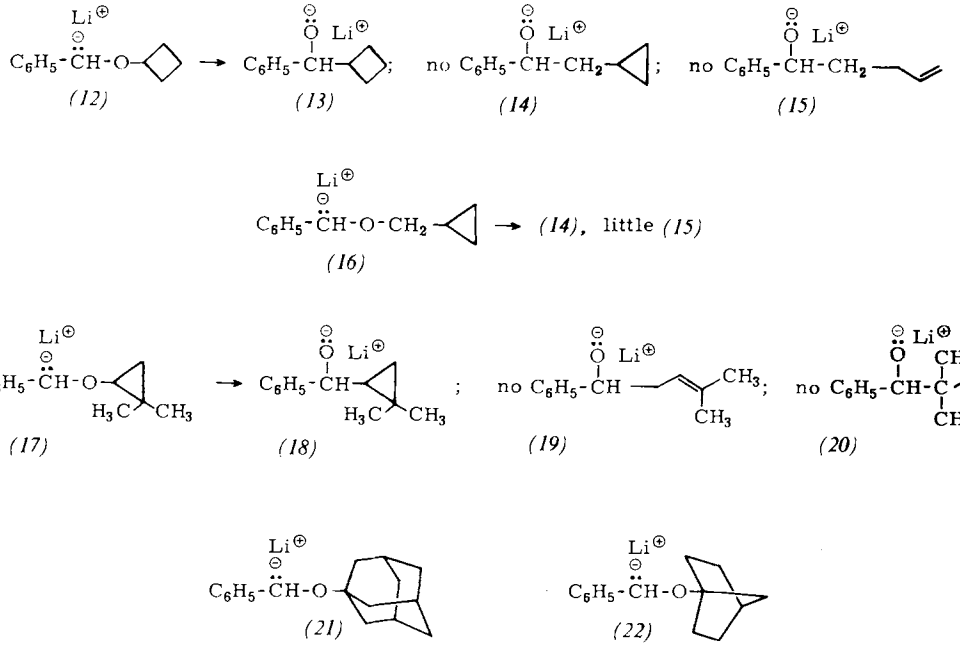
[28] On equilibrium and resonance between cyclobutyl, cyclopropylmethyl, and homoallyl cations see *M. Hanack* and *H. J. Schneider*, Fortschr. Chem. Forsch. *8*, 554 (1967); other literature cited there.

[29] On the behavior of the cyclopropylmethyl anion, see *P. T. Lansbury*, *V. A. Pattison*, *W. A. Clement*, and *J. D. Sidler*, J. Amer. Chem. Soc. *86*, 2247 (1964); cf. also *A. Maercker* and *J. D. Roberts*, *ibid. 88*, 1742 (1966).

[30] On the behavior of the cyclopropylmethyl radical, see [28], p. 597.

[31] *K. Fellenberger*, Dissertation, Universität Göttingen 1969.

[32] On the behavior of cyclopropyl cations, cf. *P. v. R. Schleyer* and *R. D. Nicholas*, J. Amer. Chem. Soc. *83*, 182 (1962); *P. v. R. Schleyer*, *ibid. 86*, 1854 (1967); *C. H. DePuy*, *L. G. Schnack*, and *J. W. Hausser*, *ibid. 88*, 3343 (1966); *P. v. R. Schleyer*, *D. W. van Diene*, *U. Schöllkopf*, and *J. Paust*, *ibid. 88*, 2868 (1966); *W. Kirmse* and *H. Schütte*, Chem. Ber. *101*, 1674 (1968); *U. Schöllkopf*, Angew. Chem. *68*, 603 (1968); Angew. Chem. internat. Edit. *7*, 588 (1968); *W. Kutzelnigg*, Tetrahedron Lett. *1967*, 4965; *D. T. Clark* and *D. R. Armstrong*, Theor. Chim. Acta *13*, 365 (1969).



It was possible to decide between the radical and the carbanion mechanisms on the basis of a series of observations, of which only the most important will be mentioned here. Lithiobenzyl 1-adamantyl ether *(21)* undergoes rearrangement, while lithiobenzyl 1-norbornyl ether *(22)* does not [33]. Since the adamantyl radical is more stable than the norbornyl radical [34], whereas the reverse is true of the organolithium compounds [35], and hence probably of the carbanions, this observation supports the radical path (b). This is also supported by the migration tendency of alkyl groups (determined for the rearrangement of lithiobenzyl alkyl ethers), which increases in the order methyl, ethyl, isopropyl, *tert*-butyl (k_{rel} = 1:40:162:2080) [36]. It is known that the rate of formation of alkyl radicals increases in this order [37], whereas that of carbanions decreases [3]. A linear relationship exists (cf. Fig. 1) between the dissociation energies of primary, secondary, and tertiary C–H bonds and the ln k_{rel} values of the rearrangement, which are in turn proportional to the differences between the activation energies; this indicates that the four alkyl residues all migrate by a similar mechanism.

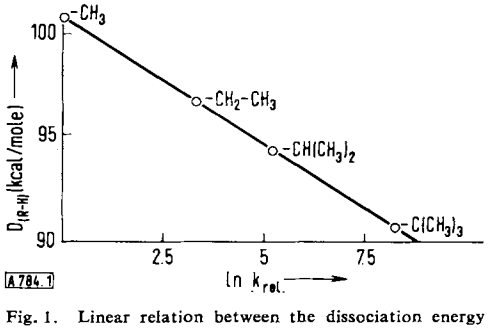


Fig. 1. Linear relation between the dissociation energy D of C–H bonds and the logarithm of the k_{rel} values for the rearrangement of alkyl groups in the reaction
C_6H_5–CHLi–O–R → C_6H_5–CHR–OLi
in tetrahydrofuran at −60 °C.

The lithium phenyl-*tert*-butylmethoxide formed on isomerization of lithiobenzyl *tert*-butyl ether exhibits a chemically induced proton spin polarization, which is recognizable in the NMR spectrum (cf. Fig. 2) [39]. This must be regarded as evidence of the intermediate formation of a radical pair of the type B during the rearrangement, since a CINP [40] is to be expected only in products formed from free-radical precursors.

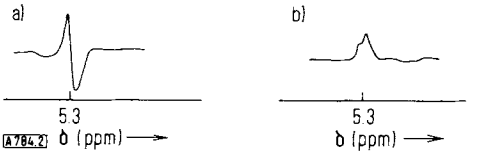


Fig. 2. NMR signal of the methine proton of lithium phenyl-*tert*-butyl-methoxide (a) immediately after the rearrangement, (b) after decay of the polarization.
(Standard: tetramethylsilane)

[33] *P. T. Lansbury, V. A. Pattison, J. D. Sidler,* and *J. B. Bieber,* J. Amer. Chem. Soc. *88,* 78 (1966).

[34] *R. C. Fortjr.* and *P. v. R. Schleyer,* Advan. Alicycl. Chem. *1,* 337 (1966).

[35] *P. T. Lansbury* and *J. D. Sidler,* Tetrahedron Lett. *1965,* 691; cf. [34], p. 353ff.

[36] *H. Schäfer, U. Schöllkopf,* and *D. Walter,* Tetrahedron Lett. *1968,* 2809.

[37] *Ch. Rüchardt* has recently pointed out [38] that the usual opinion that the ground state stability of alkyl radicals should increase in the order primary, secondary, tertiary cannot be verified experimentally. The D_{C-H} values and the activation energies of radical-forming reactions evidently run parallel only for endothermic reactions, *i.e.* when the transition state is very similar to the free radicals.

[38] *Ch. Rüchardt,* lecture to the General Meeting of the Gesellschaft Deutscher Chemiker in Hamburg, September 15–20, 1969; Angew. Chem., in the press.

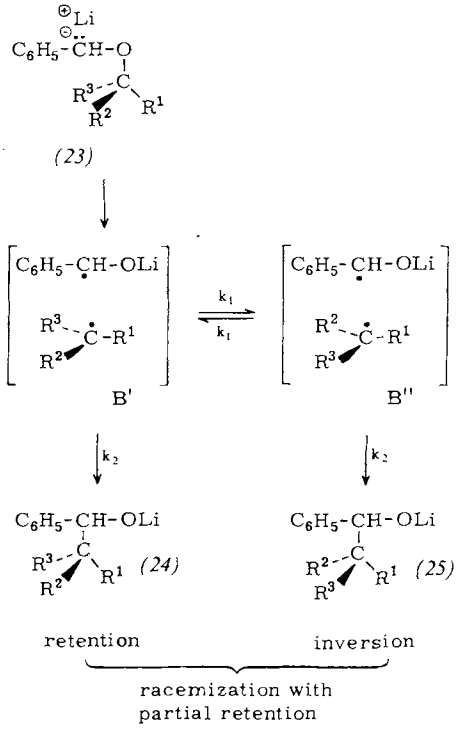
[39] *P. T. Lansbury,* private communication.

[40] *J. Bargon, H. Fischer,* and *U. Johnsen,* Z. Naturforsch. *22a,* 1551, 1556 (1967); *23a,* 2109 (1968); *H. Fischer,* Accounts Chem. Res. *2,* 110 (1969); *A. R. Ward* and *R. G. Lawler,* J. Amer. Chem. Soc. *89,* 5518 (1967); *R. G. Lawler, ibid. 89,* 5519 (1967); *A. R. Lepley, ibid. 90,* 2710 (1968); *A. R. Lepley* and *R. L. Landau, ibid. 91,* 748 (1969); *G. L. Closs* and *L. E. Closs, ibid. 91,* 4549 4550 (1969); *G. L. Closs, ibid. 31,* 4552 (1969); *R. Kaptein* and *L. J. Oosterhoff,* Chem. Phys. Letters *4,* 195, 214 (1969); *F. Gerhart* and *G. Ostermann,* Tetrahedron Lett. *1969,* 4705.

Finally, let us consider briefly how the stereochemical result, *i.e.* racemization with partial retention on the migrating carbon (cf. above), can be explained in a two-step rearrangement (cf. Scheme 4). In the radical pair B′ formed from the ionized ether *(23)* by homolysis, which has the same configuration as the starting material, some of the alkyl radicals may rotate through 180° to give the enantiomer B″ before the recombination, which occurs in the solvent cage (cage recombination)[41]. It should be noted that B′ and B″ are chiral overall, though the alkyl radicals themselves (which are assumed to be planar) are achiral, since they possess a symmetry plane. Depending on whether the recombination takes place from B′ or B″, the rearrangement product exhibits either retention or inversion of the configuration [*(24)* or *(25)*]. The ratio of retention to inversion depends on the ratio of the constants k_1 and k_2 in accordance with the relation

$$\% \text{ retention}/\% \text{ inversion} = k_2/k_1 + 1 \quad [42]$$

If $k_2/k_1 > 30$, the cage recombination proceeds with more than 97% retention, *i.e.* it is then impossible to distinguish stereochemically between an S_Ni course [in accordance with *(1)*] and a two-step mechanism. This appears to be the situation in the Stevens rearrangement (with α-phenylethyl as the migrating group)[23].



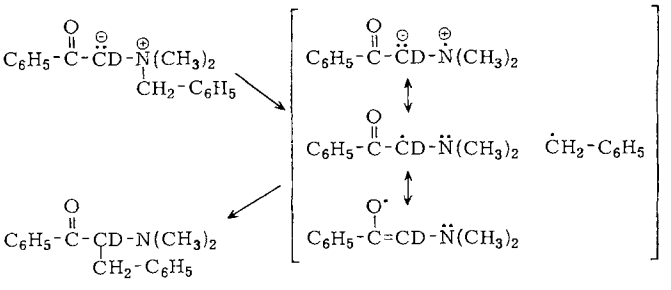
Scheme 4. Interpretation of the stereochemistry of the Wittig rearrangement (cf. text).

[41] A cross experiment has shown that the rearrangement *(6)*→*(8)* proceeds "intramolecularly" to an extent of about 90% at −60 °C; *U. Schöllkopf* and *D. Walter*, Liebigs Ann. Chem. *654*, 27 (1962).

[42] Cf. [25]; the rearrangement is formulated there as involving ion pairs, but this relation should also be valid for a radical-pair mechanism.

2.3. Mechanism of the Alkyl Migration in the Ylide Rearrangements

As was mentioned, the reacting systems of the rearrangements listed in Table 1 are isoelectronic, and the reaction courses may therefore be assumed to be similar. It has in fact recently been shown that in the ylide isomerizations[43], *i.e.* in the Stevens rearrangement[23,44], the sulfonium ylide-sulfide rearrangement[45,46], and the Meisenheimer rearrangement[47,48], the benzyl migration probably proceeds *via* a radical pair. Figures 3–5 show the courses of these rearrangement, without comment, for some typical examples, together with the characteristic NMR signals of the isomerization products. In agreement with the assumed course *via* a radical pair,



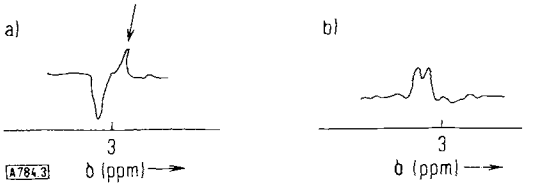


Fig. 3. Course of the Stevens rearrangement of benzyldimethylphenacylammonium ylide (in CD_3OD/CD_3ONa); NMR signal [23] of the benzyl protons of the rearrangement product (a) immediately after the isomerization, (b) after decay of the spin polarization; arrow: signal of the CH_2 protons of the by-product bibenzyl.

(Standard: tetramethylsilane).

[43] For the definition of the term ylide, see *G. Wittig* and *G. Felletschin*, Liebigs Ann. Chem. *555*, 133 (1944).

[44] *T. S. Stevens*, J. Chem. Soc. *1930*, 2107; *T. Thomson* and *T. S. Stevens*, *ibid. 1932*, 55; *J. L. Dunn* and *T. S. Stevens*, *ibid. 1932*, 1926; *1934*, 279. – *G. Wittig* recognized that the Stevens rearrangement is an ylide isomerization; see [45]. Concerning more recent work that shows the two-step course of the rearrangement, see *E. F. Jenny* and *J. Druey*, Angew. Chem. *74*, 152 (1962); Angew. Chem. internat. Edit. *1*, 155 (1962); *E. F. Jenny* and *K. Schenker*, Chimia *19*, 178 (1965); *E. F. Jenny* and *A. Melzer*, Tetrahedron Lett. *1966*, 3507 (these authors formulate the rearrangement as proceeding *via* an ion pair).

[45] *K. W. Ratts* and *A. N. Yao*, J. Org. Chem. *33*, 70 (1968); *J. Schossig*, Dissertation, Universität Göttingen 1968; *J. E. Baldwin*, *R. E. Hackler*, and *D. P. Kelly*, Chem. Commun. *1968*, 538. – Earlier literature data on the rearrangements are inaccurate, see *T. Thomson* and *T. S. Stevens*, J. Chem. Soc. *1932*, 69; *H. Böhme* and *W. Krause*, Chem. Ber. *82*, 426 (1949); cf. also *E. B. Ruiz*, Acta Salmanticensia, Ser. Cienc. *2*, No. 7 (1958), Chem. Abstr. *54*, 7623h (1960).

[46] *U. Schöllkopf*, *J. Schossig*, and *G. Ostermann*, Liebigs Ann. Chem. *737*, 158 (1970).

[47] *U. Schöllkopf* and *H. Schäfer*, Liebigs Ann. Chem. *683*, 42 (1965), earlier literature therein; *U. Schöllkopf*, *U. Ludwig*, *M. Patsch*, and *W. Franken*, *ibid. 703*, 77 (1967); *U. Schöllkopf* and *U. Ludwig*, Chem. Ber. *101*, 2224 (1968).

[48] *G. Ostermann* and *U. Schöllkopf*, Liebigs Ann. Chem. *737*, 170 (1970).

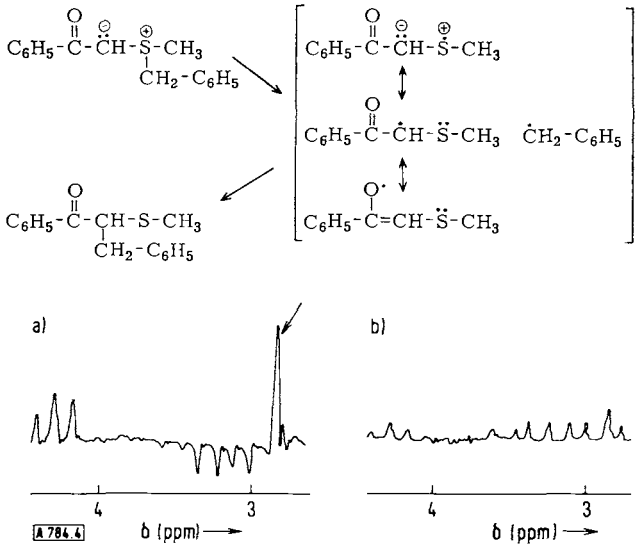


Fig. 4. Course of the rearrangement of benzylmethylphenacylsulfonium ylide; NMR signals [46] of the benzyl protons and of the methine proton of the rearrangement product (ABX spectrum) (a) immediately after isomerization, (b) after decay of the spin polarization; arrow: signal of the CH_2 protons of the by-product bibenzyl.
(Standard: tetramethylsilane.)

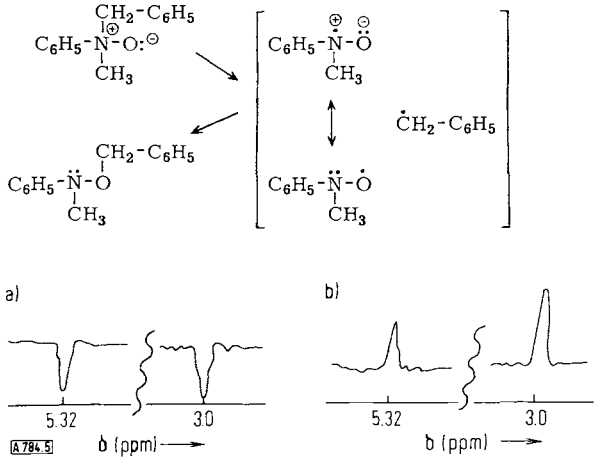
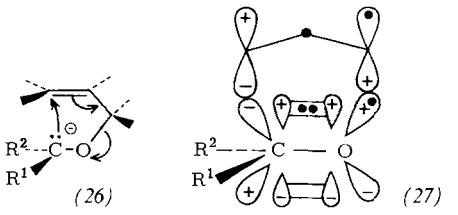


Fig. 5. Course of the Meisenheimer rearrangement of *N*-benzyl-*N*-methylaniline oxide: NMR signals [48] of the benzyl and *N*-methyl protons (a) immediately after the isomerization, (b) after decay of the spin polarization.
(Standard: tetramethylsilane.)

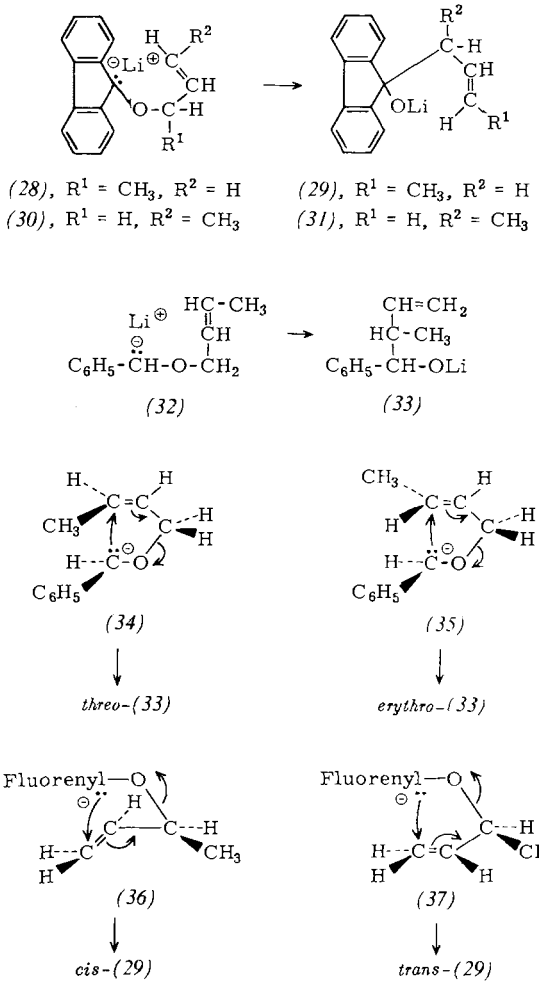
each of the three products exhibits a chemically induced proton spin polarization [40] immediately after the rearrangement.

2.4. Mechanism of the Allyl Migration

In every case examined so far, the allyl migration is accompanied by displacement of the double bond within the allyl group (allyl inversion); this can be readily explained by a one-step S_Ni' mechanism [transition state *(26)*]. Such a process is allowed according to the Woodward-Hoffmann rules [23]; the ψ_2 function of the allyl system and the π^* function of the carbonyl group are antisymmetric, so that bonding between the ends of the allyl system and the carbon and oxygen atoms of the stationary residue in *(26)* is possible [cf. *(27)*].



9-Lithio-9-fluorenyl 1-methallyl ether *(28)* gives lithium 9-*trans*-crotylfluorenolate *(29)* (>99 % *trans*), whereas the isomeric ether *(30)* changes spontaneously into lithium 9-(1-methylallyl)fluorenolate *(31)* [49–51]. Both rearrangements proceed spontaneously even at −50 to −60 °C. Lithiobenzyl crotyl ether *(32)* also isomerizes with allyl inversion, the product being a 1:2 mixture of *threo*- and *erythro*-*(33)* [52].



The preferential formation of the *erythro* isomer in this last rearrangement is as expected, since the transition state *(34)* leading to the *threo* form, in

[49] *U. Schöllkopf* and *K. Fellenberger*, Liebigs Ann. Chem. *698*, 80 (1966).

[50] *K. Fellenberger*, Diplomarbeit, Universität Heidelberg 1964.

[51] Cf. also *Y. Makisumi* and *S. Notzumoto*, Tetrahedron Lett. *1966*, 6393.

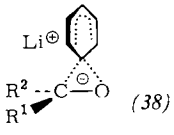
[52] *U. Schöllkopf*, *K. Fellenberger*, and *M. Rizk*, Liebigs Ann. Chem. *734*, 106 (1970). The *erythro* diastereoisomer is taken as that in which the phenyl and vinyl groups are opposite in the eclipsed conformation.

which the methyl group and the phenyl group are eclipsed, has a higher energy than the transition state *(35)* leading to the *erythro* form. On the other hand, the stereoselectivity of the rearrangement *(28)*→*(29)* (>99% *trans*[49,50]) is remarkable. The transition states *(36)* and *(37)* must differ by about 2 kcal/mole, a difference that is probably greater than that of the *cis-trans* isomeric rearrangement products *(29)*.

The results obtained in the rearrangements of *(28)* and *(30)* apparently disagree with literature data[53], according to which the isomerization not only of *(28)* but also of *(30)* (Na instead of Li, in boiling butanol with sodium butoxide) yields *(29)*; this was interpreted[54] as showing that *(28)* isomerizes by an S_Ni' mechanism and *(30)* by an S_Ni mechanism. However, the authors[53] failed to observe that under their reaction conditions *(31)* changes into *(29)*[49,50].

2.5. Mechanism of the Aryl Migration

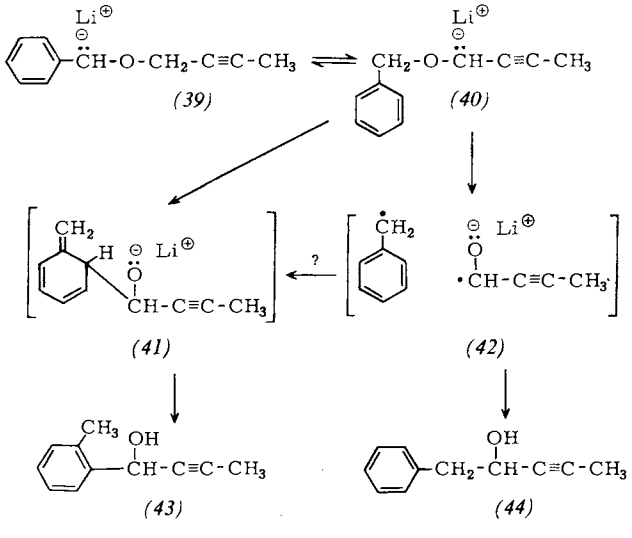
Nothing definite is known about the mechanism of the aryl migration. We regard it as an intramolecular nucleophilic substitution by the addition-elimination mechanism [intermediate *(38)*], but a cleavage-recombination mechanism *via* a radical or ion pair (cf. Scheme 3, R′ = aryl) cannot be ruled out.



(38)

2.6. *ortho* Rearrangement in Anionized Ethers

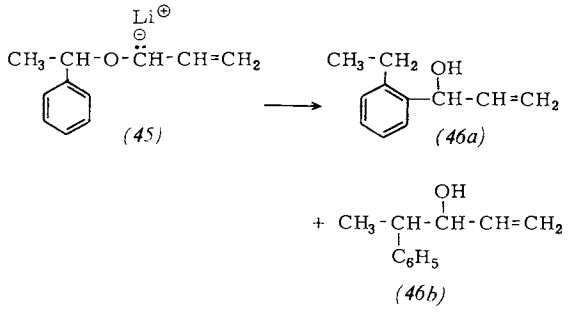
On reaction of benzyl 2-butynyl ether with butyllithium (in tetrahydrofuran at about −30 °C), 45% of 1-(*o*-tolyl)-2-butyn-1-ol *(43)* can be isolated after hydrolysis, as well as 18% of 1-phenyl-3-pentyn-2-ol *(44)*[52]. The reaction presumably leads first to lithiobenzyl 2-butynyl ether *(39)*; this is in dynamic equilibrium with 1-lithio-2-butynyl benzyl ether *(40)*, which reacts further to form *(43)* and *(44)*. *(44)* is probably formed *via* the radical pair *(42)* (cf. above), while an "allyl shift" leads to *(41)*, which rapidly tautomerizes. Owing to the resonance in the benzyl radical, however, it is conceivable that *(41)* is formed *via (42)*.



(39) *(40)* *(41)* *(42)* *(43)* *(44)*

The rearrangement *(40)*→*(43)* corresponds to the Sommelet rearrangement[55] in ammonium ylides, which has been known for some time.

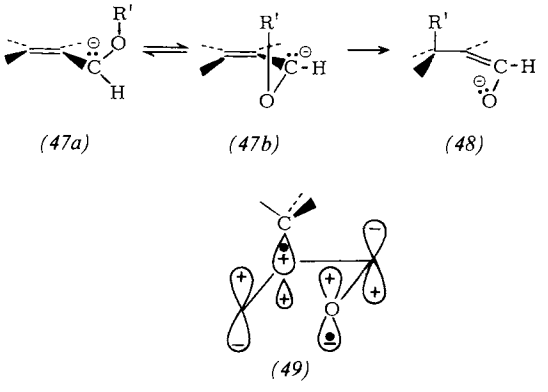
1-Lithioallyl α-methylbenzyl ether *(45)*, which is prepared from the ether and methyllithium, also undergoes *ortho* isomerization to give 1-(*o*-ethylphenyl)-2-propen-1-ol *(46a)* (after hydrolysis), as well as a Wittig rearrangement to form *(46b)*[52].



(45) *(46a)* *(46b)*

2.7. The Question of 1,4-Migration in Metalated Allyl Alkyl Ethers

According to the Woodward-Hoffmann rules, the one-step (*i.e.* suprafacial) 1,4-alkyl shift *(47)*→*(48)* is allowed by symmetry [transition state *(49)*], though it should only be possible from the "horse-shoe conformation" *(47b)* [cf. also *(49)*]. The problem has not yet been examined from this point of view. However, preparative observations[56] show that the 1,4-migration can compete successfully with the 1,2-shift in allyl alkyl ethers of the type *(47)*. Both rearrangements are formulated as proceeding *via* the same radical pair[56]. If this were so, not only the 1,2-shift but also the 1,4-migration should proceed with racemization and partial retention at the migrating carbon



(47a) *(47b)* *(48)* *(49)*

[53] *J. Cast, T. S. Stevens,* and *J. Holmes,* J. Chem. Soc. *1960,* 3521.

[54] *H. E. Zimmerman* in *P. de Mayo*: Molecular Rearrangements. Interscience, New York 1963, Vol. 1, p. 377.

[55] For definition and distinction from the Stevens rearrangement, see *G. Wittig, R. Mangold,* and *G. Felletschin,* Liebigs Ann. Chem. *560,* 116 (1948); cf. also [2].

[56] *H. Felkin* and *A. Tambuté,* Tetrahedron Lett. *1969,* 821.

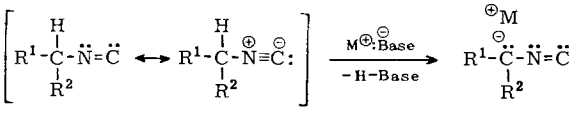
atom. If on the other hand the 1,4-migration was a sigmatropic shift, it should take place with total retention of the configuration.

In the rearrangement of (racemic) lithiobenzyl *sec*-butyl ether *(6)*, *p-sec*-butylbenzaldehyde, the result of a 1,6-migration (with subsequent hydride abstraction), can be isolated in a yield of about 4% [25]. The formation of this product can be readily explained *via* a radical pair of the type B (see Scheme 3), but not by a sigmatropic shift, since the ψ_4 of the hexatriene system is anti- symmetric.

3. Syntheses Using α-Metalated Alkyl Isocyanides

3.1. General

The α-hydrogen atoms of alkyl isocyanides [57] *[(50a)↔(50b)]* are relatively acidic, probably mainly because of the partial positive charge on the nitrogen atom [58], and can be replaced by metal with the aid of sufficiently strong bases such as butyllithium, sodium hydride, and alkali metal alkoxide [59].



(50a) *(50b)* *(51)*

M = alkali metal

The α-metalated alkyl isocyanides *(51)*, in the short time since their discovery [59], have already shown themselves to be valuable reagents, though all conceivable applications have not yet been explored [*]. They open up new possibilities for the use of isocyanides, whose chemistry was until recently thought [62] to be confined to α-elimination and α-addition at the "dicoordinate" carbon.

[57] On the syntheses of isocyanides, see *I. Ugi, U. Fetzer, U. Eholzer, H. Knupfer*, and *K. Offermann*, Angew. Chem. *77*, 492 (1965); Angew. Chem. internat. Edit. *4*, 472 (1965).

[58] *L. Pauling*: The Nature of the Chemical Bond. Cornell University Press, New York 1960, pp. 269, 338.

[59] *U. Schöllkopf* and *F. Gerhart*, Angew. Chem. *80*, 842 (1968); Angew. Chem. internat. Edit. *7*, 805 (1968); German Pat. Appl. 1812099/1 (Nov. 29, 1968), Badische Anilin- u. Soda-Fabrik; US Pat. Appl. 867941 (Nov. 20, 1969), Badische Anilin- u. Soda-Fabrik. As expected, α-alkyl substitution makes the metalation more difficult; it remains to be seen whether the butyllithium-tetramethylethylenediamine complex [60, 61] is more suitable as a metalating agent than butyllithium itself.

[60] *G. G. Eberhardt* and *W. A. Butte*, J. Org. Chem. *29*, 2928.

[61] Cf. also *D. J. Peterson*, J. Org. Chem. *32*, 1717 (1967); further literature cited therein.

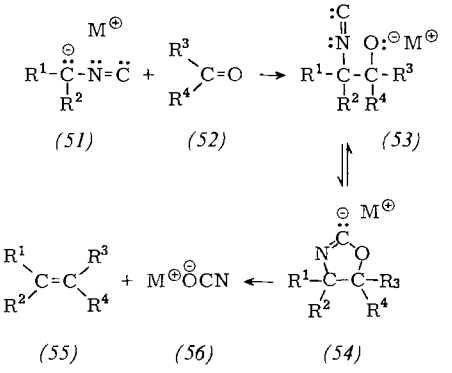
[*] Note added in proof: Meanwhile, further contributions have been published on this topic: *U. Schöllkopf* and *D. Hoppe*, Angew. Chem. *82*, 253 (1970); Angew. Chem. internat. Edit. *9*, 236 (1970); *D. Hoppe* and *U. Schöllkopf*, Angew. Chem. *82*, 290 (1970); Angew. Chem. internat. Edit. *9*, 300 (1970); *W. A. Böll, F. Gerhart, A. Nürrenbach*, and *U. Schöllkopf*, Angew. Chem. *82*, 482 (1970); Angew. Chem. internat. Edit. *9*, 459 (1970); *U. Schöllkopf* and *D. Hoppe*, Angew. Chem. *82*, 438 (1970); Angew. Chem. internat. Edit. *9*, 459 (1970); *U. Schöllkopf* in: Houben-Weyl-Müller, Vol. XIII/1. Thieme, Stuttgart, 1970, p. 239ff.

[62] See [57], p. 493.

3.2. Carbonyl Olefination

The α-metalated isocyanides *(51)* can react with aldehydes and ketones *(52)* to form olefins *(55)* and metal cyanate *(56)* [59] (cf. Table 2), the carbonyl group being replaced by the double bond.

This novel exchange reaction begins with the nucleophilic addition of *(51)* to the carbonyl group to form *(53)*. This cyclizes (presumably reversibly) to give the metalated oxazoline *(54)*, which fragments into *(55)* and *(56)* (cf. Scheme 5).



(51) *(52)* *(53)* *(55)* *(56)* *(54)*

Scheme 5. Course of the carbonyl olefination with α-metalated isocyanides *(51)*.

Table 2. Olefins *(55)* prepared by carbonyl olefination with α-metalated isocyanides [59].

(51), M = Li			*(52)*	*(55)*	Yield (%)
	R^1	R^2			
a	H	H	Benzaldehyde	Styrene	70 [a]
a	H	H	Acetophenone	α-Methylstyrene	78 [a]
a	H	H	Benzophenone	1,1-Diphenyl-ethylene	40 [b]
a	H	H	Cinnam-aldehyde	1-Phenyl-1,3-butadiene	23 [a]
b	H	C_6H_5	Acetophenone	1,2-Diphenyl-1-propene	44 [a]
b	H	C_6H_5	Cinnam-aldehyde	1,4-Diphenyl-1,3-butadiene	35 [a]
b	H	C_6H_5	Cyclo-hexanone	Benzylidene-cyclohexane	11 [a]
b	H	C_6H_5	Benzo-phenone	Triphenyl ethylene	74 [b]
c	C_6H_5	C_6H_5	Benzaldehyde	Triphenylethylene	30 [a]
d	H	$CH=CH_2$	Benzophenone	1,1-Diphenyl-1,3-butadiene	40 [b]
e	H	$CH=C(CH_3)_2$	Acetophenone	1,4,4-Trimethyl-1-phenyl-1,3-butadiene	57 [b]

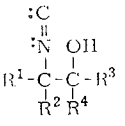
[a] In tetrahydrofuran under reflux. [b] In tetrahydrofuran at −60 °C.

In every case investigated so far the carbonyl addition (in tetrahydrofuran) proceeds very rapidly even at about −70 °C. The same is true of the cyclization *(53)→(54)*, though the equilibrium probably lies well to the left. The elimination of cyanate also proceeds at low temperatures, provided that it leads to a particularly stable olefin (cf. Table 2). In general, however, more or less prolonged refluxing in tetrahydrofuran (or standing at room temperature) will be necessary.

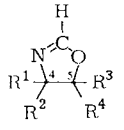
Apart from the cases in which the reaction leads to to *(55)* and *(56)* even at about −70 °C, it is possible, by suitable treatment of the reaction mixture, to iso-

late either the adducts *(53)* in the form of β-hydroxyalkyl isocyanides *(57)* or the metalated oxazolines *(54)* as oxazolines *(58)* (cf. below).

The hydroxy compounds *(57)*, which are important as precursors for the preparation of α,β-unsaturated alkyl isocyanides[63] and 2-amino 1-alcohols, are obtained by addition of the carbonyl compound *(52)* to a solution or suspension of *(51)* in tetrahydrofuran at −70 °C, followed after a few minutes by neutralization with glacial acetic acid[64]. In this way, isocyanomethyllithium *(51a)* reacts with acetophenone to give 1-isocyano-2-phenyl-2-propanol *(57a)* in 80% yield, and with benzaldehyde to give 2-isocyano-1-phenylethanol *(57b)* (75% yield)[64]. Addition of benzoyl chloride instead of glacial acetic acid gave the benzoyl derivative of *(57b)* in 78% yield[65].



(57)



(58)

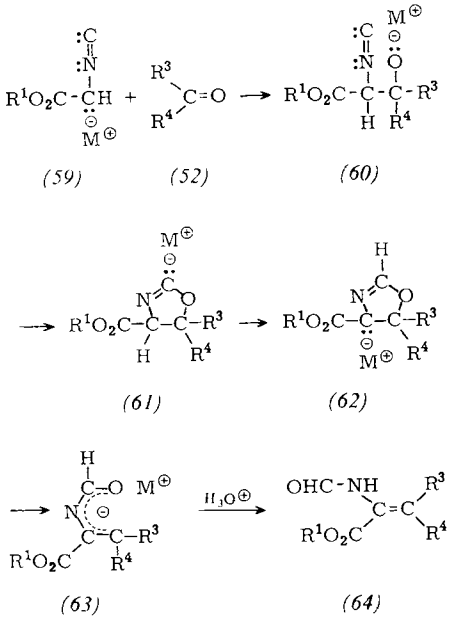
(a), $R^1 = R^2 = H$, $R^3 = C_6H_5$, $R^4 = CH_3$
(b), $R^1 = R^2 = R^3 = H$, $R^4 = C_6H_5$

Since they are less acidic than triphenylalkylphosphonium salts, alkyl isocyanides *(50)* cannot be metalated so easily. On the other hand, the compounds *(51)* add more readily to the carbonyl group than the Wittig reagents[66]. Thus α-lithiobenzyl isocyanide *(51b)* reacts with benzophenone even at −70 °C to give triphenylethylene (74%), whereas the analogous reaction with benzylidenetriphenylphosphorane proceeds only slowly even at 75 °C (in ether)[67]. α-Lithiobenzhydryl isocyanide *(51c)* also reacts readily (at about −70 °C) with benzaldehyde (cf. Table 2), whereas diphenylmethylenetriphenylphosphorane is inert toward aldehydes and ketones[68].

3.3. Formylaminoalkoxycarbonylmethylenation of Carbonyl Compounds

The reaction of metalated isocyanoacetic esters *(59)*, prepared from isocyanoacetic esters and *e.g.* butyllithium, sodium hydride, or sodium ethoxide (cf. Table 3) with aldehydes and ketones, in aprotic solvents, follows a surprising course. It leads (on acid hydrolysis) to β-substituted α-formylaminoacrylic esters *(64)*[69] (cf. Table 3), and so allows the replacement of the carbonyl oxygen by the formylaminoalkoxycarbonylmethylene group in a single operation.

Like the carbonyl olefination (cf. Section 3.2), this exchange reaction probably begins with the nucleophilic addition of *(59)* to the carbonyl group (cf. Scheme 6); this yields *(60)*, which cyclizes to form *(61)*. An intramolecular proton shift, favored by the acidity of the hydrogen atom on C-4, now leads to the 4-anionized oxazoline *(62)*, which gives the "pentadienyl anion" *(63)* by electrocyclic ring cleavage[70]. This anion can be isolated in the form of *(64)*.



(59) *(52)* *(60)* *(61)* *(62)* *(63)* *(64)*

Scheme 6. Course of formylaminoalkoxycarbonylmethylenation.

Table 3. α-Formylaminoacrylic esters *(64)* prepared by formylaminoalkoxycarbonylmethylenation with α-metalated isocyanoacetic esters *(59)* [69].

(52)	*(64)*	Yield (%)
Benzaldehyde	Ethyl α-formylamino-cinnamate	[74 [a], 69 [b], 28 [c]
Acetaldehyde	Ethyl α-formylamino-crotonate	13 [a]
Isobutyraldehyde	Ethyl α-formylamino-β-isopropylacrylate	58 [a]
Acetophenone	Ethyl α-formylamino-β-methylcinnamate	77 [a]
Acetone	Ethyl α-formylamino-β-methylcrotonate	77 [a]
Acetophenone	*tert*-Butyl α-formylamino-β-methylcinnamate	82 [a]
Cyclohexanone	Ethyl α-formylamino-cyclohexylideneacetate	87 [a]
Benzophenone	Ethyl α-formylamino-β-phenylcinnamate	81 [a]

[a] With butyllithium as base in tetrahydrofuran.
[b] With sodium hydride as base in tetrahydrofuran.
[c] With sodium ethoxide as base in ethanol; with *ca.* 65% of *(66a)*.

β-Substituted α-acylaminoacrylic acids have been synthesized in the past by condensation of acylglycines with carbonyl compounds and hydrolysis of the resulting azlactone

[63] Cf. *D. S. Matteson* and *R. A. Bailey*, J. Amer. Chem. Soc. *90*, 3761 (1968).

[64] *A. Nürrenbach* and *W. A. Böll*, private communication.

[65] *F. Gerhart*, unpublished.

[66] On the Wittig reaction see *G. Wittig* and *U. Schöllkopf*, Chem. Ber. *87*, 1318 (1954); *U. Schöllkopf*, Angew. Chem. *71*, 260 (1959); *A. Maercker*, Org. Reactions *14*, 270 (1965); literature cited there.

[67] *G. Wittig* and *W. Haag*, Chem. Ber. *88*, 1654 (1955).

[68] *H. Staudinger* and *J. Meyer*, Helv. Chim. Acta *2*, 635 (1919); cf. also *J. Meyer*, Chem. Ber. *89*, 842 (1956).

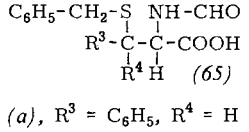
[69] *U. Schöllkopf*, *F. Gerhart*, and *R. Schröder*, Angew. Chem. *81*, 701 (1969); Angew. Chem. internat. Edit. *8*, 672 (1969); *U. Schöllkopf* and *F. Gerhart*, German Pat. Appl. 1946550/0 (Sept. 12, 1969), Badische Anilin- u. Soda-Fabrik.

[70] Check experiments with 2-oxazolines having an ethoxycarbonyl group on C-4 have shown that anions of the type *(62)* suffer ring cleavage; *M. T. Reetz*, unpublished; isoelectronic ring cleavages cf. *H. Kloosterziel*, *I. A. A. van Drunen*, and *P. Galama*, Chem. Commun. *1969*, 885.

(Erlenmeyer synthesis)[71]. However, this process requires forcing conditions, and is practically confined to carbonyl compounds that cannot undergo aldol condensation[70]. On the other hand, the reaction of *(59)*, M = Li, with cyclohexanone, which has a tendency to undergo self-addition, gives the acrylic ester in a yield of 87% (cf. Table 3).

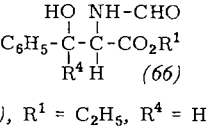
α-Acylaminoacrylic esters of the type *(64)* are of interest because of the various transformations that they can undergo, *e.g.* into α-keto and α-amino acids[71]. Unlike the acrylic acids formed in the Erlenmeyer synthesis[71], the esters *(64)* can evidently add suitable nucleophiles to their double bond after the manner of a Michael addition.

For example, if phenylmethanethiol is added to the reaction mixtures with benzaldehyde or acetone (in tetrahydrofuran with butyllithium, sodium hydride, or potassium *tert*-butoxide as the base[72]) after formation of *(64)*, the ester group then being hydrolyzed by heating with sodium hydroxide solution during isolation of the product, the reaction gives *S*-benzyl-*N*-formyl-β-phenylcysteine *(65a)* in a yield of about 70% or *S*-benzyl-*N*-formylpenicillamine *(65b)* in a yield of about 61%[73].



(65)

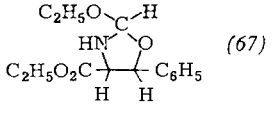
(a), $R^3 = C_6H_5$, $R^4 = H$
(b), $R^3 = R^4 = CH_3$



(66)

(a), $R^1 = C_2H_5$, $R^4 = H$
(b), $R^1 = R^4 = H$
(c), $R^1 = H$, $R^4 = CH_3$

The formation of *N*-formyl-β-phenylserine ethyl ester *(66a)* from benzaldehyde and ethyl sodioisocyanoacetate in ethanol (cf. Table 3) cannot yet be explained. It is possible that in competition with the proton migration, the intermediate *(61)* or *(62)*, $R^1 = C_2H_5$, $R^3 = C_6H_5$, $R^4 = H$, M = Na, is protonated by the solvent to form the oxazoline (cf. below). In the alkaline medium this takes up ethanol on the double bond and *(67)* is formed, which gives *(66a)* on subsequent hydrolysis in dilute acid.



(67)

N-Formyl-β-phenylserine *(66b)* and *N*-formyl-β-phenylthreonine *(66c)* can be isolated in yields of about 65 and about 50% respectively on dropwise addition of a solution of equimolar quantities of ethyl isocyanoacetate and benzaldehyde or acetophenone to a suspension of excess powdered sodium hydroxide in tetrahydrofuran, followed by stirring for a short time[74]. The details of the reaction course are again unclear.

[71] Cf. *H. E. Carter*, Org. Reactions *3*, 198 (1946); *Th. Wieland et al.* in Houben-Weyl-Müller: Methoden der Organischen Chemie. Thieme, Stuttgart 1958, p. 306ff., Vol. XI/2.

[72] For procedure see [68].

[73] *D. Hoppe*, Dissertation, Universität Göttingen, 1970.

[74] *R. Schröder*, Diplomarbeit, Universität Göttingen, 1970.

[75] *F. Gerhart* and *U. Schöllkopf*, Tetrahedron Lett. 1968, 6231; *U. Schöllkopf* and *F. Gerhart*, German Pat. Appl. 1812097/3, Badische Anilin- u. Soda-Fabrik (Nov. 29, 1968); see [64].

3.4. 2-Oxazolines from α-Metalated Isocyanides and Carbonyl Compounds

If instead of glacial acetic acid (see above), methanol or water is added in the reaction of α-metalated isocyanides *(51)* with aldehydes and ketones *(52)*, *i.e.* if the reaction mixture is worked up in the alkaline state, 2-oxazolines *(58)* can be isolated (cf. Table 3)[75].

The carbonyl adducts *(53)* (cf. Scheme 5) are evidently reversibly protonated, and the metalated oxazolines *(54)* irreversibly, in the alkaline medium. 2-Oxazolines are also formed from β-hydroxyalkyl isocyanides of the type *(57)* on treatment with methanolic sodium methoxide[64, 76].

Table 4. 2-Oxazolines *(58)* from α-metalated isocyanides *(51)* and carbonyl compounds *(52)* [75].

(51)	*(52)*	*(58)*	Yield (%)
(51a)	Benzaldehyde	5-Phenyl-2-oxazoline	60 (85) [a]
(51a)	Cinnamaldehyde	5-Styryl-2-oxazoline	58
(51a)	Furfural	5-Furyl-2-oxazoline	44
(51a)	Acetone	5,5-Dimethyl-2-oxazoline	31
(51a)	Cyclohexanone	Cyclohexanespiro-5′-(2-oxazoline)	30
(51a)	Acetophenone	5-Methyl-5-phenyl-2-oxazoline	69 (80) [a]
(51d)	Cyclohexanone	Cyclohexanespiro-5′-(4-vinyl-2-oxazoline)	13
(51b)	Cyclohexanone	Cyclohexanespiro-5′-(4-phenyl-2-oxazoline)	26
(51b)	Acetaldehyde	5-Methyl-4-phenyl-2-oxazoline	17 [77]
(51c)	Cyclohexanone	Cyclohexanespiro-5′-(4,4-diphenyl-2-oxazoline)	72
(51e)	Acetophenone	4-(β,β-Dimethylvinyl)-5-methyl-5-phenyl-2-oxazoline	46 [a]
Ethyl α-sodio-α-isocyanoacetate	Formaldehyde	4-Ethoxycarbonyl-2-oxazoline	53 [b]
[*(59)*, $R^1 = C_2H_5$, M = Na]	Benzaldehyde	4-Ethoxycarbonyl-5-phenyl-2-oxazoline	72 [b]
Ethyl α-sodio α-isocyanopropionate	Benzaldehyde	4-Ethoxycarbonyl-4-methyl-5-phenyl-2-oxazoline	86 [b]

[a] *A. Nürrenbach* and *W. A. Böll*, private communication [methanolysis a few minutes after addition of *(52)* to *(51)* in tetrahydrofuran at −70 °C].

[b] In ethanol and a little sodium cyanide as catalyst [73].

The syntheses known at present for 2-oxazolines start from *N*-acyl 2-amino 1-alcohols[78, 79], which relatively readily undergo ring closure[79], but become increasingly difficult to obtain with increasing substitution on the carbon atoms[79]. The advantage of the new synthesis is that the C-4–C-5

[76] On the cyclization of β-hydroxy isocyanides to form 2-oxazolines, see also *I. Hagedorn*, Angew. Chem. *75*, 305 (1963).

[77] *M. T. Reetz*, unpublished.

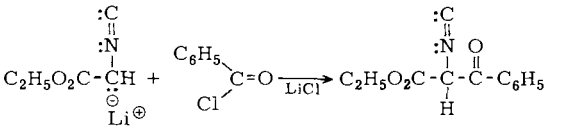
[78] Cf. *J. W. Cornforth* in *R. C. Elderfield*: Heterocyclic Compounds. Wiley, New York 1957, Vol. 5, p. 377ff.

[79] *W. Seeliger, E. Aufderhaar, W. Diepers, R. Feinauer, R. Nehring, W. Thier*, and *H. Hellmann*, Angew. Chem. *78*, 913 (1966); Angew. Chem. internat. Edit. *5*, 875 (1966).

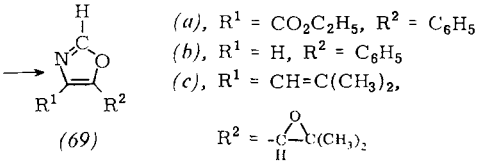
bond is formed during the reaction. The synthesis should provide a route to substituted 2-amino 1-alcohols, since 2-oxazolines are readily hydrolyzed in acidic media [78]. A synthesis of 2-amino 1-alcohols that allows wide scope for variation of the substituents on the carbon is of great interest, since many substances of this class are biologically active. In this connection, mention should be made of the 4-ethoxycarbonyl-2-oxazolines (cf. Table 4, last three lines), which can be obtained from ethyl α-isocyanoacetate or-propionate and aldehydes in ethanol with sodium cyanide as catalyst. Their hydrolysis in aqueous ethanol with a little triethylamine affords ethyl esters of *N*-formylserine and derivatives substituted in the α- or β-position [73].

3.5. Oxazoles from α-Metalated Isocyanides and Acylating Agents

On addition of benzoyl chloride to a suspension of ethyl lithioisocyanoacetate *(59a)* in tetrahydrofuran at −70 °C followed by acidic working up, 4-ethoxycarbonyl-5-phenyloxazole *(69)* can be isolated in a yield of about 80% [74]. This synthesis probably proceeds *via* the β-keto isocyanide *(68)*, which enolizes and cyclizes during working up [80]. 5-Phenyloxazole *(69)* is obtained by reaction of isocyanomethyllithium *(51a)* with *N*-methylbenzanilide and addition of methanol before working up [64]. Similarly, the oxazole *(69)* can be obtained in a yield



(59a) *(68)*



(69)

(a), $R^1 = CO_2C_2H_5$, $R^2 = C_6H_5$
(b), $R^1 = H$, $R^2 = C_6H_5$
(c), $R^1 = CH{=}C(CH_3)_2$,
$R^2 = -\overset{O}{\overset{\|}{C}}-\overset{O}{\underset{H}{\triangle}}-C(CH_3)_2$

of 50% from 1-lithio-3,3-dimethylallyl isocyanide *(51e)* and β,β-dimethylglycidic acid ethyl ester [64].

Isocyanomethyllithium *(51a)* does not appear to react uniformly with esters of carboxylic acids [64]; systematic studies will be required in order to establish which acylating reagents are most suitable for each of the compounds *(51)*.

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Translated by Express Translation Service, London

[80] For the acid-catalyzed cyclization of β-keto isocyanides, cf. *I. Hagedorn*, Angew. Chem. *73*, 26 (1961).

Chemical Lasers[**]

By K. L. Kompa[*]

Chemical lasers are based on the new principle of obtaining energy in the form of coherent radiation from chemical reactions. Since the discovery of the first laser of this type in 1965, laser emission has been investigated in a considerable number of fast gas-phase reactions. In physical chemistry such lasers provide a diagnostic tool for the detailed investigation of the energy distribution in elementary reactions. The barrier to technological use has probably also been overcome by the recent continuous operation of a chemical hydrogen fluoride laser. An attempt is made in the present article to trace the development of this still youthful field and to demonstrate the possibilities and limitations of the generation of energy with chemical lasers.

1. Introduction

Besides the well-known methods of energy production by chemical means, such as are used for heating, lighting, and driving machinery, a new principle of chemical production of energy has recently been developed. This is the total or partial liberation of the heat of a chemical reaction as stimulated emission of one or more reaction products. Reaction systems of this nature are known as chemical lasers, since the

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[**] Based on a lecture given at the General Meeting of the GDCh, September 15 to 20, Hamburg 1969.

excitation energy of the molecules, which appears as laser emission, stems from a chemical reaction. The laser is therefore chemically pumped. This principle can best be illustrated by the following specific example.

In the exothermic reaction of a fluorine atom with a hydrogen molecule to form hydrogen fluoride

$$F + H_2 \rightarrow HF + H \qquad (1)$$

(activation energy E_A = 1.7 kcal, reaction enthalpy $\Delta H = -31.6$ kcal/mole), 33.3 kcal/mole are liberated. This energy can be distributed over the translational degrees of freedom ($E_{trans.}$) of HF and H and can lead to the excitation of rotation ($E_{rot.}$) and vibration ($E_{vib.}$) of the hydrogen fluoride molecules. Electronic excitation of the reaction products requires much more energy, and is not possible here. The total energy of the hydrogen fluoride is thus

$$E = E_{vib.} + E_{rot.} + E_{trans.}$$

Provided that the system is in thermal equilibrium, the concentration of vibrationally excited molecules is given by the Boltzmann equation:

$$N_{excited} = N_0 \cdot \exp\left(-\frac{\Delta E}{kT}\right)$$

(N_0 = concentration of unexcited molecules, k = Boltzmann const., T = absolute temperature). Based on the vibrational excitation of hydrogen fluoride, with ΔE (energy for the excitation of the first vibrational state) $\approx$12 kcal or $\approx$4000 cm^{-1}, the concentration $N_{excited}$ found for room temperature, *i.e.* with $kT \approx 200\ cm^{-1}$, is negligible. However, the Boltzmann equilibrium with the environment may be considerably disturbed during or shortly after a fast chemical reaction in the gas phase, and certain molecular states may be overpopulated under these conditions of disequilibrium. The population densities of excited states may then be inverted with respect to the numbers of the Boltzmann distribution.

If one still tries to express such an inversion of population by means of a Boltzmann relation, a negative temperature value appears in the formula given. Since equilibrium is reached more rapidly for translation and rotation than for vibrational excitation, population inversions are most readily found among vibrational states. A reaction system with an overpopulation of excited molecular states constitutes a molecular amplifier, as can be easily shown. According to Beer-Lambert's law, the decrease in the intensity of a photon beam during passage through an absorbing medium is described by

$$\frac{dI}{I} = -\varepsilon c l \quad \text{or} \quad I = I_0 \cdot \exp(-\varepsilon c l)$$

(I = intensity after passing through the medium, I_0 = incident intensity, l = thickness of absorbing layer, c = concentration). If the populations of the ground and excited states are interchanged (I becomes greater than I_0), the absorption coefficient ε must become positive, and is then better named amplification coefficient. The amplification process is complementary to the absorption process.

A preliminary estimation may serve to show the energy output that can be expected from such chemical laser amplifiers. If a reaction volume of 10 l can be filled in a sufficiently short time with a total pressure of 150 torr of a 1:1 mixture of fluorine atoms and hydrogen molecules [cf. eq. (1)], corresponding to 45 mmole of each reactant, and if half of the hydrogen fluoride molecules (22.5 mmole) formed emit a vibrational quantum corresponding to $\approx$ 12 kcal/mole or $\approx$ 50 kWs/mole, the radiation pulse emitted will have an energy of >1000 Ws, which exceeds the pulsed energy output of any of the high power laser systems described so far[*]. However, it will be necessary to modify this estimate repeatedly in the course of the following discussion. A chemical laser can be constructed at relatively low experimental cost, since it merely involves a chemiluminescence experiment in a suitable optical resonator. Various methods have been used for the production of the initial concentration of a reactive species, like, for instance, fluorine atoms in the above example. Before proceeding to the description of experimental details, let us consider the reaction types and some of the reaction systems in which chemical laser emission has been observed up to now.

2. Reaction Principles

Table 1 shows the types of reaction that can lead to chemical lasers. The range extends from the photodissociation type through a number of bimolecular exchange reactions to elimination and photoelimination. All the chemical lasers described so far in the literature are listed in Table 2. The photodissociation lasers, which can only be regarded with reservation as chemical lasers, have been arranged in a separate chronological list. This list includes the first example in the production of excited iodine atoms by flash photolysis of alkyl iodides, preferably trifluoromethyl iodide. The resulting iodine laser, whose emission occurs at 1.315 μm, has an optical amplification of more than 100 dB/m[**], which is greater than that of any other known gas laser. Lasers of this type operate pulsewise, since the reaction mixture must be renewed after each "shot". Continuous operation is in principle possible in a flow system with a continuous throughput of the reaction material. The iodine atom and the bromine atom lasers are the only examples in Table 2 in which electronically excited reaction products appear. In all other cases known at present, with the exception of a hydrogen fluoride

[*] In conventional high power lasers ruby or neodymium glass is mostly used as amplifying material.

[**] dB/m = decibels per meter length of laser tube; decibel = 10 × log (output power/input power) of an amplifier.

Table 1. Types of reactions in which chemical laser emission has been observed.

Reaction type	Example	Refs.
Photodissociation	$CF_3I \xrightarrow{h\nu} I^* + CF_3$	[19, 20, 26]
Photoelimination	$CH_2CHF \xrightarrow{h\nu} HF^\dagger + C_2H_2$	[1, 17]
Abstraction	$Cl + HI \longrightarrow HCl^\dagger + I$	[10, 11, 13]
Chain reaction	$F + H_2 \longrightarrow HF^\dagger + H$	[14, 16, 25]
	$H + F_2 \longrightarrow HF^\dagger + F$	
β-Elimination	$CF_3CH_3 \longrightarrow HF^\dagger + CF_2CH_2$	[18]

* = electronic excitation. † = vibrational excitation.

Table 2. List of chemical lasers.

Pump system [a]	Method [b]	Emitting molecule	First described	Refs.
$H_2(D_2) + Cl_2$	*hv*	HCl(DCl)	1965	[2, 3]
$CS_2 + O_2$	*hv*	CO	1966	[4]
$H_2(D_2, RH) + MF_n$	*hv*	HF(DF)	1967	[5–8
$H_2(D_2) + RF$	PE	HF(DF)[c]	1967	[9]
$Cl_2 + HI$	*hv*, PE	HCl	1967	[10, 11]
$CO + O_2(+CO_2)$		CO_2	1967	[12]
$Cl_2 + HI(+CO_2)$	*hv*	CO_2	1968	[13]
$CH_3I + CF_3I$	*hv*	HF	1968	[18]
$H_2(RH) + F_2$	*hv*, PE	HF	1969	[14, 25]
$HN_3(+CO_2)$	*hv*	CO_2	1969	[15]
$H_2(D_2) + F_2(+CO_2)$		CO_2	1969	[16]
$CH_3I + N_2F_4$	*hv*	HF	1969	[27]
Photodissociation Lasers				
$CF_3I(RI)$	*hv*	I	1964	[19,20,26]
NOCl	*hv*	NO	1966	[21, 22]
$(CN)_2$	*hv*	CN	1966	[23]
IBr	*hv*	Br	1969	[24]
$CH_2CHF(Cl)$	*hv*	HF(HCl)	1969	[1, 17]

[a] Abbreviations under pump system: R = alkyl group, frequently CH_3; $(+CO_2)$ = carbon dioxide as an additive is pumped indirectly; MF_n = UF_6, SbF_5, F_2O, XeF_4, WF_6, MoF_6, XeF_2, IF_5.

[b] Abbreviations under method: *hv* = flash photolysis; PE = pulse discharge; no entry = spontaneous reaction.

[c] Rotational emission of HF also observed.

[1] *G. C. Pimentel*, 2nd. Conf. on Chemical and Molecular Lasers, St. Louis/Mo. (USA), May 1969.

[2] *J. V. V. Kasper* and *G. C. Pimentel*, Physic. Rev. Letters *14*, 352 (1965).

[3] *P. H. Corneil* and *G. C. Pimentel*, J. chem. Physics *49*, 1379 (1968).

[4] *M. A. Pollack*, Appl. Physics Letters *8*, 237 (1966).

[5] *K. L. Kompa* and *G. C. Pimentel*, J. chem. Physics *47*, 857 (1967); *K. L. Kompa, J. H. Parker*, and *G. C. Pimentel*, J. chem. Physics *49*, 4257 (1968); *K. L. Kompa, P. Gensel*, and *J. Wanner*, Chem. Physics Letters (Amsterdam) *3*, 210 (1969); *P. Gensel, K. L. Kompa, J. Wanner*, Chem. Physics Letters (Amsterdam), in press.

[6] *J. H. Parker* and *G. C. Pimentel*, J. chem. Physics *48*, 5273 (1968); *51*, 91 (1969).

[7] *R. W. T. Gross, N. Cohen*, and *T. A. Jacobs*, J. chem. Physics *48*, 3821 (1968).

[8] *G. M. Chumak, G. G. Dolgev-Saveluev*, and *V. A. Polakov*, Symposium on Chemical Lasers, Moscow, Sept. 1969, JETP Letters, in press.

[9] *T. F. Deutsch*, Appl. Physics Letters *10*, 234 (1967); *11*, 18 (1967).

[10] *J. R. Airey*, IEEE (Institute of Electrical and Electronic Engineers, New York) J. Quant. Electr. *Q* E-*3*, 208 (1967).

[11] *C. B. Moore*, IEEE J. Quant. Electr. *Q E-4*, 52 (1968).

[12] *I. Wieder*, Physics Letters *24 A*, 759 (1967).

[13] *H. L. Chen, J. C. Stephensor*, and *C. B. Moore*, Chem. Physics Letters *2*, 593 (1968).

[14] *N. G. Basov, L. V. Koulakov, E. P. Markin, A. I. Nikitin*, and *A. N. Oraevsky*, JETP Letters *9*, 375 (1969).

[15] *N. G. Basov, V. V. Gromov, E. L. Koshelev, E. P. Markin*, and *A. N. Oraevsky*, JETP Letters *10*, 2 (1969).

laser based on pure rotational excitation, vibrational-rotational emission is observed in the infrared region of the spectrum. The first really chemical laser as opposed to photodissociation was discovered in 1965 by *Kasper* and *Pimentel* in the flash-photolytically initiated hydrogen/chlorine explosion (Table 2). Vibrationally excited hydrogen chloride is formed here in the reaction of a hydrogen atom with molecular chlorine [eq. (4)]. The hydrogen atoms required are formed in the preceding reaction step (3):

$$Cl_2 \xrightarrow{h\nu} 2\ Cl \tag{2}$$

$$Cl + H_2 \rightarrow HCl + H \quad \Delta H = +1\ \text{kcal} \tag{3}$$

$$H + Cl_2 \rightarrow HCl + Cl \quad \Delta H = -45\ \text{kcal} \tag{4}$$

The nearly thermoneutral reaction (3) yields only "cold", non-vibrationally excited hydrogen chloride. In the formation of hydrogen fluoride [eq. (1)], on the other hand, even the first step of the chain reaction is exothermic, and it was this, among other reasons, that led to the discovery of hydrogen fluoride laser emission in 1967 by *Kompa* and *Pimentel*. Similar considerations also led to the development of a more effective hydrogen chloride laser, which is pumped by the reaction of chlorine atoms with hydrogen iodide molecules (Table 2). The carbon monoxide laser from the oxidation of carbon disulfide has so far received comparatively little attention. Molecular fluorine did not seem very suitable as a source of fluorine atoms for a laser according to eq. (1), owing to its problems of handling and to its low photochemical yield of fluorine atoms. On the other hand, a large number of volatile inorganic fluorides constitute photochemical fluorine atom sources with high absorption coefficients for the photolysis light; they present no difficulty in handling, even in mixtures with hydrogen, and do not attack the laser apparatus. The various fluorides exhibit characteristic differences in the emission spectra of the corresponding laser system.

Among the many hydrogen fluoride lasers, those in which excited hydrogen fluoride molecules are formed

[16] *T. A. Cool* and *R. R. Stephens*, J. chem. Physics *51*, 5175 (1969); Appl. Physics Letters, in press; cf. Laser Focus, December 1969.

[17] *M. J. Berry* and *G. C. Pimentel*, 2nd. Conf. on Chemical and Molecular Lasers, St. Louis/Mo. (USA), May 1969.

[18] *M. J. Berry* and *G. C. Pimentel*, J. chem. Physics *49*, 5190 (1968).

[19] *J. V. V. Kasper* and *G. C. Pimentel*, Appl. Physics Letters *5*, 231 (1964); *J. V. V. Kasper, J. H. Parker*, and *G. C. Pimentel*, J. chem. Physics *43*, 1827 (1965).

[20] *M. A. Pollack*, Appl. Physics Letters *8*, 36 (1966).

[21] *M. A. Pollack*, Appl. Physics Letters *9*, 94 (1966).

[22] *C. R. Giuliano* and *L. D. Hess*, J. appl. Physics *38*, 4451 (1967).

[23] *M. A. Pollack*, Appl. Physics Letters *9*, 230 (1966).

[24] *C. R. Giuliano* and *L. D. Hess*, 2nd. Conf. on Chemical and Molecular Lasers, St. Louis/Mo. (USA), May 1969.

[25] *J. F. Spinnler* and *P. A. Kittle*, 2nd. Conf. on Chemical and Molecular Lasers, St. Louis/Mo. (USA), May 1969.

[26] *C. M. Ferrar*, Appl. Physics Letters *12*, 381 (1968).

[27] *T. D. Padrick* and *G. C. Pimentel*, J. chem. Physics, in press.

by photoelimination from fluoroalkenes are a special case. It may be supposed that conclusions concerning the stereochemical course of the elimination could be drawn from the differences in the laser emission observed with *cis* and with *trans* alkenes. Laser emission is also observed on spontaneous decomposition of molecules formed by combination of free alkyl and fluoroalkyl radicals. Pure rotational laser emission has occasionally been observed to accompany the vibrational-rotational emission of hydrogen fluoride under certain conditions (cf. Table 1).

The excited vibrational states of hydrogen halide molecules are subject to extremely effective deactivation processes, which always compete with the stimulated emission. It may therefore be advantageous to transfer the excitation energy initially present in the reaction products to added molecules of an admixture that is capable of better energy storage. A number of carbon dioxide lasers can be pumped indirectly in this way. The situation is particularly favorable in the transfer of energy from hydrogen chloride or from deuterium fluoride to carbon dioxide, which is a near-resonance process. This principle of laser-pumping may be called chemosensitization. Finally, we should also mention a carbon dioxide laser that can be pumped by the oxidation of carbon compounds (Table 2). The group of indirectly chemically pumped lasers can undoubtedly be expanded further, and it is unlikely that carbon dioxide will remain the only example.

3. Experimental Arrangements

The experimental problems that arise in the operation of chemical lasers will be illustrated for the example of the flash-initiated hydrogen fluoride laser. "Classical" flash photolysis, the successful development of which earned the Nobel Prize for *R. G. W. Norrish* and *G. Porter* in 1967 [28], uses a pulse capacitor discharge through a xenon-filled quartz tube as the light source. Flash durations of between 10 and 50 μs can be achieved with discharge energies of a few thousand Ws. The half-life of reaction (1) for initial concentrations >1 torr, however, is considerably less than 1 μs. Shorter flashes are therefore desirable to achieve the full possible radiation density, *i.e.* to make full use of the possibilities offered by the high reaction rate for the fast build-up of the hydrogen fluoride concentration. An arrangement that has proved suitable for this purpose is described by *Welge et al.* [29], in which a series of spark gaps (arranged in a nitrogen atmosphere along the absorption tube) is used instead of closed xenon flash tubes for the generation of light [5, 30].

The construction principles of this apparatus are shown in Figure 1. The eight spark gaps are supplied by eight high-voltage pulse capacitors [*] (1 μF/20 kV each, E_{max} = 200 Ws). The discharge gaps are connected as in a Marx generator, and can therefore be triggered synchronously. Figure 1a shows the lucite spark chamber with the eight pairs of electrodes and the absorption tube, which is made of fused quartz with a high optical transparency, along the axis of the cylinder. Photolysis light sources of this type are characterized by good accessibility of the vacuum UV (below 2000 Å) and high reliability, as well as by the short duration of the flash. However, xenon flash tubes will retain their place for studies in which a high light yield and a good optical coupling between the photolysis lamp and the absorption cell are of primary importance. The light characteristic of such lamps can be greatly improved, with a simultaneous increase in lifetime, by effective preionization. The energy from the laser oscillator can be coupled out for instance by a partly reflecting take-off plate placed in the beam path as shown in Figure 1. A beam splitter then cuts off part of the signal for recording of the total pulse shape, while the main part of the emission is spectrally analyzed in an infrared monochromator. The individual lines in the emission signal are then recorded by a second detector placed behind the monochromator exit slit.

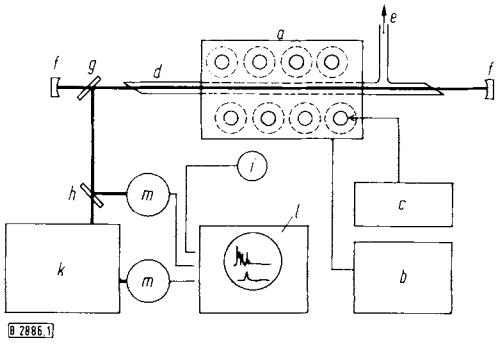


Fig. 1. Block diagram of a chemical laser apparatus.
a) Vacuum-tight spark chamber with eight spark gaps, b) 20 kV mains power supply, c) 30 kV trigger unit, d) laser tube with sapphire windows attached at the Brewster angle, e) to the vacuum line, f) spherical resonator mirrors, g) deflection plate, h) beam splitter, i) phototransistor for flash control, k) infrared monochromator, l) double-beam oscillograph, m) infrared detectors.

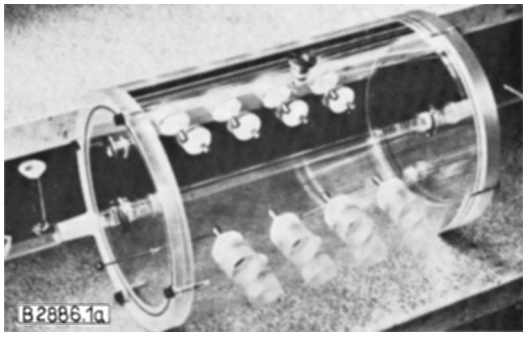


Fig. 1a. Polymethyl methacrylate spark chamber with eight pairs of electrodes and Suprasil ® laser tube at the axis of the vessel.

[28] *R. G. W. Norrish*, Angew. Chem. *80*, 868 (1968); *G. Porter*, Angew. Chem. *80*, 882 (1968).

[29] *K. H. Welge, J. Wanner, F. Stuhl*, and *A. Heindrichs*, Rev. sci. Instruments *38*, 1728 (1967).

[30] *K. L. Kompa* and *J. Wanner*, unpublished results.

[*] Hirotronic Ltd., Basingstoke/Hants. (England)

The total signal (or alternatively the flash profile) and the single-line emission are displayed on a double-beam oscilloscope and photographed.

4. Build-Up of the Laser Emission

The build-up of the laser emission is illustrated in Figure 2. The spark chamber with the eight spark gaps, the laser tube with the end windows at Brewster's angle, and the resonator mirrors are shown schematically. The photons entering the tube from the sparks first produce reactive particles, *e.g.* chlorine atoms in accordance with eq. (2) or fluorine atoms. After a certain number of collisions of the fluorine atoms with hydrogen molecules, vibrationally excited hydrogen fluoride is formed. Some of the molecules formed emit spontaneously in various directions in space and form the noise background of the oscillator. The noise components that lie in the axis of the tube undergo feedback by reflection at the mirror surfaces, are amplified, and cause the laser to start oscillating. In the arrangement shown in Figure 2, part of the power is coupled

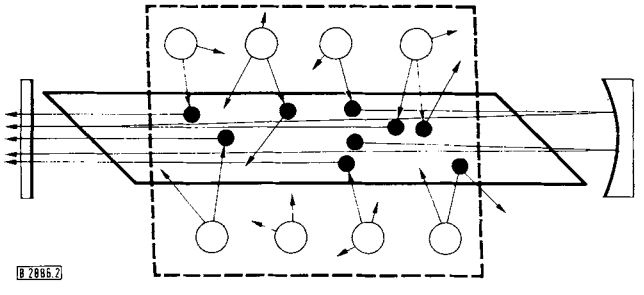


Fig. 2. Build-up of the laser emission (for explanations see text).

out by the semitransparent plane mirror shown on the left. The emission signal of a laser oscillator of this type can be further amplified by passage through other tube volumes that contain excited molecules produced in the same manner. Two additional experimental aspects deserve mention in this connection. These are the production of giant pulses and the tuning of resonators with the aid of a grating instead of a resonator mirror. The buildup of the laser emission (see Figure 2) can be divided into three steps: 1) the primary photolysis; 2) the production of energy by the chemical reaction; 3) the output of energy by stimulated emission, which occurs under the conditions described as soon as a certain threshold value is exceeded. A limited period of storage of energy in the molecules may be inserted between steps 2 and 3. To achieve this, the resonator is switched on (at a predetermined time after the photolysis flash) only when the energy is far in excess of the threshold value. Controlled switching of the resonator quality ("q-switching") leads to emission of the stored excitation energy in a very short time (a few nanoseconds) and hence to very much higher peak power outputs [31]. Variation of the switch-on time also yields information on the time dependence of the storage, and so allows conclusions to be drawn regarding the relaxation and deactivation processes in chemical laser systems [32]. Chemical lasers, like other molecular lasers, emit not only single lines but a spectrum that is more or less rich in lines. However, if a dispersing element is inserted, *e.g.* a prism or a grating in the resonator, the resonator condition can be satisfied only for a limited range of wavelengths, and hence usually only for one emission line. The resonator can then be tuned over the entire emission spectrum by grating rotation. The usefulness of such line selection in physical-chemical studies becomes apparent in the use of chemical lasers as spectroscopic light sources. On the other hand, the possibility of studying isolated single transitions allows the investigation of coupling phenomena and questions of communication between the molecular energy states involved in the emission [30].

5. Pulsed Operation of Chemical Lasers, Energy Yield

The discussion so far has been confined to the pulsed operation of chemical lasers. In every case the pumping reaction must be started by an external auxiliary energy source that provides an igniting pulse. The oscillogram in Figure 3 shows the initiating photolysis flash of an arrangement as shown in Figure 1, as well as the laser emission signal produced by it. It can be seen that the flash has a half-peak duration of 1.2 μs, whereas the laser signal lasts up to 8 μs. The laser was produced here by photolysis of a mixture of iodine pentafluoride as a source of fluorine atoms and hydrogen. Figure 4 shows a comparison of two single-line signals, which were not recorded directly in this case, but were measured with an RC integrator for better comparability of the line intensities. The change in the shape of the total emission signal as compared with Figure 3 is explained by the

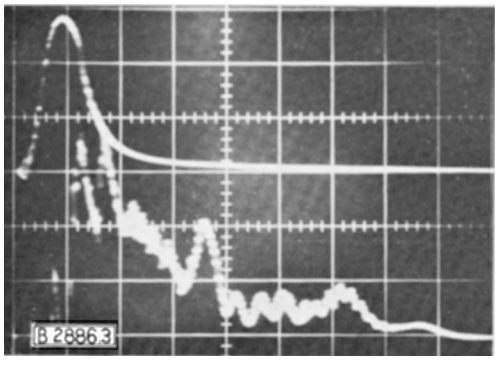


Fig. 3. Time profiles of the photolysis flash (upper trace) and of the hydrogen fluoride laser emission (lower trace): 30th illumination of a mixture of iodine pentafluoride (13 torr) and hydrogen (13 torr), time scale 1 μs/division.

[31] Cf. *e.g. W. Kleen* and *R. Müller*, Laser, Springer Verlag, Berlin-Heidelberg-New York 1969, p. 161 ff.

[32] *P. Gensel* and *K. L. Kompa*, unpublished results.

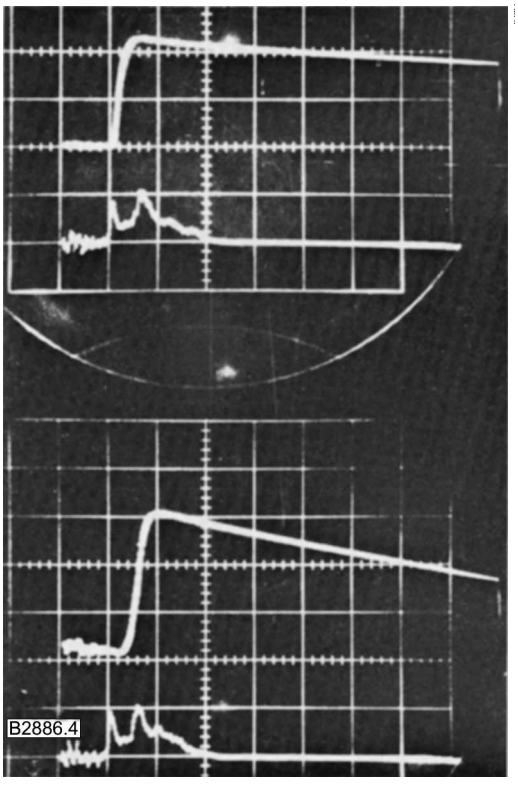


Fig. 4. Measurement of laser emission signals by a gold-doped germanium detector in an integrating circuit; upper trace in both pictures: single-line emission signal (detector Au:Ge with RC integrator), lower trace: total emission (detector InSb).

fact that tungsten hexafluoride was used as the source of fluorine atoms in this case.

If the emission in a photolytically initiated laser is pumped by only one reaction step, *e.g.* reaction (1), the radiation output of the laser is limited by the available amount of photolysis light, provided that not more than one photon can be emitted per hydrogen fluoride molecule. The quantum yield of the conversion of flash light into laser radiation cannot exceed 1. The yield can be increased in two ways. On excitation of sufficiently high vibrational states, several photons can be emitted from each hydrogen fluoride molecule formed, *e.g.* by an emission cascade *via* several vibrational states. Moreover, the use of chain reactions enables a large number of hydrogen fluoride molecules to be obtained for each fluorine atom that reacts initially. In particular, branched, self-accelerating chain reactions[33] give quantum yields that can be as high as 10^5 for the formation of hydrogen fluoride from hydrogen and molecular fluorine, depending on the reaction conditions[14]. A very small trigger pulse is then sufficient for the production of a high hydrogen fluoride concentration, and this is perhaps the greatest technological stimulus for the development of chemical lasers. The "ideal" chemical laser is thus largely or even totally independent of external energy sources. Lasers having these properties have very recently come within the bounds of technical feasibility[5,16].

[33] *N. N. Semenov*, Some Problems of Chemical Kinetics and Reactivity, Vol. II, Pergamon Press, Oxford 1959; cf. also *K. J. Laidler*, Chemical Kinetics, McGraw-Hill Book Comp., New York, Toronto-London 1950, p. 180ff.

A chain reaction for the formation of hydrogen fluoride may proceed as follows[14,33].

$$F_2 \xrightarrow{E_{diss}} 2\,F \qquad (5)$$

$$F + H_2 \rightarrow HF^* + H \qquad \Delta H \triangleq -32\ \text{kcal} \qquad (1)$$

$$H + F_2 \rightarrow HF^* + F \qquad \Delta H \triangleq -98\ \text{kcal} \qquad (6)$$

$$HF^* + F_2 \rightarrow HF + 2\,F \qquad (7)$$

Chain branching occurs here in reaction (7), where vibrationally excited hydrogen fluoride from the preceding step (6) causes fluorine molecules to dissociate in collisions. It can be seen that reaction (7) competes with the equally possible stimulated emission of the hydrogen fluoride molecules formed in (6). Chain branching therefore occurs only at certain pressures and under certain reaction conditions. Lasers having reaction (6) in addition to reaction (1) as a pumping step, which therefore have a chain length >1, have been found not only in the hydrogen/fluorine system, but also in the flash photolysis of iodine pentafluoride/hydrogen mixtures[5]. However, so far there have been no reports on accurate quantum yield determinations and energy conversion data.

6. Continuous Wave Operation

In addition to the pulsed mode described, continuous operation of a chemical laser is possible for instance in a self-propagating chain reaction. Figure 5 shows

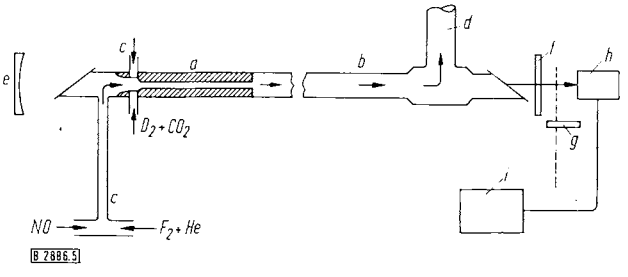


Fig. 5. Continuous operation of a hydrogen fluoride laser (after [16]). a) Teflon reaction capillary, b) Pyrex glass tube, c) gas injectors, d) to cold trap and pump, e) highly reflecting resonator mirror, f) plane mirror (0.5% transmission), g) chopper. h) bolometer, i) tuned amplifier.

the experimental arrangement used in this case. The initial concentration of fluorine atoms is produced here by the reaction:

$$NO + F_2 \rightarrow NOF + F \qquad (8)$$

The maximum output of this laser, which is still a very small device operating with a fluorine throughput of 390 μmole/s, was reported to be 0.23 W. Though this laser can be operated both as a hydrogen fluoride and as a deuterium fluoride laser, the energy transfer to carbon dioxide is advantageous.

The main reason for this is that the energy transfer largely eliminates the strong self-deactivation of the

excited hydrogen halides [*]. Another approach to the problem of self-quenching in hydrogen fluoride lasers is the use of gas-dynamic principles in addition to chemical pumping. Such a device has yielded the notable energy conversion of 12% [**] with a cw-power output of nearly 500 W [35]. Figure 5a illustrates its principles of operation. First nitrogen

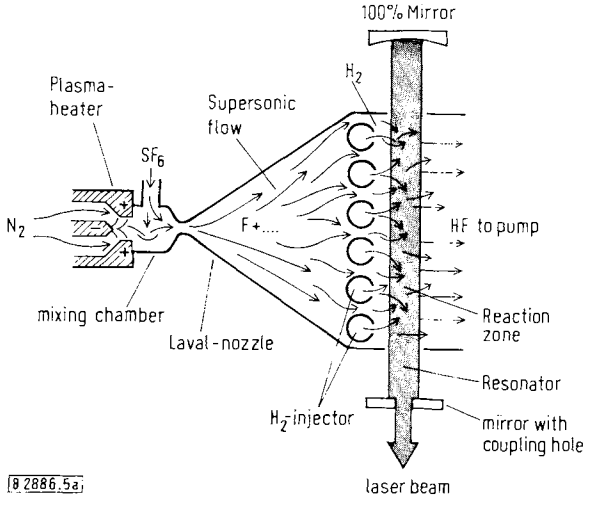


Fig. 5a. Chemical and gas-dynamic hydrogen fluoride laser.

molecules are heated to 2300 °K in a plasma heater. By subsequent mixing with sulfur hexafluoride fluorine atoms are produced thermally. The atomic fluorine flow is 0.03 moles/s. This mixture which has been cooled by rapid expansion behind a Laval nozzle to nearly room temperature is brought together with molecular hydrogen in a special injection system. The reaction zone of the mixture that is still moving with supersonic velocity is placed in an optical resonator, whose active length is only 17 cm. The number of experimental cw-laser set-ups of this type is considerably increasing at present.

7. Physico-Chemical Conditions

The choice of hydrogen fluoride for the system used as an example in the present discussion will now be explained. Figure 6 shows some energy profiles corresponding to reaction (1) for formation of various vibrational states of hydrogen fluoride. Since the energy associated with the excitation of a vibrational quantum is approximately 12 kcal/mole, the highest excited state that can be reached with the heat of reaction of this process is the third vibrational level (v = 3). The rotational states that subdivide each vibrational state are not shown in the diagram. The observed laser emission lines correspond to transitions between vibrational-rotational states, the vibrational quantum number v always changing by 1. An important advantage of the hydrogen fluoride molecule over other diatomic molecules containing heavy atoms and over compounds with three or more atoms is the relatively small number of energy states that can be occupied. Because of this, no excessive energy "dilution" occurs. Figure 6 illustrates rate

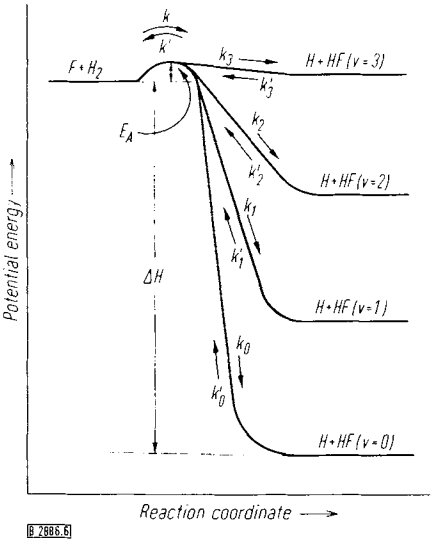


Fig. 6. Relative energies of the vibrational levels of hydrogen fluoride that can be populated by the reaction F + H_2 → H + HF (further explanations in text).

constants k_v that differ fromt he overall rate constants of the reactions in that they give the specific rates of formation of hydrogen fluoride for definite vibrational states. The differences in the constants k_v then determine the differences in the populations of the various states:

$$N_v \sim k_v \quad \text{or} \quad \frac{N_v}{N_{v-1}} = \frac{k_v}{k_{v-1}}$$

The constants k_v can be derived from the characteristics of the laser emission, which contain the excess populations of certain excitation states and hence the differences in population as the principal parameters [1,6,17,18]. The determination of these constants is of great importance to the understanding of elementary chemical reactions, and therefore appears as an important goal of chemical laser studies in physical chemistry. Investigations of this nature have given a value of 5.5 for the population ratio $N_{v=2}/N_{v=1} = k_{v=2}/k_{v=1}$ [6]. Other determinations carried out by the alternative method of observing spontaneous infrared chemiluminescence [34] gave $k_{v=2}/k_{v=1} = 3.5$ and $k_{v=3}/k_{v=2} = 0.47$. Moreover, the part of the total energy available in reaction (1) that leads to vibrational excitation, E_v/E_{total}, is found to be 57%, while only 6% appears as rotational energy and 37% as translational energy. These values show an effective conversion of the heat of reaction into vibrational energy, and also

[*] Note added in proof: A CO_2 laser operating in the arrangement shown in Fig. 5 has now been reported to have a conversion efficiency of 4% (*T. A. Cool* and *R. R. Stevens*, Appl. Phys. Lett. *16*, 55 (1970)).

[**] One should note for comparison that the carbon dioxide laser which is the most efficiently pumped gas laser so far has 15–20% energy conversion.

[34] *J. C. Polanyi* and *D. C. Tardy*, J. chem. Physics, in press; for a description of the method of investigation cf. *K. G. Anlauf, P. J. Kuntz, D. H. Maylotte, P. D. Pacey*, and *J. C. Polanyi*, Discuss. Faraday Soc. *44*, 183 (1967).

[35] *D. J. Spencer, H. Mirels, T. A. Jacobs*, and *R. W. F. Gross*, Appl. Phys. Lett. *16*, 235 (1970).

indicate a strong preference for the formation of hydrogen fluoride with v = 2. Accordingly transitions from v = 2 to v = 1 also occur preferentially in lasers pumped by reaction (1). This emission appears in the infrared region between 2.7 and 2.9 μm. In laser systems in which the additional reaction (6) contributes to the pumping, higher vibrational states up to v = 6 are excited. The emission at about 3 μm corresponds to a large number of vibrational-rotational lines, but no detailed rate constants have been published so far [5, 14]. This description of the parameters of chemical laser emission has been confined to hydrogen fluoride lasers as the area that has been most extensively studied. In view of the intense activity in this field, however, similar results may be expected in the near future for other, new chemical lasers.

8. Possible Applications

There is considerable scope for the use of these lasers in various fields. In chemistry, sources of strong monochromatic infrared radiation offer the long-term prospect of use as a "selective Bunsen burner" with the object of carrying out chemical reactions with a controlled supply of energy in certain vibrational degrees of freedom of a reaction system. Chemical lasers are also already being used as spectroscopic light sources for IR fluorescence studies [13]. An obvious point of technological interest is the possible freedom from dependence on external energy sources. Despite great hopes, it is not yet clear whether the possibly very high conversion efficiency of these lasers would make their use in high energy applications (*e.g.* for plasma production) seem interesting. No chemical laser with a pulse energy of more than 1 Ws has yet been described, but pulse energies of the order of 10^3 Ws, which correspond to the value estimated at the beginning of this article, have been predicted for laboratory systems.

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Developments in Inorganic Arc Plasma Chemistry

By U. Landt [*]

For some 10 to 15 years, plasma chemistry has been in a state of rapid development on the research side, whereas only a few reactions are at present carried out industrially in a plasma jet. After a short description of the properties of thermal plasmas, the technique of production and stabilization of arc plasmas and the various types of arc plasma generators are discussed. The course of chemical reactions at plasma temperatures is then considered, with particular reference to kinetic and thermodynamic aspects. A special part of the review is devoted to a detailed description of the inorganic reactions that have been carried out in the plasma jet (preparation e.g. of compounds containing nitrogen, C–N and C–F compounds, ozone, nitrides, cyanides, carbides, metal oxides, and metals from metal oxides and from halides).

1. Development and Present Position of Plasma Chemistry

A plasma is nowadays generally taken to be a partly or completely ionized gas that is externally electrically neutral, conducts electricity, and has a higher internal energy than an un-ionized gas. The energy required for the production and maintenance of a plasma can be supplied as heat or as electrical or mechanical energy. The most important methods for the supply of electrical energy are arc and glow discharges and electrodeless discharges (high frequency and microwave discharges). Only the arc plasma and its use will be discussed here.

The term "plasma chemistry" is at present used only reluctantly in the literature. Since chemical bonds do not exist at the high temperatures characteristic of most types of plasma, the term is really self-contradictory. Nevertheless, it is shorter than any of the

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alternatives, and will therefore be used here in the sense of the performance of chemical reactions in or with the aid of plasmas.

Chemical plasma processes have been known since the industrial production of oxides of nitrogen by "combustion of air" in the flame arc furnace (*Birkeland* and *Eyde*; *Schönherr* and *Pauling*). The development of plasma chemistry stopped for a long time after the replacement of this process by the cheaper combustion of ammonia. This standstill was mainly due to the high cost of electricity and technical problems.

For some 10 to 15 years, however, plasma chemistry has been developing rapidly, at least on the research side. The intense activity in high-temperature physics in connection with nuclear fusion, the problems encountered in space flight and supersonic technology (re-entry into the atmosphere, rocket propulsion, *etc.*), and the prospect of cheaper electricity from nuclear power stations have also led to a marked growth of interest in chemical plasma technology. This is particularly clear from the IUPAC Symposium in Moscow in 1965 on "Properties and Use of Low-Temperature Plasmas" and the Symposium on "Chemical Reactions in Electrical Discharges" at the 153rd meeting of the American Chemical Society in Miami in 1967 [1].

A number of chemical reactions under plasma conditions have been particularly intensively studied. These include the preparation of acetylene from other hydrocarbons, the chemical fixation of atmospheric nitrogen, and fluorine/carbon reactions. Many other inorganic reactions have also been carried out. Though plasma generators with powers of up to several MW have been developed, practically no use is currently being made of plasma processes in industry, apart from the arc processes for the production of acetylene (Hüls process [2], Du Pont process [3], MHD Research process [4], Knapsack AG's hydrogen arc pyrolysis process [5]). The reasons for this situation are the present high cost of power for most processes, as well as lack of knowledge of the physico-chemical principles underlying processes at plasma temperatures.

It is now becoming increasingly clear that plasma chemistry has reached a point where, after years of a predominantly empirical approach, it is necessary to make a broader study of the theoretical principles and to build up a scientifically and economically supported conceptual basis for profitable industrial use.

2. Properties of the Thermal Plasma

A plasma produced at a pressure ≥ 1 atm is characterized by high charge-carrier densities (of the order of $10^{14}/cm^3$) and a large number of collisions between electrons, ions, atoms, and molecules. To a first approximation, a plasma of this nature may be regarded as being in thermal equilibrium; it is known as a thermal plasma, and is the type that is of most interest to chemists, since all kinetic and reaction equilibria, as well as the other properties of the plasma (mean velocity of the particles, thermal conductivity, electrical conductivity, *etc.*) are functions of the temperature at constant pressure. Thermal plasmas are mainly produced by electric arcs.

At pressures lower than 1 atm, the electron and atom (or gas) temperatures differ considerably; the electron temperature can be several orders of magnitude higher than the gas temperature in such "non-thermal" plasmas.

The changes in the properties of a plasma with temperature are of the greatest importance to its practical use. Figure 1 shows the composition of a nitrogen plasma as a function of temperature. The thermal dissociation of the nitrogen molecules starts below 5000 °K, and is complete at about 12000 °K. Single ionization of the nitrogen atoms starts to become noticeable at 8000 °K and reaches a level of 50% at 15000 °K, with the result that the electrical conductivity is then comparable to that of some metals.

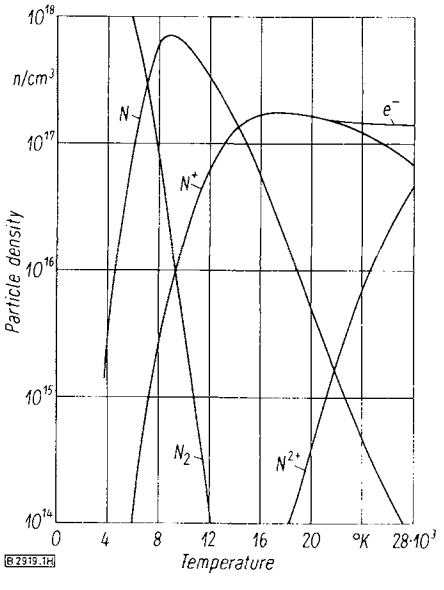


Fig. 1. Composition of nitrogen plasma as a function of the temperature (after *Burhorn* and *Wienecke* [6]); $p = 1$ atm.

The change in the enthalpies of some gases as a function of temperature is shown in Figure 2. Diatomic gases have a much higher energy content than monatomic at temperatures above 2000 °K, owing to the stored work of dissociation, and can therefore give up correspondingly greater quantities of heat without appreciably lowering the temperature of the plasma. Conversely the temperature of a monatomic

[1] *B. D. Blaustein*, Chemical Reactions in Electrical Discharges, Adv. Chem. Ser. *80*, American Chemical Society, Washington 1969.

[2] *P. Baumann*, Chemie-Ing.-Techn. *20*, 257 (1948).

[3] Chem. Week, Jan. 18, 1964, p. 64.

[4] Chem. Engng. News, Jan. 20, 1964.

[5] *K. Sennewald, E. Schallus*, and *F. Pohl*, Chemie-Ing.-Techn. *35*, 1 (1963).

[6] *F. Burhorn* and *R. Wienecke*, Z. physik. Chem. (Leipzig) *215*, 269, 285 (1960).

gas for a given value of the energy introduced into the plasma is much higher than that of a diatomic gas, as can be seen from the comparison of nitrogen and argon in Figure 3.

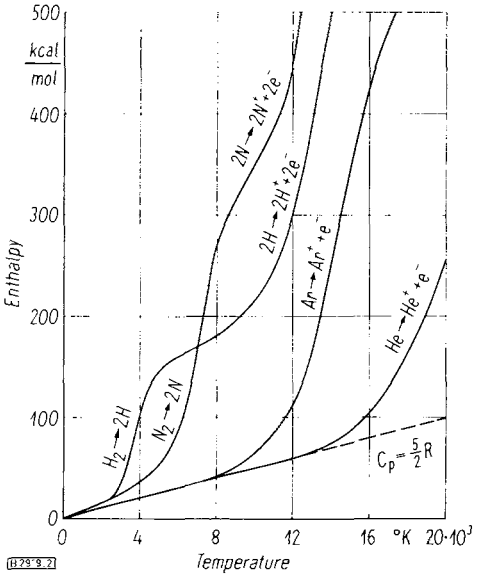


Fig. 2. Enthalpies of various gases as a function of the temperature (after *Burhorn et al.* [6] and *Drellishak et al.* [7]); p = 1 atm.

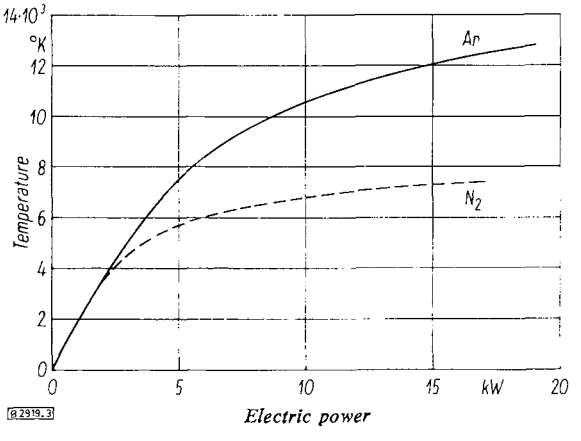


Fig. 3. Mean temperature of Ar and N_2 plasma jets as a function of the electric power of generator (after *Marchandise* [8]); gas throughput = 15 Nl/min.

3. Technology of the Arc Plasma

3.1. Technique of Production and Stabilization of Plasma Arcs

The principle of the production of plasma arcs is based on a development of the low-current carbon arc, which was known in the 19th century, and which has a column temperature of about 5000 to 6000 °C. To obtain higher arc column temperatures the current density must be increased, but the main result of an increase in the current intensity for an unconfined arc is an increase in the column volume and in the area of the anode focus. A decisive advance was achieved in 1922 by *Gerdien* and *Lotz*[9], who constricted a carbon arc to a diameter of a few millimeters by means of a water vortex; it was possible in this way to increase the current density to 10000 A/cm². The highest known arc temperature of somewhat more than 50000 °K was measured in 1951 by *Burhorn, Maecker*, and *Peters*[10] in a steam-stabilized high-current arc of this type at a current intensity of 1500 A. Though other steam-stabilized plasma jet generators have recently been constructed[11,12], this arrangement is not used in industry.

The methods used to stabilize and constrict the arc in the equipment in current use are as follows:

(a) Tangential injection of gas so that the arc becomes enclosed in a rotationally symmetrical vortex of gas (vortex or aerodynamic stabilization).

(b) Surrounding the arc with a water-cooled metal ring, which may also serve as the anode (wall stabilization).

(c) Action of a magnetic field produced either externally or inductively by the action of the arc itself (magnetic stabilization).

The constriction produced by a gas vortex or a metal ring is known as the "thermal pinch effect", and is based on the fact that the colder outer layer of gas acts as an insulator because of its low thermal and electrical conductivity, and so causes contraction of the arc. The effect produced by a magnetic field is known as the "magnetic pinch effect"; this again acts in the radial direction of the arc.

3.2. Common Types of Plasma Generators

In most modern plasma generators the arc is constricted and stabilized by a combination of the three methods described. Figure 4 shows a section through a plasma jet generator used at Knapsack AG. The arc is struck between a rod cathode, which generally consists of tungsten (+2% of thorium to reduce the work function of the electrons) or graphite, and an encircling funnel-shaped, water-cooled copper nozzle that acts as the anode. The gas, which is injected tangentially or even axially above the cathode, passes through the nozzle at a high velocity and absorbs most of the energy of the arc; while it also prevents premature striking of the arc at sporadic points on the inner wall of the nozzle. The arc can also be stabilized by an external magnet coil. The plasma jet produced by devices of this design can reach velocities ranging from subsonic to several times the speed

[7] *K. S. Drellishak, C. F. Knopp*, and *A. B. Cambel*, Phys. Fluids *6*, No. 9, p. 1280 (1963).

[8] *H. Marchandise*, Le chalumeau a plasma et ses applications, Euratom, Accord de Cooperation Euratom/Etats Unis et Programme Orgel, Travaux effectues dans le cadre du contrat Euratom/USA AT (04-3) 250 PA, No. 038, Eur 2439f, Brussels, June 1965.

[9] *H. Gerdien* and *A. Lotz*, Wiss. Veröff. Siemens-Konz. *2*, 489 (1922).

[10] *F. Burhorn, H. Maecker*, and *Th. Peters*, Z. Physik *131*, 28 (1951).

[11] *K. Jurczyk* and *G. Henzel*, DBP 954816 (1956).

[12] *A. B. Osborn*, J. Sci. Instruments *36*, 317 (1959).

of sound, depending on the diameter of the nozzle drilling; the temperatures at the core of the plasma jet can range from 8000 to 30000 °K. The temperature gradient in plasma jets is very steep (Fig. 5).

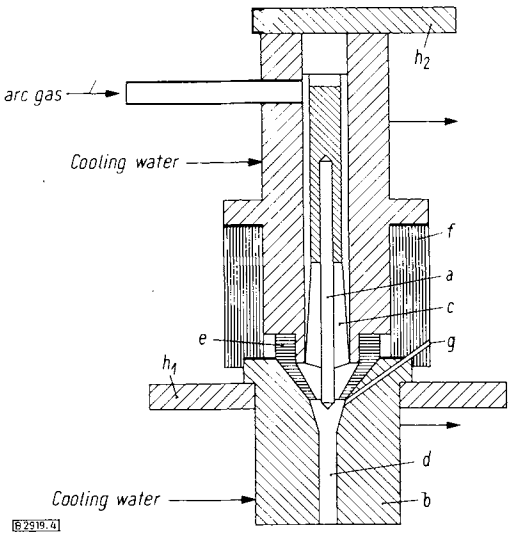


Fig. 4. Direct current plasma jet generator (Knapsack AG, Knapsack). a) Tungsten cathode, b) copper anode, c) brass clamp, d) nozzle drilling, e) ceramic body, f) insulator, g) drilling, h_1) cable terminal (+), h_2) cable terminal (−).

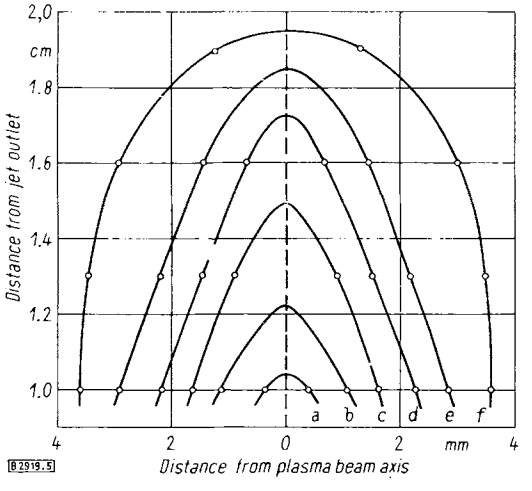


Fig. 5. Isotherms in a N_2 plasma jet (measured spectroscopically, after *Jahn* [13]).
Temperature [°K]: a) 11500, b) 11000, c) 10500, d) 10000, e) 9500, f) 9000.

Plasma generators of this design operate at voltages between 25 and 150 V, depending on the gases used. The power can be up to 100 kW; higher current densities lead to excessively strong heating of the electrodes. The thermoelectric efficiency can reach a maximum of 85 %, but is usually lower. Only argon, hydrogen, and nitrogen (and also helium in the USA) are normally used for operation of the plasma jet generators, since oxidizing gases and gases containing carbon very quickly destroy the electrodes. Corrosive reactants are introduced into the plasma jet and mixed with it underneath the anode. The plasma gas thus acts as a heat-transfer medium, though it may also be a reactant.

[13] *R. E. Jahn*, Brit. J. Appl. Physics *14*, 585 (1963).

Devices have recently been developed to allow the direct introduction of corrosive gases such as oxygen or halogens into the arc space. The normal tungsten cathode may be protected by a separate stream of inert gas or by very intensive cooling [14], or may be replaced by a zirconium cathode [15].

A plasma jet generator developed by the Westinghouse Electric Corp., Pittsburgh, Pa./USA [16, 17], in which magnetic stabilization and wall stabilization are combined, allows power consumptions of up to 20 MW and permits the direct heating of oxidizing and reducing gases (Fig. 6). A very strong external magnetic field causes the arc, which burns between two annular water-cooled copper electrodes, to rotate at a speed of about 60000 rpm; the current density can be increased in this way to 1000 A/cm². The plasma is then constricted by a water-cooled copper nozzle. This high-current arc heater can be operated either with direct current or with single-phase or multiphase alternating current.

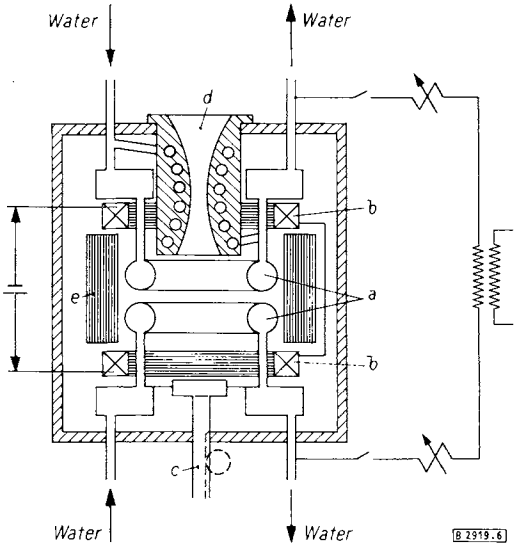


Fig. 6. Westinghouse electric-arc heater.
a) Copper electrodes, b) Magnet coils, c) Igniting device, d) water-cooled nozzle, e) heat shield.

Interest in alternating current plasma devices has recently grown because of the relatively high cost of rectifiers [18–20]. One unit of this type is the three-phase arc heater developed by Knapsack AG, Knapsack [5] for the synthesis of acetylene by the hydrogen arc pyrolysis process, which has graphite electrodes and a maximum power of 10 MW.

[14] *J. Browning*, US Pat. 3027446 (1962).

[15] *M. H. Weatherly* and *J. E. Anderson*, Electrochem. Technol. *3*, 80 (1965).

[16] *D. A. Maniera*, *P. F. Kienast*, and *C. Hirayama*, Westinghouse Engineer *26*, No. 3. p. 67 (1966).

[17] *C. Hirayama* and *D. A. Maniero*, Preprint Fuel Div., American Chemical Society, Pittsburgh, April 1966, Vol. *10*, No. 1, p. 123.

[18] *R. R. John* and *W. L. Bade*, J. Amer. Rocket Soc. *31*, 4 (1961).

[19] Materials Advisory Board Report No. MAB-167-M, Div. Eng. Ind. Res., National Research Council, Washington 1960.

[20] *W. K. Roots* and *A. H. Kadhim*, Elektrowärme int. *27*, p. 364 (1969).

Aerodynamically stabilized high-voltage plasma generators are particularly suitable for reactions with corrosive gases. *Schönherr*[21] used this principle in 1909 for the construction of an arc furnace for the production of acetylene; in this furnace, an arc 6 m long was produced between a water-cooled pot anode and a tube cathode at 4000 V and 100 A. The 8 MW arc heater used by the Chemische Werke Hüls AG, Marl, also for the production of acetylene, operates by the same principle. Aerodynamically stabilized plasma generators have recently been developed by *Thorpe*[22], *Eschenbach et al.*[23,24] (Linde Co., New York, USA), and *Browning et al*[25] (Thermal Dynamics, Lebanon, N.H./USA). Devices of this type operate in the range of 5–10 MW at voltages of 5000 to 10000 V. The enthalpy capacity is about 8000 to 11000 kcal/kg. An efficiency of 75% can be achieved.

A wall-stabilized version of the normal direct current plasma generator is the "constricted arc heater", which was first described by *Maecker*[26,27]. The cathode and the anode are separated by a series of water-cooled, mutually insulated copper rings, as shown schematically in Figure 7. Devices of this type give better transfer of the electrical energy to the arc gas than other plasma jet generators with Joule heating. Investigations and developments along this line have recently been carried out *e.g.* by *Morris et al.*[29], *Shepard et al.*[30] (NASA), and *Marlotte et al.*[31].

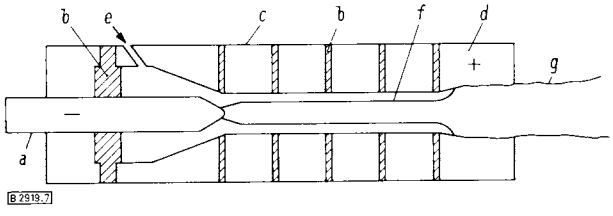


Fig. 7. Schematic cross section through a constricted arc generator (after *John* [28], cited in [65]).
a) cathode, b) insulating rings, c) water-cooled copper rings, d) anode, e) gas inlet, f) constricted arc, g) plasma jet.

A generator of this type developed by NASA, with a power of 2 MW (approx. 1500 V, 1500 A), produces *e.g.* a plasma gas with an enthalpy of about 28000 kcal/kg at pressures of 1 to 5 atm[32].

Another arrangement for the production of plasma jets was first described by *Sheer*[33,34], who used a porous, gas-cooled graphite anode instead of a water-cooled copper anode. This system, which is known as "transpiration cooling", can give an efficiency of 90%[35–40].

The plasma generators described so far produce an indirect or "non-transferred" plasma jet. If a copper or graphite crucible is situated under the copper nozzle anode of a plasma gun and connected in parallel with the anode, the resulting elongated plasma jet allows reactions with solids to be carried out directly in the crucible[22]. This arrangement is referred to as a direct or "transferred" plasma jet.

Reactions with solid reactants are often carried out with the aid of the high intensity arc; according to a comparative study by *Hall*[41] (US Naval Research Laboratory), this is much more suitable for the purpose than the conventional plasma jet. An arc of this type is produced by using relatively thin positive carbons to increase the anode current of a carbon arc to such a degree that the anode material evaporates. A long, brightly glowing jet of vapor leaves the face of the anode with a velocity of 10^3 to 10^4 cm/s and a temperature of up to 10000 °K (Fig. 8). Whereas all low-current arcs have a falling characteristic, the current intensity increases with the voltage in the high-intensity arc. 70 to 90% of the energy supplied is transformed at the anode, and since only a small portion can be dissipated by radiation or conduction through the uncooled anode, most of the energy is taken up by the plasma jet. Solids that are to react may be used in mixtures with carbon as anodes. Hollow anodes may also be used for the introduction of solid reactants. The phenomenon of the evaporating-anode high-intensity arc was discovered by *Beck* in 1910[42], and this type of electrical

[21] *O. Schönherr*, Elektrotechn. Z. *30*, 365 (1909).

[22] *M. L. Thorpe*, Res. Develop. Mag. *11*, 1 (1960).

[23] *R. C. Eschenbach*, Development of a Stable High Power High Pressure Arc Heater for a Hypersonic Tunnel, WADD-TR-61-100, July 1961.

[24] *R. J. Sarlitto* and *R. C. Eschenbach et al.*, Development of High Enthalpy, High Power Arc Air Heaters, Tech. Doc. Rep. RTD-TDR-63-4055, Feb. 1964, Speedway Research Lab., Indianapolis, Ind./USA.

[25] *J. A. Browning* and *J. W. Poole*, Arc Gas Heaters, Present and Future, AGARD Spec. Meet., Belg., Sept. 1964, AGARDograph No. 84, p. 323.

[26] *H. Maecker*, Z. Naturforsch. *11a*, 457 (1956).

[27] *H. Maecker*, Z. Physik *157*, 1 (1959); *158*, 392 (1960).

[28] *R. R. John et al.*, Theoretical and Experimental Investigation of Arc Plasma-Generation Technology, Aeronautical Systems Division, TDR 62-729, I (1962).

[29] *J. Morris, G. Back*, and *J. Yos*, Research on Radiation from Arc Heated Plasmas, AVCO RAD TR-64-10-1963.

[30] *H. Stine, V. R. Watson*, and *C. E. Shephard*, Effect of Axial Flow on the Behavior of the Wall Constricted Arc, AGARD Spec. Meet., Belg., Sept. 1964, AGARDograph No. 84, p. 451.

[31] *G. L. Marlotte, R. L. Harder*, and *R. W. Prichard*, The Radiating Arc Column, AGARD Spec. Meet., Belg., Sept. 1964, AGARDograph No. 84, p. 633.

[32] *R. R. John*, in: The Application of Plasmas to Chemical Processing (Editors: *R. F. Baddour* and *R. S. Timmins*), MIT Press, Cambridge (Mass.), London 1967, p. 18.

[33] *C. Sheer* and *S. Korman*, US Pat. 3009783 (1961, appl. 1959); US Pat. 3209193 (1965, appl. 1962).

[34] *C. Sheer*, US Pat. 3214623 (1965, appl. 1962).

[35] *E. R. G. Eckert, P. A. Schoeck*, and *E. R. F. Winter*, J. Heat Mass. Transfer *5*, 295 (1962).

[36] *R. B. Kinney, E. M. Sparrow*, and *E. R. F. Winter*, Trans. ASME Ser. *C 86*, 131 (1964).

[37] *C. Sheer, J. A. Cooney*, and *D. L. Rothacker*, AIAA Journal *2*, 2 (1964).

[38] *R. N. Jones*, US Dep. Comm. AD-610240 (1964).

[39] *E. R. G. Eckert* and *J. E. Anderson*, US Dep. Comm. AD-615903 (1965).

[40] *C. J. Cremers* and *E. R. G. Eckert*, AIAA Journal *3*, 1876 (1965).

[41] *J. M. Hall*, Synthesis of New High-Temperature Materials with the Plasma Jet, NRL Memorandum Report 1490, DDC-AD 431797.

[42] *H. Beck*, DRP 262913 (1910).

discharge was studied in detail by *Finkelnburg et al.*[43–46] and other workers[47–49].

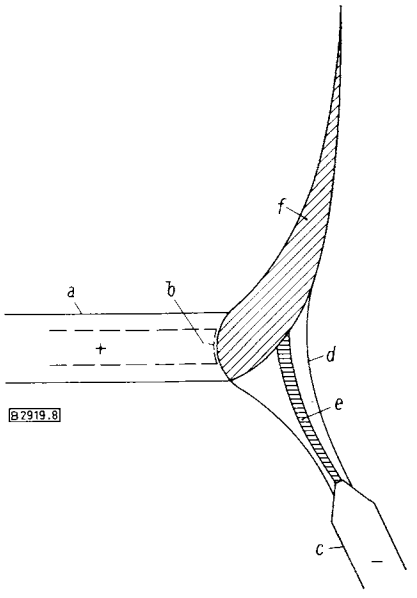


Fig. 8. Schematic drawing of a high-intensity carbon arc (after *Finkelnburg* [43]).
a) Anode, b) anode focus, c) cathode, d) arc, e) plasma jet, f) anode flame.

4. The Course of Chemical Reactions at Plasma Temperatures

4.1. General

Two steps must be distinguished in plasma-chemical processes:

(a) The introduction and mixing of the reactants with the plasma jet. The reactants are thus heated to plasma temperatures, and equilibration occurs in homogeneous gas reactions, despite the short residence times (10^{-3} to 10^{-5} s). The mixing and the energy exchange are very important to the course and the yield of plasma reactions[50–54].

(b) Quenching of the plasma jet to fix the reaction equilibria produced at high temperatures or to enable the kinetically favored recombination reactions to proceed. To be effective, the cooling rates must be of the order of 10^7 °K/s. Various quenching methods have been proposed. These include cooling the plasma jet with cooled surfaces or cold fingers, or injection of cooling liquids into the plasma jet[55,56]. The cooling liquids may also be reactants, such as liquid ammonia in the hydrazine synthesis[57] or liquid oxygen in the production of ozone[58]. Quenching processes using fluidized beds have also been devised[59–61].

4.2. Thermodynamics and Kinetics

The thermodynamic properties of gases can be calculated very accurately up to temperatures of several thousand degrees if the species existing in equilibrium are known. Where there are several reactants, however, the usual thermodynamic predictions of the equilibrium are of limited value because of the possible occurrence of unknown species. Equilibrium calculations can nevertheless be used to define the conditions for the maximum yield of the desired compound. The results of such calculations generally agree satisfactorily with the experimental observations, as is shown by detailed investigations on the systems C/H/N[62,63], C/N/F[64], and N/O[65]. Since the free enthalpy of reaction ΔG, according to the Gibbs-Helmholtz equation $\Delta G = \Delta H - T\Delta S$, is determined at very high temperatures by the entropy change ΔS, endothermic reactions resulting in an increase in entropy, which would not proceed at lower temperatures, can be carried out under plasma conditions. The products of such reactions can be obtained in high yields by quenching.

[43] *W. Finkelnburg*, The High Current Carbon Arc, FIAT Final Report 1052 (PB) 81644, US Dept. of Commerce, Washington/D.C. (1947).

[44] *W. Finkelnburg*, Hochstromkohlebogen, Springer-Verlag, Heidelberg 1948.

[45] *W. Finkelnburg*, J. Appl. Physics *20*, 468 (1949).

[46] *W. Finkelnburg* and *H. Maecker*, Elektrische Bögen und thermisches Plasma, in: Handbuch der Physik (Editor: *S. Flügge*), Vol. XXII, Gasentladungen II, Springer-Verlag, Berlin 1956, p. 254.

[47] *C. Sheer et al.*, Investigation of the High Intensity Arc Technique for Materials Testing, Rep. No. WADC-TR-58-142 (Nov. 1958).

[48] *C. Sheer, I. D. Holmgren* and *I. O. Gibson*, Characteristics of Arc Vaporized Particulates, Paper presented at Electrochemical Society Symposium, April 30, 1961 in Indianapolis, Ind./USA.

[49] *S. Korman*, High Intensity Arcs, Int. Sci. Techn., p. 90, June 1964.

[50] *M. P. Freeman* and *J. F. Skrivan*, A.I.Ch.E. Journal *8*, No. 4, p. 450 (1962).

[51] *J. Grey* and *P. F. Jacobs*, AIAA Journal *3*, 433 (1964).

[52] *J. Grey, M. P. Sherman, P. M. Williams*, and *D. B. Fradkin*, AIAA Journal *6*, 986 (1966).

[53] *D. L. Smith* and *S. W. Churchill*, Rep. 05607-1-T, Univ. Michigan, Dept. Chem. Metallurg. Eng. (1965).

[54] *R. Neubeck*, Über den Einfluß der Temperatur, Verweilzeit und Vermischung auf eine chemische Umsetzung im Lichtbogenplasma, Dissertation, TU Hannover 1969.

[55] *J. E. Anderson* and *L. K. Case*, Ind. Engng. Chem., Process Des. Dev. *1*, 161 (1962).

[56] *H. Gladisch*, Hydrocarbon Processing, Petrol. Refiner *41*, 159 (1962).

[57] *H. Harnisch, G. Heymer*, and *E. Schallus*, Chem.-Ing.-Techn. *35*, 7 (1963).

[58] *C. S. Stokes* and *L. A. Streng*, Ind. Engng. Chem., Prod. Res. Dev. *4*, 36 (1965).

[59] *W. M. Goldberger* and *J. H. Oxley*, A.I.Ch.E. Journal *9*, 778 (1963).

[60] *W. M. Goldberger* and *H. Nack*, Battelle techn. Rev. *13*, No. 11, p. 3 (1964).

[61] *J. O. Gibson* and *R. Weidman*, Brit. Chem. Engng. *8*, 300 (1963).

[62] *C. W. Marynowski, R. C. Phillips, J. R. Phillips*, and *N. K. Hiester*, Ind. Engng. Chem., Fundamentals *1*, 52 (1962).

[63] *B. R. Bronfin, M. P. Freeman, V. N. Distefano*, and *R. N. Hazlett*, 15th Chem. Inst. of Canad. Chem. Engng. Conf., Univ. Laval, Quebec City, Quebec 1965.

[64] *B. R. Bronfin* and *R. N. Hazlett*, 57th Ann. Meeting A.I.Ch.E., Boston (Mass.) 1964.

[65] *R. S. Timmins* and *P. R. Ammann*, in: The Application of Plasmas to Chemical Processing (Editors: *R. F. Baddour* and *R. S. Timmins*), MIT Press, Cambridge (Mass.), London 1967, p. 99.

If radicals that are unstable at lower temperatures are formed in the plasma, the recombination reactions that take place during quenching are kinetically controlled, since equilibration is impossible because of the short time available. The formation of thermodynamically favored condensed molecules during quenching is therefore much slower than the formation of the less stable gaseous products ("condensation barrier", *Reed*[66]). In this way, gaseous compounds can be obtained in concentrations much higher than the equilibrium concentrations calculated for room temperature.

The following reactions and systems are thus possible in plasma chemistry:

(a) Endothermic or weakly exothermic reactions whose products are stabilized at high temperatures by an increase in entropy, but are metastable at room temperature and can be obtained by rapid cooling (*e.g.* C_2H_2, NO, HCN, C_2N_2).

(b) Systems in which radicals that are normally unstable are formed at high temperatures, and recombine (on kinetic grounds) to form new compounds on quenching (*e.g.* the C/H/F system).

(c) Reactions that are thermodynamically favored at normal and high temperatures, but which require high temperatures to reach a satisfactory rate (*e.g.* the preparation of boron nitride).

Systems of types (a) and (b) may be regarded as promising for the discovery of new reactions and substances with the aid of plasma technology.

The use of plasma processes in industry is of interest only if the reaction step is particularly difficult and expensive in relation to the separation and purification steps and if the product is very valuable, *i.e.* if it has a value at least of the order of several DM/kg[67].

5. Inorganic Reactions in the Plasma Jet

5.1. Preparation of NO, HCN, C_2N_2, and N_2H_4

The problem of the direct fixation of atmospheric nitrogen with the aid of the arc process has again been extensively studied in recent years. The reasons for the renewed interest are the great importance of nitrogen compounds in the chemical industry, the favorable thermodynamics of the formation of the endothermic compounds NO, HCN, and C_2N_2 at high temperatures, and the fact that these compounds consist of small molecules having fairly simple structures. The fixation of atmospheric nitrogen with the aid of arc processes has been discussed in detail by *Timmins* and *Ammann*[65].

[66] *T. B. Reed*, Chemical Uses of Induction Plasmas, 57th Ann. Meeting, A.I.Ch.E., Boston (Mass.) Dec. 1964, publ. in: The Application of Plasmas to Chemical Processing, MIT Press, Cambridge (Mass.), London 1967, p. 32.

[67] *R. F. Baddour* and *R. S. Timmins*, in: Application of Plasmas to Chemical Processing, MIT Press, Cambridge (Mass.), London 1967, p. 12.

5.1.1. Nitrogen Monoxide

Several equilibrium calculations for the N/O system have already been published. According to these calculations, the maximum equilibrium concentration of NO at 1 atm is 5.2% at 3500 °K[65], while that at 10 to 12 atm is 8.2% between 4000 and 4500 °K[68]. *Philipps* and *Ferguson*[69] have examined important factors in the production of NO (and C_2H_2) in the plasma jet.

The maximum NO concentration obtained in the industrial arc process around the turn of the century (*Birkeland* and *Eyde*, *etc.*) was 2%. *Stokes* and *Knipe*[70] obtained an average yield of 2% (based on O_2) by injection of O_2 into a nitrogen plasma and quenching to −80 °C (laboratory scale). A similar result was obtained by *Grosse et al.*[71,72].

Using a constricted arc heater with a very small gas exit cross section, which ensures a very high quenching rate, *Timmins* and *Ammann*[65,73] were able to increase the NO concentration in the exhaust gas to 6–7%. The authors generally consider it possible to reach an NO concentration of 5% by heating air in the arc to an optimum temperature of 3500 °K, followed by very rapid quenching. With an electrothermal efficiency of 65%, the power consumption would be about 44 kWh/kg of NO, and the cost of power would thus be many times that for the production of NH_3[65]. Recent Russian investigations show that industrially acceptable NO concentrations can be obtained by reaction of an N_2 plasma jet with H_2O or superheated steam, or by injection of an excess of O_2 into the N_2 plasma at 3000 to 4000 °K, followed by quenching. Calculations have shown that NO can be produced more cheaply in a plasma jet at 3100 to 3200 °K and 20 to 30 atm than by the combustion of NH_3. Experiments at 5 to 10 atm have been reported, though no yields are indicated[74].

Kozlov et al.[75] used a 40 kW plasmatron and obtained NO concentrations of up to 12% by blowing H_2O or steam into an N_2 plasma. The dependence of the NO yield on the N_2/H_2O ratio and on the flow rate were also investigated.

[68] *S. N. Ganz*, *A. P. Melnik*, *L. S. Polak*, *V. S. Shchipachev*, and *P. A. Yamnov*, Khim.-Tekhnol. Respub. Mezhvedom. Nauch-Tekh. Sb *1967*, No. 7, p. 26.

[69] *R. C. Phillips* and *F. A. Ferguson*, in: Proceedings of an International Symposium on High Temperature Technology, McGraw Hill, New York 1960, p. 192.

[70] *C. S. Stokes* and *W. W. Knipe*, Ind. Engng. Chem. *52*, 287 (1960).

[71] *A. W. Grosse*, *H. W. Leutner*, and *C. S. Stokes*, Plasma Jet Chemistry, First Annual Report under ONR Contract Nonr 3085 (02), The Research Institute of Temple University, Philadelphia, Pa./USA 1961.

[72] *A. V. Grosse*, *C. S. Stokes*, *J. A. Cahill*, and *J. J. Correa*, US Dept. Comm., Office Tech. Serv. AD 418483 (1963).

[73] *R. S. Timmins* and *P. R. Ammann*, Chemical Reactions in a Constricted Arc. National Meeting of A.I.Ch.E., Boston, Mass./USA, Dec. 1964.

[74] *L. S. Polak* and *V. S. Shchipachev*, Kinetika i. Termodinam. Chim. Reaktsii v Nizkotemperaturnoi Plazme, Akad. Nauk SSR, Inst. Neftekhim. Sinteza 1965, p. 151.

[75] *G. I. Kozlov*, *G. N. Khudyakov*, and *Yu. N. Kobzev*, Chim. Vys. Energ. *1*, 495 (1967).

According to reports by other Russian authors, the maximum NO yield obtained by injection of air into an N_2 plasma at atmospheric pressure is only 3.6% [76]. *Kozlov et al.* have patented the production of NO by injection of superheated steam into an N_2 plasma at 6000 °K [77].

5.1.2. Hydrocyanic Acid

Various processes for the production of HCN in the plasma arc have been tried on the semi-industrial scale. The starting materials are H_2, N_2, NH_3, and C or CH_4. Equilibrium calculations carried out by *Marynowski et al.* (Stanford Research Institute) [62] for the system C/H/N show that the maximum equlibrium concentration of HCN occurs at 3000 °K. *Freeman et al.* (American Cyanamid Co., New York) [50, 78–80] have investigated the production of HCN by heating an N_2/CH_4 mixture in a 24 kW direct current plasma jet. They obtained a yield of 0.115 mole of HCN/mole of N_2 at a power consumption of 68 kWh/kg of HCN. *Stokes, Leutner et al.* (Research Institute of Temple University) [71, 81, 82] carried out a series of investigations. *Leutner* [82] reported the investigation of four reactions for the production of HCN: 1) from the elements in accordance with the equation $2C + H_2 + N_2 \rightarrow 2HCN$ using a consumable graphite cathode as the source of carbon; 2) from C and NH_3 (again with a graphite cathode); 3) from CH_4 and N_2; and 4) from CH_4 and NH_3.

A conversion of more than 50% (based on the carbon introduced) was achieved; the main by-product was C_2H_2. The highest yields were obtained with the elements as the starting materials. The most important parameter in all the experiments was the cooling rate.

5.1.3. Cyanogen

According to calculations by Russian authors [83], the maximum equilibrium concentration of CN occurs at about 4000 °K. They claim to have obtained a conversion of about 60% in their experiments on the synthesis of C_2N_2 from the elements. The power consumption was 0.48 kWh/mole of C_2N_2.

Suzuki et al. [84] studied the formation of C_2N_2 from coal gas, natural gas, or propane and nitrogen in an arc between carbon and tungsten electrodes. However, the yields were small. *Stokes* and *Knipe* [70] prepared C_2N_2 by injection of fluidized carbon powder into an N_2 plasma; the conversion (based on carbon) was 2%. Conversions of up to 15% (based on C) were obtained by the use of a plasma reactor with a graphite cathode and N_2 or an N_2/Ar mixture as the plasma gas [71, 86]. The problem of using vaporizing graphite electrodes as the source of carbon (high-intensity arc) was examined in detail by *Blanchet* and *Baddour* [87] and by *Ammann et al.* [88].

5.1.4. Hydrazine

Though the formation of N_2H_4, both from the elements and from NH_3, is endothermic, it is associated with a decrease in entropy, unlike the formation of the other nitrogen compounds discussed. Hydrazine formation may therefore be expected only *via* free radicals. The yields in the plasma process are correspondingly low. In the direct reaction of H_2 with N_2, N_2H_4 is formed only in traces [71]. According to *Harnisch, Heymer,* and *Schallus* [57] the synthesis proceeds in a yield of about 0.5% (based on the NH_3 throughput) on injection of liquid NH_3 into an N_2 or Ar plasma. *Neubeck* [54] obtained a yield of only 0.02% at a power of about 4 kW in his investigations on the influence of various factors on the synthesis of N_2H_4.

5.2. Synthesis of Carbon-Fluorine and Nitrogen-Fluorine compounds

A comprehensive review on the preparation of fluorine compounds in a plasma has been published by *Bronfin* [89]. The article also contains detailed thermodynamic data on the systems C/F, N/F, and C/N/F as well as the corresponding references.

5.2.1. C–F Compounds

Numerous studies have been carried out on the preparation of C–F compounds in arcs, in most cases using a high-intensity arc. In this arrangement, the carbon evaporating from the graphite anode can take part in the reaction. The procedure used by

[76] *S. N. Ganz* and *A. P. Melnik*, Chim. Technol. Miner. Udobr. *1966*, p. 44.

[77] *G. V. Gulyaev, G. I. Kozlov, L. S. Polak, G. N. Khudyakov,* and *V. S. Shchipachev*, Russ. Pat. 208695 (Cl. C 01 b), Jan. 1, 1968, Appl. March 30, 1963.

[78] *H. M. Hulburt* and *M. P. Freeman*, Trans. New York Acad. Sci., Ser. II, *25*, No. 7, p. 770 (1963).

[79] *M. P. Freeman*, The Nature and Quantitative Determination of the Reactive Species in a Nitrogen Plasma Jet, 147th National Meeting of ACS, Vol. 8, No. 2 (1964).

[80] *M. P. Freeman*, Advances Chem. Ser. *1969*, No. 80, p. 406.

[81] *H. W. Leutner* and *C. S. Stokes*, Ind. Engng. Chem. *53*, 341 (1951).

[82] *H. W. Leutner*, Ind. Engng. Chem., Process Des. Dev. *2*, 315 (1966).

[83] *S. N. Ganz, Yu. I. Krasnokutskii,* and *L. A. Ashkinazi*, Ž. Prikl. Chim. (Leningrad) *42*, No. 4, p. 761 (1969).

[84] *M. Suzuki* and *S. Takahashi*, J. chem. Soc. Japan, Pure Chem. Sect. *77*, 594 (1956).

[85] *M. Suzuki* and *S. Takahashi*, J. chem. Soc. Japan, Pure Chem. Sect. *77*, 573 (1956).

[86] *H. W. Leutner*, Ind. Engng. Chem., Process Des. Dev. *1*, No. 3, p. 166 (1962).

[87] *J. L. Blanchet*, Reactions of Carbon Vapor with Hydrogen and with Methane in a High Intensity Arc, Sc. D. Thesis, Department of Chem. Engineering, MIT, Cambridge, Mass./USA, June 1963.

[88] *P. R. Ammann, R. F. Baddour, M. M. Johnson, T. W. Mix,* and *R. S. Timmins*, Chem. Engng. Progr. *60*, 52 (1964).

[89] *B. R. Bronfin*, in: The Application of Plasmas to Chemical Processing (Editors: *R. F. Baddour* and *R. S. Timmins*), MIT Press, Cambridge (Mass.), London 1967, p. 157.

Baddour and *Bronfin* [90,91] for the conversion of CF_4 into C_2F_4 in a carbon arc is representative of a whole series of fluorocarbon syntheses in a thermal plasma. The highest C_2F_4 concentration of 69 mole-% was obtained at 0.1 atm and 17 kW. The C_2F_4 yield decreased with rising pressure and increased with increasing electric power. The quenched gas contained only a small quantity of other fluorocarbons (C_2F_6, C_3F_8), the remainder being CF_4. *Denison et al.* [92] led CF_4 into a high-intensity arc at 75 torr and quenched the reaction gas with the aid of a fluidized carbon bed. They obtained a C_2F_4 concentration of 75 mole-%. PF_5, SF_6, or AsF_3 may be used instead of CF_4 as the fluorinating agent.

The preparation of C_2F_4 in the carbon arc is described in a number of patents. The Du Pont de Nemours Co., Inc., Wilmington, Del./USA has patented a furnace with a rotating arc, in which *e.g.* C_2F_4 can be prepared from CF_4 or PF_5 to give a concentration of 81 % in the quenched gas [93]. The principal product formed from CF_4, as also from higher fluorocarbons is C_2F_4 [94–96]; the same result is obtained when CF_4 is allowed to react with various hydrocarbons in the carbon arc [97]. The presence of hydrogen (*e.g.* as HF) leads to the formation of partly fluorinated hydrocarbons [98], whereas mixed chlorofluorocarbons are formed in the presence of chlorine [99, 100]. It is interesting to note that the principal product obtained on heating CF_2Cl_2 or $C_2F_4Cl_2$ is again C_2F_4 [100]. Further information may be found in the more detailed review by *Bronfin* [89].

5.2.2. N–F Compounds

Interest in the N/F system is evidently focused mainly on the compounds NF_3, N_2F_4, and N_2F_2. However, the concentration of the nitrogen fluorides formed is low in most arc syntheses. *Bronfin* and *Hazlett* [64] used a 20 kW N_2 plasma jet, into which CF_4 or SF_6 was injected as the fluorinating agent. The addition of CF_4 leads to a mixture of nitrogen fluorides and fluorocarbons, with NF_3 as the main product; only NF_3 was formed on introduction of SF_6. However, the conversion of nitrogen into nitrogen fluorides was only 1 mole-% in both cases. *Lipscomb* [101] obtained an NF_3 concentration of 1.7 to 2.5 mole-% in the exhaust gas in the reaction of CF_4 with NO in a 2 kW low-current carbon arc at about 50 torr. Other syntheses in the C/N/F system with a carbon arc have been carried out by *Lipscomb* and *Smith* [102] and by *Farlow* [103].

5.3. Other Gas/Gas and Gas/Liquid Reactions

5.3.1. Carbon Disulfide

Plasmachem. Inc. (Newport Beach, Calif./USA) proposed the preparation of CS_2 from H_2S and CH_4 or natural gas by a plasma-chemical process (presumably in the plasma arc). The cost of construction of a plant having a capacity of 50000 t/year is claimed to be only one half to two thirds of the cost of a plant based on the catalytic process. No further details were published [104].

5.3.2. Ozone

Stokes and *Streng* [58] described a new method for the synthesis of O_3. Liquid oxygen is injected into a helium plasma, and the O_3 formed is quenched in excess O_2. The conversion is low; the production rate is 0.5 kg/h at a power of 10 kW. *Grosse* and *Stokes* have patented this process [105].

5.3.3. Oxygen from Carbon Dioxide

Experiments have recently been carried out on the cleavage of CO_2 into CO and O_2 in a plasma jet [106, 107]. However, the O_2 yield was barely 3 % at a burner power of 6 kW.

5.4. Nitrides, Cyanides, and Carbides

5.4.1. Nitrides and Cyanides

Harnisch and *Heymer* [57, 108, 109] have produced finely divided nitrides (particle size <0.1 μm) of the elements boron, aluminum, silicon, titanium, and zirconium in yields of 90 to almost 100 % by reaction of the vaporized halides of the elements with NH_3 in

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[91] *R. F. Baddour* and *B. R. Bronfin*, Ind. Engng. Chem., Process Des. Dev. *4*, 162 (1965).

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[93] *R. E. Burk*, E.I. Du Pont de Nemours Co, Inc., Wilmington, Del./USA, DBP 1038535, US Prior. (June 15, 1955).

[94] *M. W. Farlow*, US Pat. 2081245 (1963).

[95] *M. W. Farlow*, US Pat. 2709182 (1955).

[96] *M. W. Farlow* and *E. L. Muetterties*, US Pat. 2709190 (1955).

[97] *M. W. Farlow* and *E. L. Muetterties*, US Pat. 2981761 (1961).

[98] *M. W. Farlow* and *R. M. Joyce*, US Pat. 2709183 (1955).

[99] *C. S. Cleaver*, *M. Crest*, and *M. W. Farlow*, US Pat. 2757212 (1956).

[100] *M. W. Farlow* and *E. L. Muetterties*, US Pat. 2725410 (1955).

[101] *R. D. Lipscomb*, US Pat. 3043662 (1962).

[102] *R. D. Lipscomb* and *W. C. Smith*, US Pat. 3008798 (1961).

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[104] Chem. Ind. *20*, No. 1, p. 19 (1968).

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[106] *F. P. Rudek* and *H. Warner*, Research on Electrical Arc Reduction of Carbon Dioxide, Aerospace Medical Research Lab. U.S.A.F., Rep. AMRL-TDR-64-62 (1964).

[107] *J. L. Blanchet*, *J. R. Parent*, and *H. C. Lavallee*, Canad. J. Chem. Engng. *47*, p. 160, April (1969).

[108] *G. Heymer* and *H. Harnisch* (Knapsack AG, Knapsack), DBP 1160831 (1964).

[109] *G. Heymer* and *H. Harnisch* (Knapsack AG, Knapsack), DBP 1193485 (1966).

a direct current H_2 or N_2 plasma jet. A similar process for the production of ultrafine nitrides of refractory metals has been published by *Neuenschwander* [110] (Ciba AG, Basel), who prepared *e.g.* TaN from the chloride in an H_2/N_2 plasma jet. Other methods start with metal powders. However, these methods are very unsatisfactory because of the very short times spent by the reactants in the plasma jet (of the order of 10^{-3} to 10^{-5} s), the small size of the hot zone, the steep temperature gradient, and the difficulties presented by the introduction of solids into the plasma jet. *Stokes* and *Knipe* [70] prepared TiN and Mg_3N_2 in yields of 30 to 40% by blowing the metal powder into a nitrogen plasma. *Stokes* [111] reported an improvement of the process for the production of TiN, and also described the preparation of tungsten nitride WN. Fine BN was prepared by *Bosch* and *De Vynck* [112] by introduction of powdered boron into an N_2/NH_3 plasma jet. No information on yields was given. Nitrides and oxide nitrides of metals have been obtained from the oxides in an Ar/N_2 plasma jet [113].

The use of a "transferred" plasma jet for the preparation of the nitrides of Ta [114], Mo [115], W [116], Ti [117], Al [118], and Zr [119] from the metals and from the oxides [120–122] has been described in a series of Japanese papers. The starting materials were nitrated with a N_2 plasma jet in a water-cooled copper crucible or in a graphite crucible, which acted as a second anode. Physico-chemical and analytical data for these reactions have been reported [122]. The procedure appears to be of value only for laboratory investigations. The preparation of AlN, Si_3N_4, ZrN, TiN, and HfN is described in another Japanese study [123, 124], in which yields of more than 80% were obtained. No further details are known. *Winterhager* and *Hanusch* [125] recently examined the current methods for the production of TiN in direct current plasma jets. The dependence of the yield on various parameters was investigated. The production of metal cyanides from metal oxide and graphite powder or propane in a N_2 plasma jet has been investigated by *De Vynck* [126]. However, the yields were unsatisfactory.

5.4.2. Carbides

A process for the production of finely divided transition metal carbides has been described by *Neuenschwander* (Ciba AG, Basel) [110, 127]. The carbides of Ta, Nb, and Ti were prepared in a hydrogen plasma with addition of CH_4. The products have particle sizes of 0.01 to 0.1 μm.

The same is true of the reactions with solid starting materials as in the case of the nitrides. *Correa, Stokes et al.* [128–130] obtained tantalum carbides by treatment of tantalum powder or Ta_2O_5 with CH_4 in an H_2 plasma jet. The yields of TaC and Ta_2C were 46 and 86% respectively. It was found in a similar study that the metal powder is a better starting material than the trioxide for the preparation of tungsten carbides. The conversion in this case is about 50%.

Small quantities of magnesium carbides and Al_4C_3 were formed on reaction of Mg or MgO and of Al_2O_3 with propane in an Ar/H_2 plasma jet [126]. B_4C is obtained on introduction of boron powder into a H_2/Ar plasma and injection of a propane/butane mixture. The yield here was again low [112]. ZrC was prepared by reaction of zirconium powder or ZrO_2 with benzene vapor in an argon plasma [113, 131]. NbC has been obtained from a mixture of Nb_2O_5 and C in a copper crucible with the aid of a "transferred" plasma flame [132].

The reactions

$$MO + 3\,C \rightarrow MC + 2\,CO \quad (M = Ti, Si)$$

$$M_2O_5 + 7\,C \rightarrow 2\,MC + 5\,CO \quad (M = V, Ta)$$

were evidently also carried out and investigated in a "transferred" plasma flame [133].

The high-intensity arc is much more suitable than the plasma jet for the production of carbides from solid

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[113] *F. Leprince-Ringuet*, *A. M. Lojus*, and *R. Collongues*, C. R. *258*, No. 1, p. 221 (1964).

[114] *O. Matsumoto* and *Y. Hayakawa*, Denki Kagaku *34*, 775 (1966).

[115] *O. Matsumoto*, Denki Kagaku *34*, 872 (1966).

[116] *O. Matsumoto*, Denki Kagaku *35*, 488 (1967).

[117] *O. Matsumoto*, Denki Kagaku *35*, 625 (1967).

[118] *O. Matsumoto*, Denki Kagaku *35*, 697 (1967).

[119] *O. Matsumoto*, Denki Kagaku *35*, 870 (1967).

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[124] *Y. Hayashi*, *K. Okada*, and *S. Koide*, Yogyo Kyokai Zasshi (J. Jap. ceram. Assoc.) *76*, (877), 307 (1968).

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[132] *R. Ishizuka*, *K. Akashi*, and *I. Egami*, Seisan-Kenkyn *20*, No. 11, p. 572 (1968).

[133] *H. Triche* and *C. Butti*, Method. Phys. Anal. *4*, No. 4, p. 379 (1968).

starting materials[41]. *Korman, Sheer et al.*[134] (Vitro Laboratories, West Orange, N.J./USA) have made a detailed study of the use of the high-intensity arc for chemical reactions involving solid starting materials; the production of uranium carbide has already been carried out on the 20 t scale. In this process, UO_2 and carbon are compressed into electrically conducting rods, sintered, and used in this form as consumable anodes. The uranium carbide is obtained in the form of spherical fused particles[135].

5.5. Preparation of Metal Oxides

Many attempts have been made to prepare finely divided metal oxides by oxidation of metal powders or metal chlorides with the aid of plasma techniques[136]. Attempts of this nature are usually made in an induction plasma, since corrosion problems can arise when an electrode plasma is used. However, devices have been developed to allow the introduction even of oxygen (or halogens) into the plasma jet without attack of the electrodes[137,138].

Processes and equipment for the production of finely divided metal and metalloid oxides, particularly TiO_2 as a white pigment, ZrO_2, SiO_2, Al_2O_3, Fe_2O_3, and antimony oxide, by oxidation of the corresponding halides, especially the chlorides, have been patented by a number of companies[139–144]. The Farbenfabriken Bayer AG[145] has proposed that at least one of the two preheated reactants be brought to a sufficiently high temperature by a high-voltage discharge between two electrodes. According to another suggestion, an oxidizing gas is heated in a high-intensity arc, and is then allowed to react with the metal chloride vapor. In this case the carbon electrodes should contain 20 to 70% of oxides, carbides, or halides of the corresponding metal as nucleating material[146].

The vaporization of coarse TiO_2 or SiO_2 in a plasma jet followed by condensation to form a fine powder has also been suggested[147,148].

Sheer and *Korman* have described a method for the production of finely divided SiO_2 by vaporization of SiO_2 from the anode of a high-intensity arc, followed by condensation[134].

5.6. Reductions

5.6.1. Reduction of Metal Oxides and Oxide Ores

TiO_2 is reduced to titanium in a plasma reactor in which the continuously introduced oxide is first melted. The finely divided liquid oxide droplets are reduced with a H_2 plasma jet to fine droplets of metal. The resulting titanium is reported to have a purity of 99.8%[149]. The production of tungsten powder by reduction of WO_3 in an Ar/H_2 plasma was studied by *Tsetkov et al.*[150], who also developed an industrial method for the production of ultrafine powders with spherical particles. Metallic vanadium has been prepared by reduction of a $V_2O_3/CaCl_2$ melt with calcium vapor produced under the action of an argon plasma. The vanadium is removed from the liquid slag by centrifugation (Centre National de la Recherche Scientifique, Paris)[151].

Grosse, Stokes et al.[152] described the reduction of WO_3 (95% yield), Fe_2O_3 (100%), Ta_2O_5 (26%), and Al_2O_3 (2 to 5%) with a hydrogen plasma. It was not possible to reduce TiO_2 and ZrO_2 by this method. The Ciba AG, Basel, has patented a process[153] in which the oxides of Re, Mo, and W, as well as ammonium tungstate, are reduced to fine metal powders by introduction into a horizontal H_2 plasma jet. The dependence of the grain size of the metal powder on the experimental conditions for the reduction of oxides in a plasma jet has been investigated by *Panfilov* and *Tsetkov*[154].

The feasibility of the carbothermic reduction of metal oxides in the vapor phase with the aid of a high-

[134] *C. Sheer* and *S. Korman*, The High Intensity Arc in Process Chemistry, in: Arcs in Inert Atmospheres and Vacuum, Proc. Symp. Electrothermics and Metallurgy Division, Electrochemical Society, San Francisco, Calif./USA, 30. 4.–1. 5. 1956.

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[139] *K. Arkless* and *D. Cleaver* (British Titan Products Co., Ltd., London), DAS 1226082 (1966; Brit. Prior. 6. 2. 1962).

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[149] *W. J. McLaughlin* (Aerojet-General Corp., Claremont, Calif./USA), US Pat. 3429691 (1969).

[150] *Yu. V. Tsvetkov, S. S. Deinecka, D. M. Chizhikov, J. K. Tagirov*, and *J. Ya. Basieva*, Porosh. Met. Novoi Tech. *1968*, p. 143.

[151] *M. Foex* (Centre National de la Recherche Scientifique), US Pat. 3257196 (1966).

[152] *C. S. Stokes, J. A. Cahill, J. J. Correa*, and *A. V. Grosse*, US Dept. Comm., Clearinghouse Sci. Techn. Inform. AD 625591 (1964).

[153] Ciba AG, Basel, Austrian Pat. 263388 (1968; Swiss Prior. 1965).

[154] *S. A. Panfilov* and *Yu. V. Tsvetkov*, Met. Tsvet. Redk. Metal. Akad. Nauk SSSR, Inst. Met. *1967*, p. 128.

intensity arc has been studied by *Sheer* and *Korman* [134, 155, 156]. The principal problem in such a process is the prevention of the reoxidation of the metals by fast and efficient quenching.

Kusch [157] used hollow graphite anodes for his reduction experiments in the high-intensity arc, the metal oxide/carbon moldings being introduced through these anodes. The reaction products were deposited on cooled surfaces. The yields of metal (*e.g.* Fe, Al, Mg) were up to 80%.

The Union Carbide Co., New York, has patented the reduction of molten oxide ores over a liquid metal by an inert gas plasma to which *e.g.* CH_4 is added [158].

The reduction of iron ores by plasma techniques has been discussed by *Gilles* [159], who obtained degrees of reduction of 33 to 69% with a H_2 plasma jet at temperatures ranging from about 3000 to 5700 °K. This author assumed that the most important factor influencing the reduction process is the heat transfer. The reduction of molten iron ores with reducing gases heated by one or more plasma generators is described in two patents [160, 161]. The consumption of electrical power is reported to be 1110 kWh/t of crude iron.

5.6.2. Reduction of Halides

Finely divided, nonpyrophoric powders of the metals of groups IVb, Vb, and VIb and of the actinide metals can be obtained by introduction of the corresponding chlorides (or oxide chlorides), with Ar as a carrier gas, into a hydrogen plasma. An excess of 5–10 moles of H_2/mole of metal halide is necessary, and the yields obtained were around 90% [162].

A complicated process for the reduction of the halides of Ti, Zr, Nb, Ta, Mo, and W is described in two patents granted to the Rio Algom Mines Ltd., Toronto, Ontario/Canada [163]. The halides are introduced into a plasma jet together with liquid Na or powdered Mg as the reducing agent. Pure titanium is obtained in a yield of 80 to 90% from $TiCl_4$ and liquid Na.

WF_6 can be reduced to the metal with a H_2 plasma jet. The resulting powder has a specific surface area of between 3 and 35 m^2/g [164]. Powders of other refractory metals can be prepared in the same manner. The reduction of the halides of Be, B, Al, Si, Ti, Nb, Ta, Cr, Mo, and W in a hydrogen plasma is described in a patent by the Union Carbide Co., New York [165]; yields and the power consumption are also given.

The production of boron is described in a U.S. Atomic Energy Commission report [166]. BF_3 or BCl_3 was reduced in a H_2 arc plasma; the yields were 30 and 60% respectively. Silicon and titanium halides can be reduced in a similar manner to very pure metals [167].

A reduction of silicon and titanium halides that does not yield the metal is also possible. *Harnisch et al.* [57, 168] have prepared $TiCl_3$ by reaction of $TiCl_4$ in a H_2 plasma jet at temperatures between 2500 and 3000 °K followed by quenching at −120 °C. By maintaining a molar ratio $H_2/TiCl_4 < 6$, it was possible to obtain almost pure $TiCl_3$. By reducing $SiCl_4$ under similar conditions, the same authors obtained a mixture of chlorosilanes from which the principal product, $SiHCl_3$, could be readily obtained by fractional distillation [57, 169]. Trichlorosilane is a very suitable starting material for the production of high-purity silicon. The power consumption is reported to be 4 kWh/kg of $SiHCl_3$.

5.7. Various Other Plasma Reactions

Korman and *Sheer* have devised further uses of the high-intensity arc. Thus, because of the very short reaction times in the vapor phase, complex oxides can be decomposed into simpler oxides with no possibility of reformation of the original complexes [134]. The method has been successfully used for the decomposition of the manganese ore rhodonite ($MnSiO_3$); the condensate contained MnO and SiO_2 [170]. The same method has been suggested for the preparation of metals such as uranium, beryllium, and lithium.

This pyrolysis method has very recently been applied to iron titanates in the USSR and in Poland. With anodes containing 70% of ilmenite/30% of graphite and use of O_2 for arc operation, the oxides TiO_2,

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Fe_2O_3, Fe_3O_4, and SiO_2 were found in the condensate; the TiO_2 (90%) collected mainly in the reaction zone[171]. With N_2 as the arc gas, the main products were Fe, TiC, and CO together with TiN[172]. The decomposition of ilmenite in a thermal plasma has been examined in another Polish investigation[173]. $ZrSiO_4$ can also be decomposed into ZrO_2 and SiO_2 by this method[174].

Another use of carbon arc is for the vapor-phase halogenation of oxides[134]. On evaporation of an anode containing ore in an atmosphere of chlorine, the oxide is quantitatively converted into the chloride in accordance with the equation

$$MO + Cl_2 + C \rightarrow MCl_2 + CO$$

This method has been used by *Warren* and *Shimizu*[174], for the preparation of $NbCl_5$ from Nb_2O_5 and of $AlCl_3$ from Al_2O_3. *Orbach et al.*[175] have patented a process for the halogenation of BeO in a plasma burner with nonreacting electrodes. BeO is introduced into the N_2 plasma jet together with petroleum coke and Cl_2. The conversion is 62.6%.

The production of mixed oxides *e.g.* from ZrO_2 and Cr_2O_3[176] or from TiO_2 and other oxides[177] and the preparation of spinels[178] in plasma jets have also been described. *Papp*[179] studied the possibility of using plasma techniques for the production of phosphorus, mainly from the thermodynamic standpoint.

A combination of a fluidized bed reactor and a plasma jet has been developed by *Goldberger*[59,60,180], at the Battelle Institute. The fluidized bed may be used as a quenching device or as an inert heat store; however, if it consists of electrically conducting particles (*e.g.* carbon), it can also act as an "electrode" for the formation of the plasma arc. The preparation of phosphorus by reduction of $Ca_3(PO_4)_2$ with this arrangement has been investigated in detail; the thermal efficiency increased with the throughput and reached a maximum of 70%. CaC_2 has also been prepared by this method.

The synthesis of H_2S from the elements in a plasma jet has been reported by *Stokes* and *Cahill*[129]. H_2S was obtained in a yield of 37% (based on S) on introduction of sulfur powder into a He/H_2 plasma (electric power 7.75 kW).

Very recent Russian articles describe investigations on the possibility of thermal decomposition of phosphate ores in a plasma jet[181,182]. It is shown that insoluble P_2O_5 can be converted into citric acid-soluble P_2O_5 in a yield of 96.5% by treatment of a phosphate ore/SiO_2 mixture (30% SiO_2) in a plasma jet at 4130 °K. The power consumption found in the experiments was between 3150 and 6850 kWh/t of starting crude phosphate.

6. Closing Remarks

It can be seen from the large number of investigations described here that the plasma jet is a very interesting and valuable new aid for the research chemist. There is no doubt that some of the known plasma-chemical processes, and probably also some that have not yet been developed, will be used industrially in the future, though it cannot be said at present when this will be.

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Novel Ring Opening of Hydroxyphenylcyclobutenedione[1] [**]

By *Walter Ried* and *Günter Isenbruck*[*]

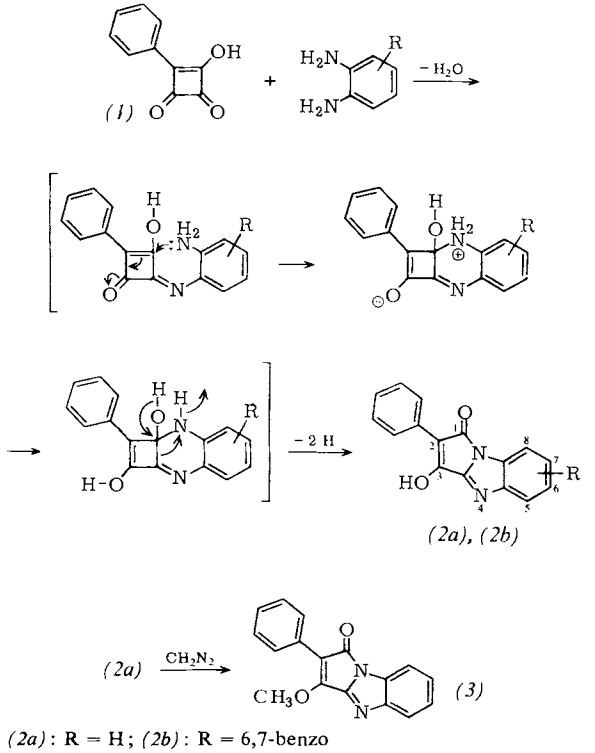
Dedicated to Professor H. Beyer on the occasion of his 65th birthday

3-Hydroxy-4-phenyl-3-cyclobutene-1,2-dione *(1)* reacts with primary aromatic amines to give 2-anilino-4-phenylcyclobutenediylium diolates [2], and with aliphatic amines to give ammonium salts which can be converted into the 2-amino-4-phenylcyclobutenediylium diolates[3].

Compound *(1)* reacts with aromatic 1,2-diamines with loss of H_2O and 2H to give a red crystalline substance[4], whose IR spectrum contains a carbonyl absorption at 1755 cm^{-1} indicative of a carbonyl group in a four or five membered ring. If *(2)* is assumed to have the structure given below, then methylation of *(2a)* with diazomethane must lead to formation of *(3)*.

The UV spectrum of *(3)* in CH_3OH shows absorption maxima at 229, 267, and 269, and a broad maximum at 323 nm ($\log \varepsilon = 4.07$) that is characteristic of pyrroloimidazole[5]. 2,3-Diphenylpyrrolo[1,2-*a*]benzimidazol-1-one, which is formed on condensation of diphenylmaleic anhydride and *o*-phenylenediamine[6], also shows a broad maximum at 325 nm ($\log \varepsilon = 3.88$) and a carbonyl absorption at 1755 cm^{-1}.

According to the spectra, elemental analysis, and molecular weight determination (262), compound *(2a)* can be formulated as 3-hydroxy-2-phenylpyrrolo[1,2-*a*]benzimidazol-1-one. Since hydroxyphenylmaleic anhydride does not react under the conditions used for the preparation of *(2)* it cannot be formed as intermediate. We suggest, therefore, the following reaction mechanism.



(2a): R = H; *(2b)*: R = 6,7-benzo

Experimental:

To a solution of *(1)* (5 mmoles, 870 mg) in glacial acetic acid (30 ml) is added with stirring a solution of the diamine (5–6 mmoles) in glacial acetic acid (20 ml) at room temperature. The solution turns deep red and gradually becomes cloudy. Precipitation is brought to completion by stirring for a few hours; the product is recrystallized from DMF/CH_3OH, yield 70–75 %.

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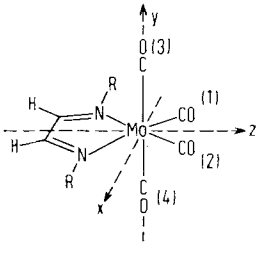
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Dependence of Solvatochromism on the Ground State in 1,4-Heterobutadienecarbonylmolybdenum Complexes

By *Heindirk tom Dieck* and *Ingo W. Renk*[*]

The color of solutions of *N,N'*-di-*tert*-butyl-1,4-diazabutadienetetracarbonylmolybdenum *(1)*, as well as of other 1,4-diazabutadienecarbonylmetal complexes[1], depends considerably on the polarity of the solvent (cf. Table)[2].

Strong solvatochromism is to be expected when the ground state of the dissolved complex is polar, *i.e.* when the polar solvent molecules exhibit a high degree of short range order. The excitation ought to be antiparallel to the ground-state dipole moment μ_G since a particularly strong destabilizing solvation then occurs in the excited state.



(1), R = $C(CH_3)_3$

In complexes of Type *(1)* with C_{2v} symmetry the z-axis and direction of μ_G are coincident; in C_{2v} both are totally symmetric. Electron excitations in $\pm z$ direction must have ground and excited states of the same symmetry since with the given symmetry of the z vector only the product of two identical representations of C_{2v} gives a totally symmetric integrand of the transition moment and thereby a permitted transition.

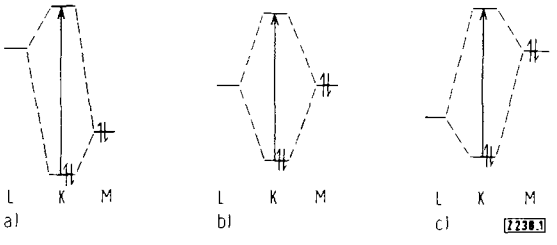
In *(1)* the occupied metal d-orbitals fall into the symmetry classes A_1, A_2, and B_2. The lowest unoccupied orbital is ψ_3 on the four-center π system which likewise has symmetry B_2.

In B_2, metal and ligand orbital also have the strongest overlapping which is of importance for the magnitude of the interaction term and the intensity of the electron excitation.

According to the values given in the Table, the longest wavelength transition of *(1)* with extinctions between 12000 (cyclohexane) and 5000 l $mole^{-1}$ cm^{-1} (dimethyl

sulfoxide) shows a solvatochromic effect, which can only occur by excitation from the metal to the four-center ligand — antiparallel to μ_G; the excitation can be considered as a metal-ligand charge transfer (CT), despite the interaction terms $\langle b_2/b_2 \rangle$ to be expected.

Electron spectroscopic measurements give no indication of the magnitude of this interaction or whether the solvatochromism occurs as a result of a stabilization of the ground state or of a destabilization of the excited state. In addition to ν_{CT} values, the Table contains the wave numbers of the four IR-active carbonyl frequencies. An unusually strong solvent dependence is found for the CO groups CO-1 and CO-2 situated *trans* to the diazabutadiene ligands (L), whereas in the case of CO-3 and CO-4 the changes lie within the error of measurement. This indicates, however, that considerable solvent-dependent polarization occurs in the ground state in the z direction [3]. As expected, the ν_{CT} and ν_{CO} values are linearly dependent quantities. Slight deviations from linearity are observed in the case of solvents such as chloroform and boron trifluoride-dibutyl ether, which interact particularly strongly with the carbonyl oxygen atoms [5].



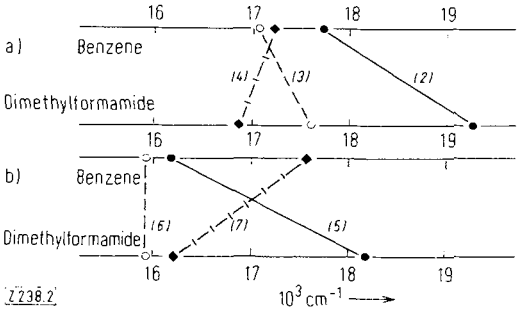
Scheme 1. L = ligand, K = complex M = metal.

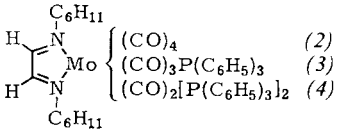
The invariance of $\nu_{CO-3,4}$ is interpreted as a good indication of the possible inductive (!) perturbation of the metal terms, *e.g.*, in the substitution of these carbonyl groups by phosphanes [5].

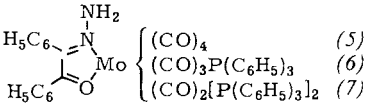
If, in accordance with Scheme 1a, the metal orbital is originally lower [6] than the ligand orbital, the coefficient of the former in the ground state is $> \sqrt{0.5}$, and the excitation will have metal→ligand CT character (Case 1). Correspondingly, the same negative solvatochromism will also occur as in *(1)*. Raising the metal orbital or lowering the ligand orbital reduces solvatochromism, which vanishes completely at energy balance; in this case the interaction term can be determined experimentally (Case 2): it is equal to half the excitation energy. If the metal orbital (Scheme 1c) is raised so as to be slightly higher than ψ_3, the complex ground state is predominantly a ligand state without μ_G changing its direction. Here, excitation occurs from the ligand to the metal, *i.e.* in the direction of μ_G; the solvatochromism is positive (Case 3).

In Scheme 2 the absorption maxima for two complex groups with increasingly destabilized metal d-electrons in two rather extreme solvents, benzene and dimethyl formamide (cf. Table), are outlined. Scheme (2a) contains the values for *N,N'*-dicyclohexyl-1,4-diazabutadienecarbonylmolybdenum complexes *(2)*, *(3)*, and *(4)* with four [4], three, and two CO groups and correspondingly none, one, or two triphenylphosphanes in place of CO-3 or CO-4 — (2b) shows the behavior of the analogous *N*-amino-2,3-diphenyl-1-oxa-4-azabutadiene complexes *(5)*, *(6)*, and *(7)* [5].

Compounds *(1)*, *(2)*, *(3)*, and *(5)* are examples of Case 1 and, therefore, according to their ground state configuration are metal(0) complexes insofar as assignment of oxidation numbers for metals in low valence states appears reasonable. In the case of *(6)*, the position of ν_m is found to be exactly the same in all common solvents [5]; this is a case of accidental degeneracy b_2/b_2. The interaction term, in this instance the stabilization by π back-donation, corresponds to $1/2\ \nu_m \approx 8000\ cm^{-1}$.







Scheme 2. Magnitude and direction of the solvatochromism in diaza- and oxaazabutadienecarbonylmolybdenum complexes.

Compounds *(4)* and *(7)* with positive solvatochromism correspond to Case 3 and are to be regarded as cation complexes of the metal.

Table. Solvent-dependence of the CT absorption and the CO frequencies (in cm^{-1}) of *(1)*.

Solvent	CT Absorption	CO-1 A_1	CO-2 B_1	CO-3 A_1	CO-4 B_2
Dimethyl sulfoxide	21120	1878	1828	2023	1908
Dimethylformamide	20960	1880	1832	2024	1908
Acetonitrile	20830	1883	1832	2024	1912
Acetone	20400	1887	1836	2024	1912
$(C_4H_9)_2O \cdot BF_3$	20200	1882	1832	2024	1912
Nitropropane	20190	1885	1835	2024	1912
Methanol	19880	1887	1838	2024	1913
Methylene chloride	19380	1886	1835	2026	1912
Dioxane	19230	1892	1842	2022	Sch
Chloroform	18930	1890	1838	2024	1915
Mesitylene	18590	1901	1848	2024	1910
Carbon tetrachloride	18020	1910	1855	2024	1915
Carbon disulfide	17950	(1913)	1860	2024	(1913)
Cyclohexane	17745	1914	1864	2024	1923

Thus, these complexes of 1,4-diazabutadienes and 1-oxa-4-azabutadienes are systems having a delocalized ground state, similar to many transition complexes of the four center system S—C—C—S [7]. Generally, there is no need for ascribing aromatic character to such five-membered chelate rings [4].

Substitution at any center of the ligand π system, by exchange of carbonyl groups for other ligands or by changing the metal, affords a suitable model which is explained quite well by an extended perturbation theory and is supported by ESR [8] and polarographic [5] experiments.

Procedures:

Stable tetracarbonyl compounds such as *(1)* can be prepared by heating of ligand and metal hexacarbonyl in benzene: Boiling a mixture of *N,N'*-di-*tert*-butyl-1,4-diazabutadiene [9] (1.5 g) and $MoCO_6$ (2.34 g) (9 moles of each) for 6 hours yields fine long needles (3.2 g, 94%; decomp. 217 °C) of the desired compound.

Less stable tetracarbonyl compounds such as *(5)* are obtained from bis(dialkylcyanamide)- or bis(triphenylphosphine oxide)tetracarbonylmolybdenum by substitution below room temperature [10].

Tricarbonyl compounds such as *(3)* or *(6)* can be prepared — if the tetracarbonyls are not sufficiently stable — by reaction of tris(acetonitrile)tricarbonylmolybdenum with equimolar quantities of $P(C_6H_5)_3$ and chelate ligand: A mixture of $(CH_3CN)_3Mo(CO)_3$ (0.76 g), $P(C_6H_5)_3$ (0.66 g), and benzilmonohydrazone (0.65 g) (2.5 mmoles of each) is stirred for 14 h at 18 °C; deep-blue soluble crystals of *(6)* having a copper luster are formed [0.9 g (54%), (further 0.7 g from mother liquid); decomp. 104 °C].

The thermally labile *dicarbonyl compounds* such as *(4)* and *(7)* are obtained from bis(acetonitrile)bis(triphenylphosphine)dicarbonylmolybdenum by substituting acetonitrile below room temperature[11]. Reaction of equimolar amounts proceeds quantitatively if the acetonitrile liberated is pumped off from the higher boiling solvent. Recrystallization leads to disproportionation products.

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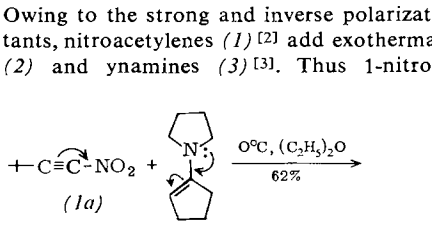
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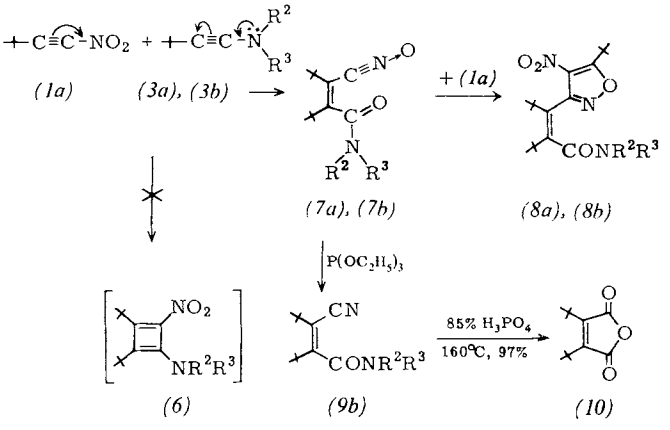
Addition of Nitroacetylenes to Enamines and Ynamines[1]

By *Volker Jäger* and *Heinz Günter Viehe* [*]

Owing to the strong and inverse polarization of the reactants, nitroacetylenes *(1)*[2] add exothermally to enamines *(2)* and ynamines *(3)*[3]. Thus 1-nitro-3,3-dimethyl-1-butyne *(1a)* and 1-pyrrolidinocyclopentene *(2a)* undergo a generalizable C_2-ring expansion reaction[4,5] to give the nitrocycloheptadienylamine *(4)*. This affords the α-nitro ketone *(5)*[6] on hydrolysis.



Reaction of *(1a)* with ynamines *(3a)* and *(3b)* yields not the electronically and sterically stabilized cyclobutadienes *(6)*[7] but their isomers, the nitrile oxides *(7a)* and *(7b)*, respectively. The structures of *(7a)* and *(7b)* were established by spectroscopic means and by their reaction with additional *(1a)* to give the isoxazoles *(8a)* and *(8b)*, respectively. The orientation of the substituents in *(8)* is formulated by analogy with the results of previous 1,3-dipolar cycloadditions of nitrile oxides[8]. Degradation of the nitrile oxide *(7b)* by reduction[9] to the nitrile *(9b)* and subsequent hydrolysis gives the maleic anhydride *(10)*. This compound is remarkable because of its adjacent *tert*-butyl groups.



(a), $R^2=R^3=CH_3$; *(b)*, $R^2=CH_3$, $R^3=C_6H_5$, + = $(CH_3)_3C$

Reactants	Product	Yield (%)	M.p. (°C)
(1a) + *(3a)* 1:1	*(7a)*	29 [a]	82–83
(1a) + *(3a)* 2:1	*(8a)*	44	115
(1a) + *(3b)* 1:1	*(7b)*	21	138
	and *(8b)*	41	131–132
(1a) + *(3b)* 1:4	*(7b)*	66	138

[a] Formed quantitatively according to IR spectrum but decomposes on recrystallization.

3-tert-Butyl-2-nitro-1-pyrrolidino-1,3-cycloheptadiene (4)

Compound *(1a)* (636.5 mg, 5.0 mmoles) in ether (10 ml) is added dropwise at 0 °C to *(2a)* (688 mg, 5.0 mmoles), also in ether (10 ml). Removal of solvent and recrystallization from CH_2Cl_2/light petroleum (b.p. 40–60 °C) gave compound *(4)* (yield 826 mg, 62%) as yellow needles, m.p. 187–188 °C (decomp.); NMR ($CDCl_3$, δ_{TMS} = 0): olefinic proton at δ = 6.05 ppm, $J \approx 6.5$ Hz; UV (C_2H_5OH): λ_{max} = 277.5 nm (log ε = 3.7), 391.5 (4.0).

2,3-Di-tert-butyl-4-(N-methyl-N-phenylamino)-4-oxo-2-butenenitrile oxide (7b) and di-tert-butylmaleic anhydride (10)

Compound *(1a)* (640 mg, 5.04 mmoles) in ether (4 ml) is added slowly to a solution of *N*-methyl-*N*-phenyl-3,3-dimethyl-1-butynylamine *(3b)* (4.0 g, 21.4 mmoles) in ether (5 ml). After 12 h, the precipitated colorless crystals are washed several times with *n*-pentane; yield of *(7b)* = 1.04 g (66%), m.p. 138 °C, IR (in KBr): 2285, 1330, (C≡N→O); 1635 (C=O), 1598 and 1495 cm^{-1} (aromatic).

Reduction of *(7b)*[9] gives the nitrile *(9b)* in 90% yield; m.p. 146 °C, IR (in KBr): 2205 (C≡N), 1635 (C=O), 1595 and 1495 cm^{-1} (aromatic).

Compound *(9b)* (190 mg) was heated to 160 °C in 85% phosphoric acid (5 ml) for 20 h; after neutralization with a concentrated solution of $NaHCO_3$ the product was ex-

tracted with ether. Recrystallization from *n*-pentane/ether gave 130 mg (97 %) of the anhydride *(10)*, m.p. 88.5–89.5 °C, IR (in KBr): 1835, 1755, 1260 cm^{-1} (CO stretching); UV (*n*-hexane): λ_{max} = 209 nm (log ε = 3.9); 251.5 (3.8).

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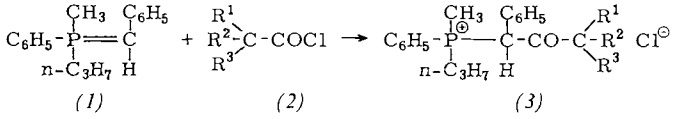
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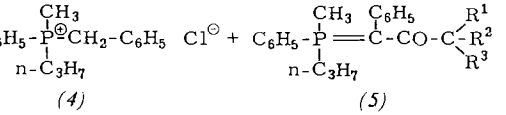
New Method for Determination of the Absolute Configuration of Carboxylic Acids [1]

By *Hans-Jürgen Bestmann, Herbert Scholz,* and *Eckart Kranz* [*]

When two moles of the racemate of benzylidene(methyl)(phenyl)(*n*-propyl)phosphorane *(1)* is treated with one mole of an optically active acid chloride *(2)*, partial kinetic resolution occurs [2]: the acylated phosphonium salt *(3)* is formed from *(1)* and *(2)* and, since *(2)* reacts preferentially with one of the enantiomers of *(1)*, the other enantiomer becomes enriched in solution and then reacts by transylidation [3] with the initial product *(3)*; this affords the optically active phosphonium chloride *(4)* which is precipitated, while the diastereoisomeric acyl ylide *(5)* remains dissolved in the tetrahydrofuran solution. The absolute configuration of *(4)* was proved by chemical correlation with the configuration of the corresponding bromide that had been determined by X-ray structure analysis [4].



(1) *(2)* *(3)*

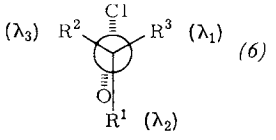


(4) *(5)*

Using this reaction we have now developed a method of determining the absolute configuration of centrochiral carboxylic acids [5] by qualitative application of *Ugi*'s [6] and *Ruch*'s [7,8] stereochemical structural model without the necessity of considering conformations.

For this purpose two equivalents of *(1)* are treated with one equivalent of the optically active acid chloride *(2)* whose absolute configuration is to be determined; then the specific rotation of the precipitated phosphonium chloride *(4)* is measured (see below).

The ligand constants λ_n of the three ligands of the acid chloride are next assigned as described by *Ugi* and *Ruch* [6–8] and are numbered clockwise; for our purposes it is immaterial with which λ the enumeration begins but it is important that the reacting acid chloride group be placed behind the projection plane of the Newman projection. This is illustrated in *(6)*.



(6)

The asymmetric induction of the acid chloride is then given by a chirality product χ determined from the equation:

$$\chi = (\lambda_1 - \lambda_2)(\lambda_2 - \lambda_3)(\lambda_3 - \lambda_1).$$

We have found that the mathematical sign of the chirality product χ of the optically active acid chloride *(2)* agrees with the sign of the specific rotation of the precipitated phosphonium salt *(4)* (measured in methanol at 589 nm) in all cases where *(2)* has been written in the correct absolute configuration [9].

When the specific rotation of *(4)* has been determined, the substituents R^1, R^3, and R^3 of *(2)* are arranged arbitrarily around the asymmetric carbon atom, *e.g.*, as in *(6)*, and their ligand constants are numbered clockwise. A qualitative order for the numerical magnitudes of the λ values is then set up by using the known constants [6] and, for unknown λ, by basing them on the space-filling by the substituents. Such a series is, for instance, $\lambda_2 > \lambda_1 > \lambda_3$. The mathematical sign of λ is now determined qualitatively. For the relative series just stated the value of χ is found to be positive. If this sign agrees with the sign of the specific rotation of the phosphonium chloride *(4)* as obtained in the kinetic resolution, then the arbitrarily assigned absolute configuration of the acid chloride is correct. If these two signs are of opposite sense, then the positions of two ligands must be exchanged, *e.g.*, R^2 and R^3; then, to retain the clockwise numbering of λ_n, the ligand constants must be assigned as $R^2 = \lambda_1$ and R^3 as λ_3; the order of magnitude of the λ values thus becomes $\lambda_2 > \lambda_3 > \lambda_1$, and, since the equation for χ is inversion-asymmetric, the sign of χ changes when the relative sizes of two λ values are changed: in our case χ becomes negative, and the exchange of two ligands which results in a change of absolute configuration thus leads to the required agreement between the sign of χ and the sign found for the specific rotation of *(4)*.

The Table sets out the results of our experiments: in all cases the absolute configurations determined by the new rule agrees with those recorded in the literature.

Examples 9 and 10 are of particular interest: here a phthaloylimido group has been replaced by a methoxy group but both compounds belong to the (*S*)-series; in no. 9 $\lambda_{N\text{-phthaloyl}} > \lambda_{CH_3}$, but according to *Ugi* [6] in no. 10 $\lambda_{CH_3} > \lambda_{OCH_3}$; it thus transpires that, although no. 10 is still in the (*S*)-configuration, the sign of its χ becomes negative; our rule requires that the sign of the optical rotation of *(4)* must then also become negative, and that is the experimental result. Comparison of examples 6 and 7 gives qualitatively similar results. It follows further from the Table that

$\lambda_{CH_3} > \lambda_{acetoxy}$, $\lambda_{CH_3} > \lambda_{benzoyloxy}$, and $\lambda_{Cl} > \lambda_{CH_3}$.

Table. Determination of the absolute configuration of acid chlorides *(2)*.

No.	Acid chloride *(2)* used	Sign of sp. rotn. of *(4)* at 589 nm in CH_3OH	Sign of chirality parameter of *(2)*	Absolute configuration	
				Found	Literature
1	(+)-Hydratropoyl	−	−	*S*	*S*
2	(−)-Hydratropoyl	+	+	*R*	*R*
3	(−)-2-Phenylbutyryl	+	+	*R*	*R*
4	(+)-2-Phenylbutyryl	−	−	*S*	*S*
5	(−)-*N*-Phthaloylvalyl	+	+	*S*	*S*
6	(−)-*N*-Phthaloylphenylalanyl	+	+	*S*	*S*
7	(+)-*O*-Methylmandeloyl	−	−	*S*	*S*
8	(−)-*O*-Methylmandeloyl	+	+	*R*	*R*
9	(−)-*N*-Phthaloylalanyl	+	+	*S*	*S*
10	(−)-*O*-Methyllactoyl	−	−	*S*	*S*
11	(−)-*O*-Acetyllactoyl [10]	+	+	*R*	*R*
12	(−)-*O*-Benzoyllactoyl	+	+	*R*	*R*
13	(−)-*N*-Phthaloylleucyl	+	+	*S*	*S*
14	(+)-*cis*-1-Methyl-2-phenylcyclopropanecarbonyl [11]	−	−	1*S*:2*R*	1*S*:2*R*
15	(−)-2-Chloro-4-methylvaleryl	+	+	*S*	*S*
16	(+)-2-Chloropropionyl	+	+	*S*	*S*
17	(+)-2-Chloro-3-methylbutyryl	+	+	*S*	*S*
18	(+)-2-Chloro-3-phenylpropionyl	+	+	*S*	*S*
19	(−)-Menthyloxyformyl	+	+	3*R*	3*R*
20	(−)-3β-Acetoxy-Δ5-etiocholenoyl	+	+	17*R*	unknown

Experimental:

A filtered solution of the ylide *(1)* in tetrahydrofuran is prepared from benzyl(methyl)(phenyl)(*n*-propyl)phosphonium bromide (6.76 g, 20 mmoles) by the sodium amide method (0.5 g of sodium)[3,12]. A solution of the optically active acid chloride *(2)* (10 mmoles) in anhydrous tetrahydrofuran is dropped into this solution with stirring at room temperature. This precipitates *(4)*, and the orange color of the solution of *(1)* changes to the yellow color of *(5)*. Up to this point the work must be with protection by nitrogen and exclusion of moisture. The phosphonium chloride *(4)* is then filtered off, washed with benzene, collected, and dried, after which its specific rotation is determined. The optical yield is 6—7%. The following values were found for (+)-(*S*)-(4) with an optical purity of 86%: $[\alpha]_{589} = +36.2$, $[\alpha]_{578} = +38.5$, $[\alpha]_{546} = +44.9$, $[\alpha]_{436} = +84.6$, $[\alpha]_{365} = +150.7$ (*c* = 0.54 in methanol).

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Synthesis and Reactions of Substituted (Dibenzoyldioxyiodo)benzenes; A New Class of Organic Oxidants[**]

By *Božo Plesničar* and *Glen A. Russell*[*]

The reaction of iodosobenzenes with substituted perbenzoic acids in chloroform/methanol (8:1) at 0 °C yields highly reactive (dibenzoyldioxyiodo)benzenes *(1)* containing trivalent iodine.

$$X\text{–}Ar\text{–}IO + 2\ Y\text{–}Ar\text{–}CO_3H \rightarrow X\text{-}Ar\text{-}I(O\text{–}O\text{–}CO\text{–}Ar\text{–}Y)_2 \quad (1)$$

$$X\text{–}Ar\text{–}IO + 2\ Y\text{–}Ar\text{–}CO_2H \rightarrow X\text{–}Ar\text{–}I(O\text{–}CO\text{–}Ar\text{–}Y)_2 \quad (2)$$

	X	Y	Yield (%)	M.p. (°C)	νCO (cm^{-1}) [a]	Active oxygen calc.	found [b]
(1a)	H	*m*-Cl	70	93 (dec.)	1744s, 1725s	8.77	8.7
(2a)	H	*m*-Cl	60	136—137	1650s, 1630w	3.10	3.2
(1b)	H	*p*-NO_2	70	115 (dec.)	1749s, 1729s	8.44	8.4
(2b)	H	*p*-NO_2	63	211—212 [c]	1651	2.98	2.8
(1c)	*p*-Cl	*m*-Cl	83	78 (dec.)	1735s, 1720s	8.25	8.1
(2c)	*p*-Cl	*m*-Cl	58	164—165	1655s, 1630w	2.91	2.8
(1d)	*p*-Cl	*p*-NO_2	70	103 (dec.)	1747s, 1726s	7.94	8.0
(2d)	*p*-Cl	*p*-NO_2	49	213—214	1665w, 1642s	2.80	2.7
(1e)	*o*-CH_3	*p*-NO_2	79	98 (dec.)	1740	8.24	8.3

[a] In Nujol. [b] Determined iodometrically. [c] M.p. 209 °C [1].

The (dibenzoyldioxyiodo)benzenes *(1)* are white or yellow amorphous compounds which detonate at 80—120 °C and which may undergo spontaneous ignition or detonation upon manipulation in the solid state at room temperature. They react with iodide ion to liberate 3 moles of iodine per mole of *(1)*.

The Table summarizes the physical properties of compounds *(1)* as well as the properties of the corresponding (dibenzoyloxyiodo)benzenes *(2)* formed from the reaction of iodosobenzene and benzoic acids in chloroform/methanol (5:1) [1].

We were surprised that the (dibenzoyldioxyiodo)benzenes *(1)* could be isolated. They are more powerful oxidizing agents than the peracids. Moreover, they appear to transfer two oxygen atoms to substrates such as sulfides or aryl iodides (Scheme 1); compound *(2)* was the reduction product in each case except for iodide ion and for triphenylphosphine where iodobenzene was formed. Dibenzyl sulfide and iodobenzene were still oxidized to the sulfone and iodoxybenzene when a great excess of the substrate was employed (reactions followed by NMR).

(1a) + CH_3SOCH_3 → $CH_3SO_2CH_3$ + *(2a)* (20 min, 100 %)

(1a) + $C_6H_5CH_2SCH_2C_6H_5$ → $C_6H_5CH_2SO_2CH_2C_6H_5$ + *(2a)* (20 min, 100 %)

(1a) + pyridine → pyridine *N*-oxide + *(2a)* (30 min, 85 %)

(1a) + C_6H_5I → $C_6H_5IO_2$ + *(2a)* (60 min, 72 %)

(1a) + $(C_6H_5)_3P$ → $(C_6H_5)_3PO$ + C_6H_5I (10 min, 85 %)

(1a) + styrene → styrene oxide + *(2a)* (45 min, > 80 %)

(1a) + *trans*-stilbene → *trans*-stilbene oxide + *(2a)* (90 min, > 90 %)

Scheme 1. Reactions of [bis(*m*-chlorobenzoyldioxy)iodo]benzene *(1a)* at 28 °C in CH_2Cl_2, 20 % excess of *(1a)* (calculated on the assumption that *(1a)* contains two active oxygen atoms).

The low solubilities of (dibenzoyldioxyiodo)benzenes *(1)* made homogeneous decomposition studies difficult. Solutions of *(1a)* and *(1b)* (0.02 M) in methylene chloride and chloroform yielded iodoxybenzene *(3)*, the diaroyl peroxide, and the arenecarboxylic acid after a few hours at room temperature. Decomposition was faster in chloroform than in methylene chloride but in neither solvent was biphenyl or carbon dioxide detected. This suggests that the (dibenzoyldioxyiodo)benzene *(1)* are excellent traps for aroyloxy radicals. Hydrolysis of compounds *(1)* by traces of moisture may be a complicating factor [2], but we believe the major decomposition route is one of homolysis.

(1a) $\xrightarrow[28\,^\circ C]{5\ h,\ CHCl_3}$ $C_6H_5IO_2$ + *m*-$ClC_6H_4CO_2H$ + (*m*-$ClC_6H_4CO_2)_2$

(1.0 mole) *(3)* (0.8 mole) (1.7 mole) (0.1 mole)

(1b) $\xrightarrow[28\,^\circ C]{5\ h,\ CHCl_3}$ $C_6H_5IO_2$ + *p*-$NO_2C_6H_4CO_2H$ + (*p*-$NO_2C_6H_4CO_2)_2$

(1.0 mole) *(3)* (0.9 mole) (1.4 mole) (0.5 mole)

Preparation of (dibenzoyldioxyiodo)benzenes (1):

The substituted perbenzoic acid (15 mmoles) was dissolved in 100 ml of chloroform/methanol (8:1) at 0—5 °C. Iodosobenzene (5 mmoles) was added with stirring. After 15 minutes' stirring, most of the solvent was removed in a rotary evaporator. The precipitate was washed twice with dilute sodium bicarbonate (20 ml of 5 % solution), with ether, and dried *in vacuo* over P_2O_5. The crude products, which were estimated to be 98—99 % pure by infrared spectroscopy, were purified by dissolution in methylene chloride, the solution being quickly filtered to remove traces of iodosobenzene or iodoxybenzene. The solvent was quickly evaporated and the product dried under vacuum.

Warning: All the (dibenzoyldioxyiodo)benzenes *(1)* are explosive when dry, and manipulation with metal spatulas is not recommended. Avoid any heating.

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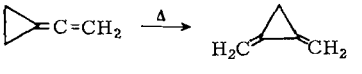
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Dimethylenecyclopropane

By *Robert Bloch*, *Pierre Le Perchec*, and *Jean-Marie Conia* [*]

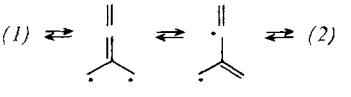
Although derivatives of dimethylenecyclopropane are known and have attracted considerable interest on account of their heat of formation and strain energy [1,2], the parent compound *(2)* has not hitherto been obtained. We are now able to report the preparation of this highly volatile and unstable species.



(1) *(2)*

On heating to 320 °C under vacuum for 3 min (static gas-phase technique), vinylidenecyclopropane *(1)* [3] gives a mixture of *(2)* (30 %) and *(1)* (20 %) and polymers, which are easily separated by gas chromatography.

This simple thermal conversion, already observed with methyl derivatives of *(2)* [2], is apparently promoted by a cyclopropane ring cleavage which leads to a highly delocalized biradical closely related to trimethylenemethane.

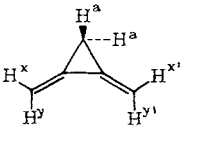


The low yield of the conversion of *(1)* into *(2)* is due to the unavoidable polymerization of *(2)*. Even at −10 °C a white solid is precipitated from a pure sample of *(2)* after one hour's standing. Attempts to form the tetracyanoethylene adduct under the usual conditions were unsuccessful. The structure of *(2)* is established by spectrometry.

Mass spectrum: *m/e* 39 (100 %), 65 ($(M-1)^+$, 92 %, characteristic of many cyclopropane derivatives [4]), 66 (M^+, 87 %).

IR (in CCl_4): ν = 3.24, 3.33, 3.35, 3.40 (νC—H), 5.65 s, 6.20 (νC=C), 9.90 μm (cyclopropane).

UV (in hexane): λ_{max} = 232 (ε = 11000), 225 (9700), 240 nm (10000) [cf. 1,2-dimethylenecyclopentane: 248 (ε = 10400) and 1,2-dimethylenecyclobutane: 248 nm (10100)].



NMR: $A_2XX'YY'$ system with three symmetric multiplets (9 lines each) centered respectively at δ = 1.56 ($2H^a$), 5.27 (H^x,$H^{x'}$), 5.50 ppm (H^y,$H^{y'}$); J_{ay} = 2.6, J_{ax} = 1.7,

$J_{x'y,xy'} = {}^1/_2 (J_{x',y} + J_{y',x}) = \pm 0.85$ Hz[**]. The magnitude of J_{ay} and J_{ax} suggests a large σ-π overlap and therefore a large external H^a—C—H^a angle.

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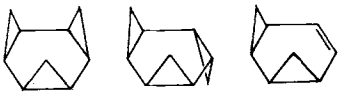
[**] Solvent CCl_4; external standard $Si(CH_3)_4$.

Monohetero Derivatives of Bis- and Trishomobenzenes[1] [**]

By *Horst Prinzbach* and *Dieter Stusche* [*]

In this communication we report on the compounds *(10a)*, *(10b)*, and *(11a)*, which are the first isolable monohetero derivatives of the trishomobenzene series *(1a)* and *(1b)*; we have also prepared *(7a)*, *(9a)*, and *(9b)* as hetero derivatives of the bishomobenzene series *(2)* [2].

4,5-Bis(methoxycarbonyl)oxepin *(3a)* [3] and -*N*-tosylazepine *(3b)* [4] add diazomethane, reacting as the bicyclic structures *(4a)* and *(4b)* [5], respectively; the preferred



(1a) *(1b)* *(2)*

products are the all-*cis*-pyrazolines *(5a)*, *(6a)*, and *(6b)* respectively.

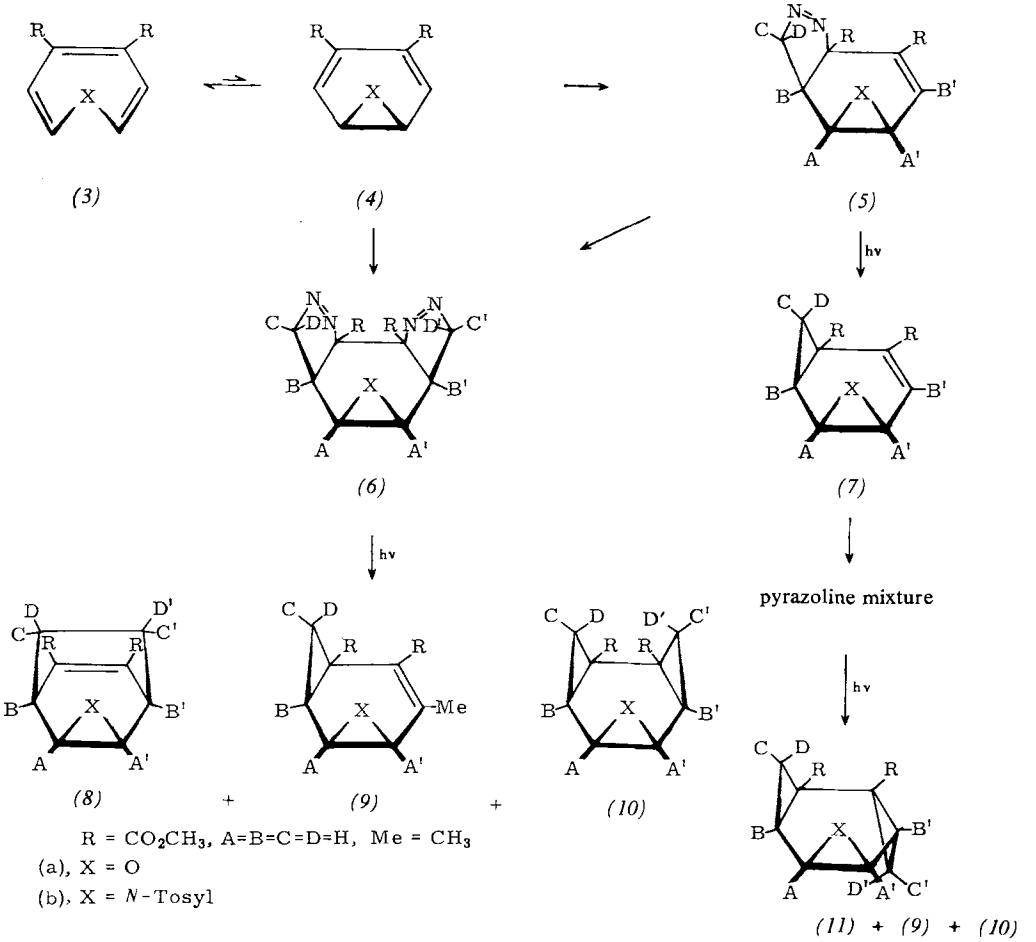
The monoadduct *(5a)* crystallizes out when diazomethane (0.5 g, 12 mmoles) is added to a solution of *(3a)* (2.1 g, 10 mmoles) in ether (100 ml) in a yield of 65–70 %. The bisadduct *(6a)* was prepared by the same method as was previously used for *(6b)* [5], *i.e.* by precipitation with ether from a mixture of *(3a)* (1 g, 4.7 mmoles) and diazomethane (0.42 g, 10 mmoles) in dichloromethane (100 ml) that has been allowed to stand for 72 h (yield 65–70 %).

On photolysis (300 ml solvent, −20 °C, Hanau Q 81 high pressure mercury lamp), *(5a)* (0.6 g, 2.4 mmoles; methanol; 2 h) affords the oxabishomobenzene *(7a)* (80–90 %); *(6a)* and *(6b)* (4.0 mmoles; acetone; 2 h) give *(8a)* and *(8b)* (60–65 %), *(9a)* and *(9b)* (5–10 %), and *(10a)* and *(10b)* (20–25 %), respectively, after thin-layer chromatography (silica gel/benzene).

The product ratio in the photolysis of *(6a)* and *(6b)* varies with the solvent. In methanol the amount of *(9a)* and *(9b)* is increased considerably at the expense of *(8a)* and *(8b)*.

The bishomobenzene *(7a)* adds diazomethane [0.5 g, 2.2 mmoles of *(7a)* in ether (100 ml); 0.13 g, 3.1 mmoles of CH_2N_2; 1 week; 10 °C] to give a mixture of pyrazolines, which is photolyzed directly (methanol; 2 h). The crude product consists of *(9a)* (12 %), *(10a)* (25 %), and *(11a)* (27 %) (separated by preparative thin layer chromatography; silica gel/benzene).

The structures of the new compounds prepared were confirmed by elemental analysis and spectral data (see Table). In the case of the pyrazolines *(5a)*, *(6a)*, and *(6b)*, the ex-



Cpd. M.p. (°C)	NMR (τ)								UV [d] λ_{max} (nm; ε)
	H^A	$H^{A'}$	H^B	$H^{B'}$	H^C	$H^{C'}$	H^D	$H^{D'}$	
(5a) 112–114 (dec.)	6.49 (2,M) [a] J_{AB} *ca.* 3 Hz		7.43 (1,M) J_{BC} = 2.5 Hz J_{BD} = 8.0 Hz	2.44 (1,M)	4.85 (1,M) J_{CD} = 17.5 Hz		5.31 (1,M)		322 (180) 232 (5900)
(6a) 135–136 (dec.)	6.63 (2, M) [a] $J_{AA'}$ = 3.8 Hz $J_{AB} = J_{A'B'}$ = 4.6 Hz		7.10 (2, M) $J_{BB'} \leqslant 0.1$ Hz $J_{AB'} = J_{A'B}$ = −0.2 Hz		5.03 (2, M) $J_{CD} = J_{C'D'}$ = 17.0 Hz $J_{BC} = J_{B'C'}$ = 8.0 Hz		5.53 (2, M) $J_{BD} = J_{B'D'}$ = 5.5 Hz		321 (360)
(6b) 116 (dec.)	6.65 (2, M) [a] $J_{AA'}$ = 6.7 Hz $J_{AB} = J_{A'B'}$ = 6.3 Hz		7.30 (2, M) $J_{BB'} \leqslant 0.1$ Hz $J_{AB'} = J_{A'B}$ = −0.3 Hz		5.25 (2, M) $J_{CD} = J_{C'D'}$ = 17.0 Hz $J_{BC} = J_{B'C'}$ = 7.5 Hz		5.85 (2, M) $J_{BD} = J_{B'D'}$ = 5.5 Hz		322 (400) 272 (510) 262 (740) 254 (680)
(7a)	6.77 (1, M) $J_{AA'}$ = 3.6 Hz J_{AB} = 4.1 Hz	7.10 (1, M) [b] $J_{A'B'}$ = 3.7 Hz	8.30 (1, M) J_{BD} = 5.7 Hz J_{BC} = 9.3 Hz	3.03 (1, D)	8.00 (1, M) J_{CD} = 3.2 Hz		9.33 (1, M)		
(8a) 68–69	6.77 (2, M) [b]		7.0 (2, M)		8.2 (2, M) 9.1 (2, M)				239 (4900)
(8b) 118.5–119	6.60 (2, M) [a]		6.9 (2, M)		8.15 (2, M) 9.0 (2, M)				273 (950) 267 (1220) 261 (1610) ε_{245} = 3800
(9a) 82–83	*ca.* 6.3 $J_{AA'}$ = 3.6 Hz	6.88 (1,D) [c]	$H^B + H^C$ 8.0–8.2 (2, M)	Me 7.77 (3, S)			9.33 (1, M)		
(9b) 134	6.53 (1, M) $J_{AA'}$ = 6.5 Hz	6.98 (1, D) [c]	$H^B + H^C$ 7.9–8.3 (2, M)	Me 8.02 (3, S)			9.25 (1, M)		
(10a) [e] 76.5–77	6.57 (2, M) [c] $J_{AA'}$ = 4.1 Hz $J_{AB} = J_{A'B'}$ = 4.9 Hz		8.30 (2, M) $J_{BB'} \leqslant 0.1$ Hz $J_{AB'} = J_{A'B}$ = −0.2 Hz		8.80 (2, M) $J_{CD} = J_{C'D'}$ = 5.2 Hz $J_{BC} = J_{B'C'}$ = 9.8 Hz		9.65 (2, M) $J_{BD} = J_{B'D'}$ = 5.9 Hz		ε_{229} = 200
(10b) [f] 111–112	6.65 (2, M) [a] $J_{AA'}$ = 7.6 Hz $J_{AB} = J_{A'B'}$ = 6.4 Hz		8.25 (2, M) $J_{BB'} \leqslant 0.01$ Hz $J_{AB'} = J_{A'B}$ = −0.2 Hz		8.75 (2, M) $J_{CD} = J_{C'D'}$ = 5.6 Hz $J_{BC} = J_{B'C'}$ = 9.8 Hz		9.63 (2, M) $J_{BD} = J_{B'D'}$ = 6.3 Hz		273 (1000) 267 (1000)
(11a) 51.5–52	6.6–7.0 (2, M) [c] $J_{AA'}$ = 4.1 Hz		8.0–8.6 (4, M) J_{AB} = 4.9 Hz $J_{AB'}$ = 0.8 Hz J_{BC} = 9.6 Hz $J_{A'B'}$ = 1.4 Hz $J_{A'B} \leqslant 0.1$ Hz $J_{B'C'}$ = 9.1 Hz $J_{BB'} \leqslant 0.1$ Hz				9.20 (1, M) J_{CD} = 3.7 Hz J_{BD} = 5.7 Hz	8.90 (1, M) $J_{C'D'}$ = 3.8 Hz $J_{B'D'}$ = 6.4 Hz	ε_{230} = 250

[a] In $CDCl_3$. [b] In C_6H_6. [c] In CCl_4. [d] In CH_3OH. [e] Molecular ion *m/e* 238. [f] Molecular ion *m/e* 391.

pected $n \rightarrow \pi^*$ bands and the typically large coupling constants of the methylene protons were observed. The spatial relationships of the three-membered rings in *(7a)*, *(10a)*, *(10b)*, and *(11a)*, and hence those also of the rings in *(5a)*, *(6a)*, and *(6b)*, follow from J_{AB} and $J_{A'B'}$ [6]. Compound *(8a)* is identical with the partially hydrogenated adduct of dimethyl acetylenedicarboxylate and oxepin [7]. Its formation from *(6a)* affords additional proof of the *cis* arrangement of the three hetero rings in *(6a)*.

The crystalline trishomobenzenes *(10a)*, *(10b)*, and *(11a)*, which are stable at room temperature, differ considerably in their thermal behavior. Whereas *(11a)* remains unchanged at temperatures up to about 160 °C, *(10a)* and *(10b)* isomerize smoothly at 70 °C to form hetero-2,5,8-cyclononatriene derivatives [8].

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Stable Complexes of Bullvalene [**]

By *Rudolf Aumann* [*]

Bullvalene [1] *(1)* is a notorious case of a molecule with degenerate valence isomerization, in which all the H atoms are magnetically equivalent on the NMR time scale at temperatures above 80 °C. This degeneracy disappears with introduction of a substituent into *(1)*. In this connection, particular interest attaches to the study of metal complexes

in which the bullvalene skeleton is unchanged, but where two double bonds are employed in coordination to the metal. Previous attempts[2] to prepare such complexes were unsuccessful, except for a bullvalene-$Ag(H_2O)^+$ complex[3], because of the great ease with which compound *(1)* rearranges in the presence of metals. We have now been able to prepare stable bullvalene complexes of composition bullvalene-$M(CO)_4$ *(2)* [*(2a)*: M = Cr (dec. 120 °C); *(2b)*: M = Mo (dec. 119 to 120 °C); *(2c)*: M = W (dec. 135 to 136 °C)] by reaction of *(1)* with the corresponding acetonitrile-$M(CO)_3$ complexes in dioxane[4] in 40—70% yield, and have analyzed them by spectroscopy.

The presence of a rigid bullvalene skeleton with an intact cyclopropane ring in *(2b)* and *(2c)* was established by a ^{1}H-NMR double resonance experiment. H^7 and H^8 of the uncomplexed vinyl group form an AB system (cf. Figure), $J_{7,8}$ = 11 Hz, with further splitting in the A ($J_{6,7}$ = 8 Hz; $J_{1,7}$ = 1 Hz) and B parts ($J_{1,8}$ = 8 Hz). In the complexed vinyl group, $J_{2,3}$ (= $J_{9,10}$) is reduced to 7 Hz. It was not possible to demonstrate a degenerate Cope rearrangement with cyclopropane ring shift from skeletal positions 4, 5, 6 to 1, 2, 10 with a concomitant metal shift on the NMR time scale, either by line broadening of the peaks or by use of the Forsén-Hoffman method[5].

Unlike *(2b)* and *(2c)*, which decompose irreversibly to paramagnetic products on heating, even in inert solvents such as cyclohexane, compound *(2a)* rearranges quantitatively to a new complex *(3)* (m.p. 161—162 °C) above about 80 °C. Complex *(3)* was identified by its ^{1}H-NMR spectrum (in C_6D_6 with TMS as internal standard; chemical shifts[6] in τ: $H^{1,6}$ = 7.26, $H^{2,5}$ = 6.56, $H^{3,4}$ = 5.65, $H^{7,8}$ = 6.71, $H^{9,10}$ = 4.81; assigned by double resonance experiments), as well as by its IR and mass spectra.

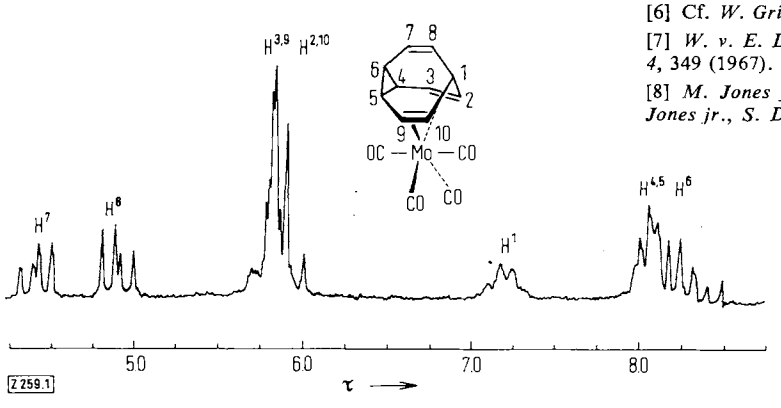
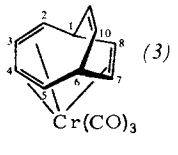


Figure: ^{1}H-NMR spectrum of *(2b)*; C_6D_6 solution, TMS as internal standard, 100 MHz.

(2a) —80°C→ *(3)*



In the presence of NH_3, complex *(3)* slowly decomposes to $(NH_3)_3Cr(CO)_3$ and bicyclo[4.2.2]deca-2,4,7,9-tetraene *(4)*. *(4)* could be identified by its IR and ^{1}H-NMR spectra[7] after isolation by gas chromatography.

Remarkably, *(4)* is not formed on thermolysis[7] of *(1)* but only on photolysis[8]; this demonstrates that under the influence of the metal a rearrangement occurs that is otherwise only permitted photochemically.

The complexes *(2)* are stable as crystals for several months under argon. In benzene they decompose slowly at 30 °C to benzene-$M(CO)_3$ and *(1)*. In the presence of carbon monoxide, rapid decomposition to *(1)* and to the corresponding $M(CO)_6$ complex occurs. After isolation by gas chromatography, *(1)* was identified by its IR and ^{1}H-NMR spectra.

In the 20-eV mass spectra of *(2)*, the molecular ions with the expected isotopic ratios are accompanied by fragments resulting from the successive loss of the four CO groups.

The IR spectra (cyclohexane solution) of *(2)* contain four ν_{CO} bands in intensity ratios that are characteristic of tetracarbonylmetal moieties (ν_{CO} in cm^{-1}: *(2a)* 2028, 1946, 1930, 1904; *(2b)* 2039, 1947, 1941, 1902; *(2c)* 2039, 1947, 1941, 1902).

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New Tetrachalcogenide Chelates[**]

By *Hartmut Köpf*, *Werner Kahl*, and *Alexander Wirl*[*]

Bis(π-cyclopentadienyl)tetrasulfidomolybdenum(IV) *(1)*, which is formed according to the reaction scheme (M^{IV} = Mo; X = S):

$$(C_5H_5)_2M^{IV}Cl_2 + M^{I}{}_2X_5 \longrightarrow (C_5H_5)_2M^{IV}\begin{matrix}X\\X\\X\\X\end{matrix} \quad (1)\text{-}(4)$$

$$+ 2\ M^{I}Cl + \tfrac{1}{8}X_8$$

was recently characterized as the first chelate complex of a dianionic tetrachalcogenide ligand[1]. We have now also successfully carried out this reaction with M^{IV} = W and X = Se and obtained the tetrachalcogenides $(C_5H_5)_2WS_4$ *(2)*, $(C_5H_5)_2WSe_4$ *(3)*, and $(C_5H_5)_2MoSe_4$ *(4)* as further examples of the selective formation of polychalcogenide five-membered ring chelates with central ions having a d^2 electronic configuration. In contrast, only the six-membered ring chelates $(C_5H_5)_2TiX_5$ could be isolated with the d^0 central ion Ti^{IV}, irrespective of the chalcogen (X = S or Se)[2]. Compounds *(2)* and *(3)* are the first polychalcogenide chelates of tungsten, and *(3)* and *(4)* are the first hetero derivatives of the yet unknown cyclopentaselenium system.

On reaction of bis(π-cyclopentadienyl)metal(IV) chlorides[3] with ammonium pentasulfide in aqueous ethanol or with sodium pentaselenide in ethanol, *(2)—(4)* are obtained as brown precipitates that are only sparingly soluble in all the usual solvents except dimethylformamide (DMF) and dimethyl sulfoxide (DMSO). Recrystallization under mild conditions from DMF affords deeply colored crystals that are stable towards air and which appear uniform under a microscope. The composition $(C_5H_5)_2MX_4$ was established unequivocally by elemental analysis. Although the solubility of the compounds decreases rapidly along the series *(1)* > *(2)* ⋙ *(3)* ≈ *(4)*, the molecular weights determined cryoscopically in DMSO[4] after calibration with $(C_5H_5)_2TiS_5$ show that *(2)—(4)* are also present in the monomeric ring form in their solutions.

Like that of *(1)*[1], the ^{1}H-NMR spectra of *(2)—(4)* recorded in DMF show, in the expected region[5,6], a sharp singlet for the cyclopentadienyl protons which is not split, even when the temperature is lowered[7] to −60 °C.

	M^{IV}	X	M^I	Decomp. (°C)	τC_5H_5 (ppm) [a]	νCH (cm^{-1}) [b]	ωCC	δCH	γCH	ωSS	not assigned
(2)	W	S	NH_4	above 180	4.85 [c]	3080 m	1435 s 1410 s 1360 w 1115 w	1075 m 1063 w 1020 m 1010 s 998 vs	950 w 924 w 874 s 836 vs 824 vs	488 m [d]	587 w 405 w 364 m
(3)	W	Se	Na	225	4.78	3075 m	1420 m 1355 w 1114 vw	1060 m 1011 m 992 m	949 vw 930 vw 860 Sh 832 vs 823 Sh		585 vw 377 m 360 m
(4)	Mo	Se	Na	215	4.83	3085 w	1425 m 1405 m 1360 Sh 1110 w	1060 w 1012 m 993 m	860 Sh 830 Sh 816 vs		388 s

[a] In DMF; TMS as external standard. [b] KBr disks. [c] Cf. *(1)*: 4.86. [d] Cf. *(1)*: 482 w.

Such behavior at low temperature indicates that the five-membered MX_4 rings of *(2)—(4)* adopt a non-planar conformation similar to that postulated for *(1)*[1].

Bis(π-cyclopentadienyl)tetrasulfidotungsten(IV) (2), -tetraselenidotungsten(IV) (3), and tetraselenidomolybdenum(IV) (4)

An aqueous solution of $(NH_4)_2S_5$ obtained according to ref.[8] is used for further reaction without any attempt being made to crystallize $(NH_4)_2S_5$. An air-sensitive, alcoholic solution of 2 mmoles of Na_2Se_5 is prepared under an inert gas (argon or nitrogen) by dissolution of sodium (0.09 g, 4 mg-atoms) and red selenium (0.79 g, 10 mg-atoms) in liquid ammonia (50 ml), evaporation of the ammonia in a stream of inert gas, and dissolution of the residue in degassed ethanol (25 ml). — Under an inert gas a stirred suspension of $(C_5H_5)_2WCl_2$[3] (0.77 g, 2 mmoles) in degassed ethanol (25 ml) is treated with 2 ml of the solution of $(NH_4)_2S_5$ containing about 2.5 mmoles/ml or added dropwise to the Na_2Se_5 solution and the stirred reaction mixture is brought almost to boiling over a period of one hour. The brown precipitate is filtered off, washed with aqueous ethanol and carbon disulfide, and dried *in vacuo*. Extraction with DMF at *ca.* 80 °C and recrystallization at −30 °C affords *(2)* (0.66 g, 75%) as brownish-red crystals that are also slightly soluble in acetone or *(3)* (1.08 g, 86%) as brownish-violet platelets; similarly, $(C_5H_5)_2MoCl_2$[3] (0.59 g, 2 mmoles) gives a somewhat lower yield of *(4)* (0.39 g, 36%) as lustrous reddish-black platelets.

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Tellurium Halide Systems: Te_2Br and Te_3Cl_2

By *Albrecht Rabenau, Hans Rau*, and *Götz Rosenstein*[*]

Of the lower tellurium halides Te_yX (X = Cl, Br, I; $y \geq 1$), only the iodides have hitherto been described[1–3]. According to thermoanalytical findings by *Damiens*[4], such compounds should also be formed in the systems tellurium-bromine and tellurium-chlorine (regarded as solid solutions of tellurium in the respective tetrahalide by the author!). In connection with our studies on the systems formed by tellurium with its tetrahalides, we have now been able to isolate and identify the compounds Te_2Br and Te_3Cl_2. They cannot be prepared in pure form by reaction of stoichiometric amounts of the elements; instead their synthesis requires starting materials containing more halogen.

One arm of a two-arm quartz-glass tube contains powdered tellurium and the other arm contains liquid halogen in the ratio 1 Te: 1 Br or 1 Te : 2 Cl. The tellurium is heated to 220—260 °C; in the other arm the bromine is heated slowly from room temperature to 50 °C, or the chlorine from 0 °C to room temperature, as the reaction progresses. After consumption of the free halogen, the reaction tube is heated to 300—350 °C (muffle furnace) and shaken. The homogeneous melt is quenched with water and the product is then annealed for 2—3 weeks at 165 (bromide) or 180 °C (chloride) to promote solid-state equilibrium. Reaction to Te_2Br and $TeBr_4$ or Te_3Cl_2 and $TeCl_4$ is then complete. Gray needle-like crystals (up to 5 mm length) of Te_2Br or silver-gray compact crystals (1 mm) of Te_3Cl_2 are formed at various parts of the wall of the tube; the crystals prove suitable for X-ray studies.

Larger amounts of Te_2Br or Te_3Cl_2 are obtained by extraction of the tetrahalide from the respective reaction mixture by organic solvents. Here, however, the reactions

$$4\ Te_2Br_{(solid)} \rightleftharpoons 7\ Te_{(solid)} + TeBr_{4(dissolved)}$$

$$2\ Te_3Cl_{2(solid)} \rightleftharpoons 5\ Te_{(solid)} + TeCl_{4(dissolved)}$$

play a role.

Since the concentration of dissolved tetrahalide in equilibrium with the solid Te_2Br or Te_3Cl_2 is lower than the saturation concentration under the same conditions, the end of the separation process is indicated when the concentration falls below the latter value. Thus it is first necessary to determine the saturation concentration in a suitable solvent (diethyl phthalate at 80 °C for the bromides and toluene/light petroleum (b.p. 100—140 °C) (1:1) at room temperature for the chlorides). The reaction mixture is first stirred with the dry solvent for a few minutes in absence of air. Part of the solution is then removed by filtration under suction and replaced by fresh solvent. The concentration of halide in the extract, and thus the amount of halogen extracted, can be determined potentiometrically. The process is repeated — in small steps near the desired composition — until the concentration falls below the value at saturation. Only a single solid phase is then present. Depending on the solvent used, the last traces thereof are removed *in vacuo* or by washing with light petroleum. According to X-ray studies and elemental analysis, this technique yields pure Te_2Br or Te_3Cl_2. It is essential that the operation be carried out rapidly, particularly with the chlorides because $TeCl_4$ reacts with the solvent.

Te_2Br and Te_3Cl_2 melt peritectically at 224 and 238 °C respectively. Both compounds are stable towards air. They are soluble in hot acids and bases.

X-ray data: Te_2Br, orthorhombic: $a = 15.04$, $b = 12.96$, $c = 4.030$ Å; $Z = 8$; $d_{X\text{-ray}} = 5.67$, $d_{exp} = 5.61$ g cm^{-3}; probable space groups $Pna2_1$ and Pnam. Te_3Cl_2, monoclinic: $a = 7.069$, $b = 8.652$, $c = 11.26$ Å; $\beta = 117.51°$; $Z = 4$; $d_{X\text{-ray}} = 4.93$, $d_{exp} = 4.90$ g cm^{-3}; probable space group $P2_1/c$.

The tellurium halides known to date — except the fluorides — are summarized in the Table.

Table. Tellurium halides.

$TeCl_4$	$TeBr_4$	TeI_4
$TeCl_2$ [a]	$TeBr_2$ [a]	
		TeI [1, 2]
Te_3Cl_2	Te_2Br [5]	Te_xI [3]

[a] The dihalides appear incapable of existence in the crystalline state; their presence in the gaseous phase has been established.

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[1] *W. R. Blackmore, S. C. Abrahams*, and *J. Kalnajs*, Acta Crystallogr. *9*, 295 (1956).

[2] *S. A. Ivashin, E. S. Petrov*, and *T. I. Samsonova*, Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk *1969*, 51.

[3] *A. Rabenau, H. Rau*, and *G. Rosenstein*, Angew. Chem. *79*, 688 (1967); Angew. Chem. internat. Edit. *6*, 706 (1967).

[4] *A. Damiens*, Ann. Chim. *19*, 44 (1923).

[5] In the meantime, the existence of Te_2Br in the system Te/Br has been established and reported on: *S. A. Ivashin* and *E. S. Petrov*, Isv. Sib. Obd. Akad. Nauk SSSR, Ser. Khim Nauk *1970*, 149.

Fourier-Transform ^{13}C-NMR Spectroscopy of Polyols[**]

By *Wolfgang Voelter, Eberhard Breitmaier, Günther Jung, Toni Keller*, and *Dieter Hiss*[*]

The electron distribution in organic molecules, which can be approximated by quantum-mechanical calculations and described by molecular orbitals and substituent effects, is concerned primarily with the carbon atoms. The consideration of open-chain aliphatic polyalcohols shows that ^{13}C-NMR often provides more direct information about molecular configurations than proton magnetic resonance. Polyols widely occur in nature and are important for the characterization of sugars as their reduction products.

The Table lists the chemical shifts of the C atoms of a number of polyols measured relative to CS_2 as external standard. The shifts are determined from the accumulated Fourier-transform ^{13}C-NMR spectra decoupled from the ^{1}H noise. The following points warrant attention:

1) Replacement of an H atom in a polyol (*e.g.* 1,2-propanediol with $\delta_{C\text{-}3} = 171.05$ ppm) by a further OH group causes a downfield shift that is much greater than as observed in ^{1}H resonance (*e.g.* glycerol with $\delta_{C\text{-}1,3} = 127.1$).

2) The ^{13}C signals of primary C atoms in vicinal polyols are found between 126 and 130 ppm.

3) The ^{13}C signals of secondary C atoms in vicinal polyols are located between 117 and 122 ppm.

4) For polyols having a symmetric configuration such as ribitol *(9)* and xylitol *(10)* and D-mannitol *(12)* and galactitol *(14)*, the ^{13}C signals for C-1,5, C-2,4, and C-1,6, C-2,5, C-3,4, respectively, are found in pairs, so that only three signals are observed (Fig. 1a).

5) For polyols having an asymmetric configuration such as D-arabitol *(11)* and D-sorbitol *(13)* one signal for each C atom (Fig. 1b) is observed.

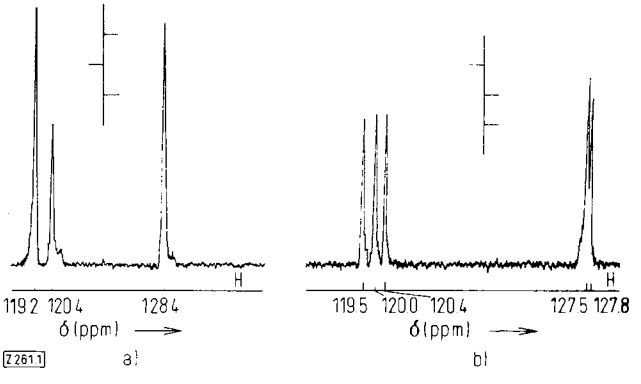


Fig. 1. Fourier-transform ^{13}C-NMR spectrum of a) xylitol *(10)* and b) D-arabitol *(11)*.

The signals of *(2)* to *(7)* are assigned by considering the ^{13}C-^{1}H spin multiplets of the partially decoupled spectra. The ^{13}C signals of the compounds *(8)* to *(10)* can be assigned unequivocally from the intensity ratios. Thus the signal for C-3 in *(10)* appears upfield, and the corresponding signal of *(9)* downfield, from the unresolved signal for C-2,4 (see Table). On the basis of this finding, a partial assignment of the spectra of the polyols *(11)* to *(14)* is possible by comparison of configurations (see Table). For instance, the configurations of C-1,4 in xylitol and D-sorbitol are the same; consequently, the ^{13}C signal for C-3 of D-sorbitol is found upfield ($\delta = 121.1$ ppm) and the signal for C-5 downfield ($\delta = 117.9$ ppm) when compared with those of the C-2,4 group ($\delta = 119.5$ and 119.7 ppm).

The ^{1}H-noise-decoupled Fourier-transform ^{13}C-NMR spectra were recorded with 20% aqueous solutions on a Bruker HX 90 14″ spectrometer at 50 °C, 22.63 MHz, and

Table. ^{13}C chemical shifts of polyols.

		δ (ppm)							
		—C—	$-CH_3$	$-CH_2-$	CH_2OH	2-CHOH	3-CHOH	4-CHOH	5-CHOH
Glycol	*(1)*	—	—	—	126.7	—	—	—	—
1,2-Propanediol	*(2)*	—	171.05	—	122.4	121.3	—	—	—
1,3-Butanediol	*(3)*	—	167.1	149.2	130.8	—	124.7	—	—
1,4-Butanediol	*(4)*	—	—	162.3	128.5	—	—	—	—
Glycerol	*(5)*	—	—	—	127.1	117.6	—	—	—
Erythritol [a]	*(6)*	—	—	—	127.1	118	118	—	—
Erythritol [a]	*(7)*	—	—	—	127.8	118.7	118.7	—	—
Pentaerythritol	*(8)*	145.7	—	—	129.7	—	—		—
Ribitol	*(9)*	—	—	—	128.5	118.65	118.4	118.65	—
Xylitol	*(10)*	—	—	—	128.15	118.8	120.1	118.8	—
D-Arabitol	*(11)*	—	—	—	127.5 127.8	120.4	120	119.5	—
D-Mannitol	*(12)*	—	—	—	126.7	118.7	120.4	120.4	118.7
D-Sorbitol	*(13)*	—	—	—	128.25 127.9	119.5 119.7	121.1	119.5 119.7	117.9
Galactitol	*(14)*	—	—	—	127.8	120.7	121.4	121.4	120.7

[a] Different sources.

a pulse duration of 40 μs with accumulation of 500 to 1000 scans of 0.8 s (^{19}F peak of hexafluorobenzene used for stabilization). The chemical shifts initially recorded relative to TMS as external reference were converted to the usual δ_{CS_2} values according to the relationship $\delta_{CS_2} = \delta_{TMS} + 194$ (ppm). Owing to the large magnitude of the shifts, susceptibility corrections can be neglected.

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[**] 1st communication on Fourier-Transform ^{13}C-NMR Spectroscopy.

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Radical 1,3-Migration of Arylazo Groups – CIDNP Effect with *p*-Tolyl Protons

By *Jochen Hollaender* and *Wilhelm P. Neumann* [*]

In our investigations of free radical reactions of azo compounds [1] we examined the spontaneous decomposition of 1,3,5-triarylpentazadienes *(1)*—*(4)* [2]. It proceeds in accordance with eq. (1) [3].

However, we also found that a very rapid 1,3-migration of arylazo groups occurs which affords mixtures of *(2a)* and *(2b)* and of *(3a)* and *(3b)* from *(2a)* and *(3a)* respectively. This migration must proceed intramolecularly since no mixed pentazadienes *(2)* or *(3)* occur in the mixture of triphenyl- *(1)* and tri-*p*-tolyl derivative *(4)*. A radical pair is formed (in a solvent cage) as intermediate, as we were able to confirm by the appearance of a "chemically induced dynamic nuclear polarization" (CIDNP) [4] of the methyl protons in the ^1H-NMR spectrum of *(2)*—*(4)* [5].

$$Ar^1\text{-}N{=}N\text{-}\underset{\bullet}{N}\text{-}Ar^3 + \dot{A}r^5 \xrightarrow{-N_2} \underset{\text{(1)-(4)}}{Ar^1\text{-}N{=}N\text{-}\underset{\displaystyle Ar^3}{\underset{|}{N}}\text{-}N{=}N\text{-}Ar^5} \xrightarrow{-N_2} \dot{A}r^1 + Ar^3\text{-}\dot{N}\text{-}N{=}N\text{-}Ar^5 \qquad (1)$$

	Ar^1	Ar^2	Ar^5
(1)	C_6H_5	C_6H_5	C_6H_5
(2a)	C_6H_5	C_6H_5	p-CH_3—C_6H_4
(2b)	C_6H_5	p-CH_3—C_6H_4	C_6H_5
(3a)	p-CH_3—C_6H_4	p-CH_3—C_6H_4	C_6H_5
(3b)	p-CH_3—C_6H_4	C_6H_5	p-CH_3—C_6H_4
(4)	p-CH_3—C_6H_4	p-CH_3—C_6H_4	p-CH_3—C_6H_4

In the case of *(4)* reactants and rearrangement products are chemically identical [eq. (2)]. An NMR signal of the CH_3 protons (τ = 7.96 in benzene, 70 °C) appears momentarily as emission (negative polarization) and then later, after quenching the mixture, as normal absorption. The situation is much clearer in chloroform solution at 40 °C (cf. Figure).

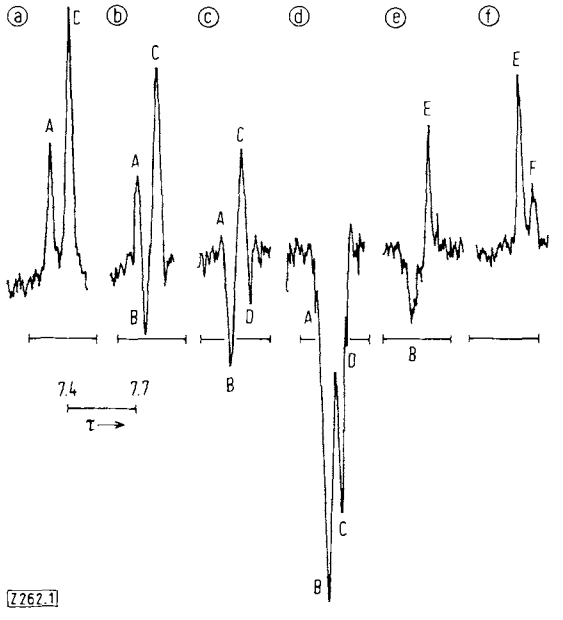
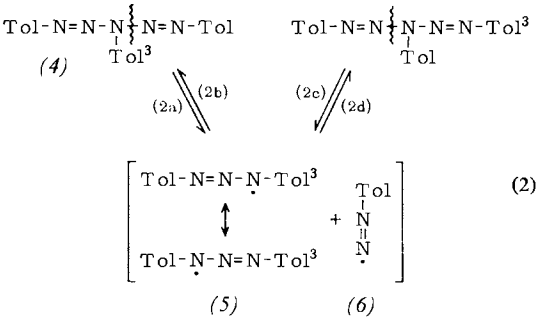


Figure. ^1H-NMR spectrum of 1,3,5-tri-*p*-tolylpentazadiene *(4)* during decomposition in $CHCl_3$: a—e) within 50 s, f) after 1h. A—C: see text; D—F: signals of products [6].

The CH_3 signals of the central *p*-tolyl group like those of the terminal *p*-tolyl groups A and C (τ = 7.49 and 7.57 resp.) appear as emission caused by radical pair recombination without isomerization, *i.e.* corresponding to eq. (2a) + (2b) and (2c) + (2d). In recombination with isomerization, *i.e.* according to eq. (2a) + (2d) and (2c) + (2b), central and terminal tolyl groups exchange positions, thus leading to a new orientation of the CH_3 protons. We ascribe the strongest emission B at τ = 7.52, which must be referred to as a coalescence signal [6], to this effect.



(2)

The above mentioned emissions can be ascribed to that part of the molecule which is formed from the intermediate spin-delocalized triazenyl radical *(5)* in the recombination. The part arising from the *p*-tolylazo radical *(6)* apparently does not play any effective role in the polarization of CH_3 protons, as we have been able to show in our experiments with *p*-tolylazotriphenylmethane.

These findings confirm the existence of arylazo radicals, *e.g. (6)*, which have already been formulated on many occasions as reactive intermediates[7] and support the idea of CIDNP in radical pair recombination in the solvent cage[4c].

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[1] Previous communication: *W. P. Neumann, H. Lind,* and *G. Alester,* Chem. Ber. *101*, 2845 (1968).

[2] Prepared according to *H. v. Pechmann* and *L. Frobenius,* Ber. Dtsch. Chem. Ges. *28*, 170 (1895), with coupling, however, at –20 °C.

[3] *E.g. (1)*, 0.1 M in cumene at 25 °C, has a half-life of 18.5 min.

[4] a) *J. Bargon, H. Fischer,* and *U. Johnson,* Z. Naturforsch. *22a*, 1551 (1967); b) *H. R. Ward* and *R. G. Lawler,* J. Amer. Chem. Soc. *89*, 5518 (1967); c) *G. L. Closs* and *A. D. Trifunac, ibid. 92*, 2186 (1970), and literature cited therein.

[5] The detection of CIDNP on aryl protons in *(1)–(4)* is rendered difficult by the simultaneously occurring emissions from the degradation products.

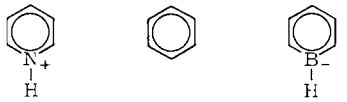
[6] Further observed CIDNP phenomena (emissions and enhanced absorptions) and their ascription to the degradation products cannot be dealt with here.

[7] *J. F. Garst* and *G. S. Hammond,* J. Org. Chem. *23*, 98 (1958); *W. A. Pryor* and *K. Smith,* J. Amer. Chem. Soc. *89*, 1741 (1967).

A Novel Aromatic Boron Heterocycle as Ligand in a Transition Metal π-Complex[**]

By *Gerhard E. Herberich, Georg Greiss,* and *Horst F. Heil*[*]

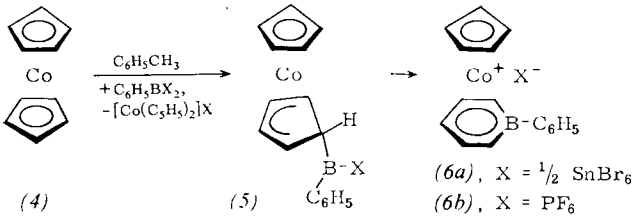
Pyridinium ion *(1)*, benzene *(2)*, and the hitherto unknown hydridoborinate ion *(3)* are members of an isoelectronic series:



(1) *(2)* *(3)*

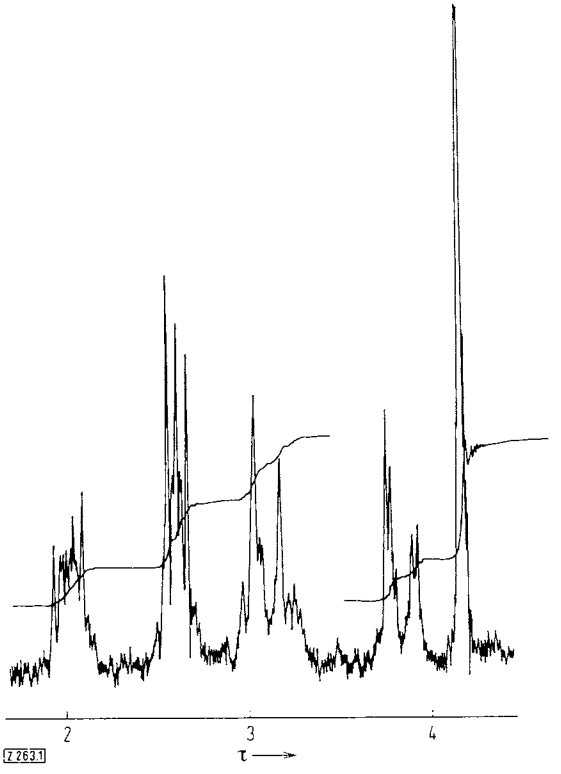
We have now synthesized the first transition metal π-complexes containing ligands of type *(3)* by using bis(cyclopentadienyl)cobalt *(4)* and boron halides or organoboron halides as starting materials.

By analogy with previous investigations on the reaction of *(4)* with organohalides[1,2] and on the ring expansion of the 5-*exo*-halogenomethyl derivatives of cyclopentadiene-cyclopentadienylcobalt[3,4] one could expect a reaction scheme for the reaction of *(4)* with boron halides and organoboron halides as exemplified here for phenylboron dibromide (with X = Br):



(4) *(5)* *(6a)*, X = ½ $SnBr_6$ *(6b)*, X = PF_6

In fact *(4)* reacts with phenylboron dibromide[5] at –50 °C in toluene to give bis(cyclopentadienyl)cobalt bromide and a red unstable solution[6]. Salts *(6)* separate upon treatment with halide acceptors at room temperature. Thus addition of $SnBr_4$ produces the hexabromostannate *(6a)*, which can be converted into the hexafluorophosphate *(6b)* (orange red needles, m.p. 139 °C, stable in air) by hydrolysis and subsequent precipitation with NH_4PF_6 solution.



The ^{1}H-NMR spectrum (see Figure) of *(6b)* (in CD_3COCD_3, TMS as internal standard, at 60 MHz, 30 °C) contains the singlet of the cyclopentadienyl ring at τ = 4.16, two multiplets of the phenyl group at τ = 2.0 and 2.6, and two multiplets of the remaining five protons at τ = 3.1 and 3.83. The latter signals appear within a remarkably narrow range of less than 0.8 ppm and further downfield than the signal of the C_5H_5 ring. The ^{11}B-NMR spectrum[7] (in CD_3COCD_3, external $BF_3 \cdot O(C_2H_5)_2$, at 100 MHz, room temperature) shows a singlet at δ = –23.3 ppm. These data indicate a planar benzenoid six-membered ring structure[8] of the C_5H_5B grouping in *(6)*. The boron atom, thus being part of a 6π electron system, fully participates in the bonding to the metal. Alternative structures with aliphatic protons, B–H bonds, or a diene grouping can be disregarded[9]. Furthermore, a non-planar structure similar to that of cyclohexadienyl ligands[10], in which the phenylborylene group would be displaced by about 40–50° from the

plane of the dienyl carbon atoms, is not consistent with the NMR data[9,11].

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[3] *G. E. Herberich* and *J. Schwarzer*, Angew. Chem. *81*, 153 (1969); Angew. Chem. internat. Edit. *8*, 143 (1969).

[4] *G. E. Herberich* and *J. Schwarzer*, Chem. Ber. *103*, 2016 (1970); *G. E. Herberich, G. Greiß*, and *H. F. Heil*, J. Organometal. Chem. *22*, 723 (1970).

[5] *H. Nöth* and *H. Vahrenkamp*, J. Organometal. Chem. *11*, 399 (1968).

[6] Presumably of the intermediate *(5)*, which has not yet been isolated on account of its extreme sensitivity.

[7] Measurements by Dipl.-Chem. *Schmidt-Sudhoff*, Universität München. We thank Dr. *H. Nöth* for his valuable suggestions.

[8] X-ray structure analysis ought to provide direct proof of such a structure. Measurements are at present being carried out on $Co(C_5H_5BOCH_3)_2$; *G. Huttner* and *B. Krieg*, unpublished.

[9] Cf: *M. L. Maddox, S. L. Stafford*, and *H. D. Kaesz*, Advan. Organometal. Chem. *3*, 1 (1965); *J. W. Emsley, J. Feeney*, and *L. H. Sutcliffe*: High Resolution Nuclear Magnetic Resonance Spectroscopy, Vol. 2, Pergamon Press, London 1968.

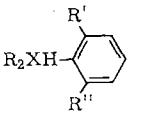
[10] *P. H. Bird* and *M. R. Churchill*, Chem. Commun. *1967*, 777; *M. R. Churchill* and *F. R. Scholer*, Inorg. Chem. *8*, 1950 (1969).

[11] For such a structure having tricovalent boron an ^{11}B-resonance would be expected at $\delta = -50$ to -80 ppm; the signals of the dienyl protons should appear in the range $\tau = 2.5$ to 6.0; cf. [3, 9].

Conformations of *ortho*-Disubstituted Aniline and Toluene Derivatives. Proton Magnetic Resonance and Semiempirical Energy Calculation[1] [**]

By *Albrecht Mannschreck, Ludger Ernst*, and *Elmar Keck* [*]

Compared to the situation at sp^3-sp^3 and sp^2-sp^2 valences, little is known about the conformations resulting from rotation about sp^2-sp^3 bonds or about their relative energies. Compounds of types *(1)* and *(2)* are suited to experimental study of the possible conformers because their lifetimes are especially long. Such rotamers have been



(1), X = $N^{\oplus}$
(2), X = C

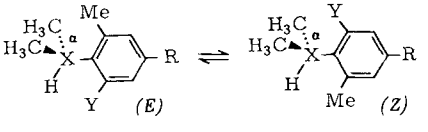
described for *N,N*-dibenzylanilinium ions *(1)*[2] and for 9-arylfluorenes[3], which may be regarded as toluene derivatives *(2)*. It has repeatedly been suggested[2–6] that those conformations are most favored in which the proton at the sp^3 center eclipses an *ortho* substituent. This assumption is now strongly supported by semiempirical energy calculations on toluenes *(2)* for which we also determined, for the first time, the most unfavorable conformation, *i.e.* the transition state of the sp^2-sp^3 rotation. Moreover our calculations reproduce the rotamer equilibria which we were able to measure for the structurally simple toluenes *(5)* and *(6)* and for the isoelectronic *N,N*-dimethylanilinium ions *(3)* and *(4)*.

Reaction of 6-chloro-2-methylaniline and 6-bromo-2,4-dimethylaniline, respectively, with dimethyl sulfate yielded the corresponding *N,N*-dimethyl compounds (b.p. 84-85 °C/12 torr, n_D^{25} 1.5248, and b.p. 65–67 °C/0.001 torr, n_D^{25} 1.5433, resp.) which on dissolution in CF_3CO_2H gave the anilinium ions *(3)* and *(4)*. We obtained *(5)* from 5-chloro-1,3-dimethylbenzene and isopropanol/H_2SO_4; after purification by GLC the sample of *(5)* still contained 5 % of 5-chloro-1,3-dimethyl-2-isopropylbenzene. Bromination of 4-nitro-2-methyl-1-isopropylbenzene[7] in the presence of Ag_2SO_4/H_2SO_4 yielded *(6)* which, after separation by GLC, was still contaminated by 25 % of 5-bromo-4-nitro-2-methyl-1-isopropylbenzene (m.p. 50–52 °C). The absorptions of this by-product, however, did not interfere with those of *(6)*.

For *(3)* and *(4)* in CF_3CO_2H at +27 °C as well as for *(5)* and *(6)* in CS_2 at −55 °C we found two sets of ^1H-NMR signals which are due to rotamers (*E*) and (*Z*) (Table) and coalesce upon raising the temperature[5]. The assignment of signals to rotamers will be explained for the case of (*E*)-*(5)* and (*Z*)-*(5)*. The α-CH septet at $\tau = 6.69$ (CH) is due to isomer (*Z*)-*(5)* where the methine proton and the *ortho* methyl group experience the same environment as in the symmetrical toluene *(7)* showing $\tau = 6.81$ (CH) (CS_2, −60 °C)[5]. In (*E*)-*(5)*, however, the methine proton is adjacent to the chlorine atom, which causes a deshielding through space and shifts the α-CH resonance to $\tau = 6.18$ (CH) (septet). The α-methyl protons of (*E*)-*(5)* and (*Z*)-*(5)* give rise to doublets at $\tau = 8.74$ and 8.65, respectively, which were correlated in the same way.

The energy *E* of a conformation was calculated by addition of the following partial energies[8]: a) stretching energy

Table. Rotamer percentages P and chemical shifts τ in anilinium ions (X=$N^{\oplus}$, CF_3CO_2H, + 27 °C) and toluenes (X=C, CS_2, −55 °C) as determined by ^1H-NMR.

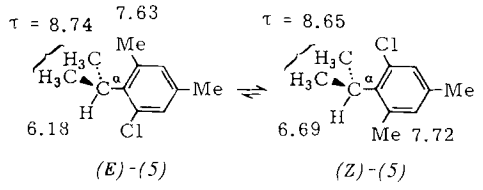


(*E*) ⇌ (*Z*)

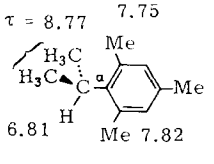
	X	Y	R	(*E*) P (%)	(*E*) τ(α-CH_3) [a]	(*E*) τ(*o*-CH_3)	(*Z*) P (%)	(*Z*) τ(α-CH_3) [a]	(*Z*) τ(*o*-CH_3)
(3)	$N^{\oplus}$	Cl	H	45	6.34	7.22	55	6.24	7.34
(4)	$N^{\oplus}$	Br	Me	62	6.37	7.27	38	6.25	7.39
(5)	C	Cl	Me	33	8.74	7.63	67	8.65	7.72
(6)	C	Br	NO_2	54	8.58	7.34	46	8.50	7.42

[a] Doublets by coupling with the $NH^{\oplus}$-proton ($J = 5$ Hz) of the anilinium ions (X=$N^{\oplus}$) and with the CH-proton ($J = 7$ Hz) of the toluene derivatives (X=C), resp.

of the bond between the α-C atom and the benzene ring; b) bending energy of the angles at the α-C atom and the angles formed by the bonds of the *ortho* substituents and the

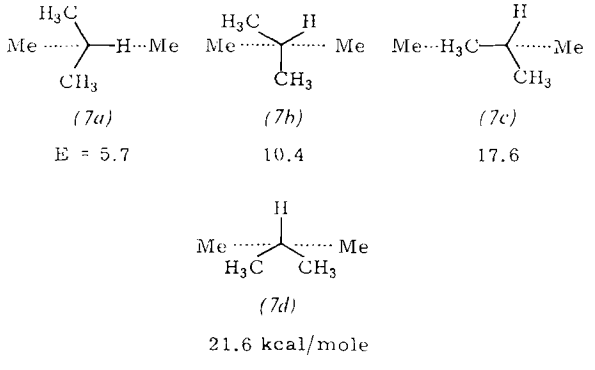


(E)-(5) *(Z)-(5)*



(7)

C—C bonds of the benzene ring; c) nonbonded interactions[9] between each *ortho* substituent and the neighboring *meta* proton on the one hand and the three α-substituents CH_3, CH_3, and H on the other. The specific geometry of a conformation was found by varying the C-aryl bond length and the above mentioned angles in small steps and by calculating the energies of all resulting combinations. The lowest energy combination was regarded as representing the geometry of that conformation.



(7a) *(7b)* *(7c)* *(7d)*

E = 5.7 10.4 17.6

21.6 kcal/mole

Thus for α,α,2,4,6-pentamethyltoluene *(7)* we found that conformation *(7a)* indeed shows the lowest energy. Compared to *(7a)*, *(7b)* is destabilized both by additional bond angle deformations and by a more unfavorable Me/CH_3 interaction. As shown by our calculation, this Me/CH_3 interaction (dihedral angle 0 °) is less repulsive in *(7c)* than the corresponding interaction *via ca.* 30 ° in *(7d)* which has to be counted twice. The transition state of the sp^2-sp^3 rotation is thus represented by *(7d)*. We obtained analogous results for α,α,2,4,6-pentachlorotoluene[6] as well as for *(5)* and *(6)*.

The calculation for these two toluene derivatives yielded energy differences between the (*E*)- and (*Z*)-rotamers. From these differences we obtained (with $\Delta S = 0$) rotamer equilibria (33 % (*E*)-*(5)* and 50 % (*E*)-*(6)*, resp.) which agree fairly well with the NMR results (Table). As to the corresponding anilinium ions *(3)* and *(4)*, their (*E*)-isomers are somewhat more favorable (Table) than (*E*)-*(5)* and (*E*)-*(6)*. This is perhaps due to weak intramolecular hydrogen bonds N—H···Y in (*E*)-*(3)* and (*E*)-*(4)* which, however, have still to be proved.

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] Part 7 of the series "Protonenresonanz-Untersuchungen zur inneren Rotation". – Part 6: *A. Jaeschke, H. Münsch, H. G. Schmid, H. Friebolin*, and *A. Mannschreck*, J. Mol. Spectrosc. *31*, 14 (1969).

[2] *A. Mannschreck* and *H. Münsch*, Tetrahedron Lett. *1968*, 3227.

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[4] *P. C. Myhre, J. W. Edmonds*, and *J. D. Kruger*, J. Amer. Chem. Soc. *88*, 2459 (1966); *E. A. Chandros* and *C. F. Sheley jr., ibid. 90*, 4345 (1968); *H. Kessler, A. Moosmayer*, and *A. Rieker*, Tetrahedron *25*, 287 (1969).

[5] Cf. *A. Mannschreck* and *L. Ernst*, Tetrahedron Lett. *1968*, 5939; Chem. Ber., submitted.

[6] Cf. *B. J. Fuhr, B. W. Goodwin, H. M. Hutton*, and *T. Schaefer*, Can. J. Chem. *48*, 1558 (1970).

[7] M.p. 33–34 °C. Prepared by $NaBH_4$ reduction of 4-nitro-2-chloromethyl-1-isopropylbenzene in dimethyl sulfoxide.

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"Single Vessel Reaction" for the Synthesis of Various Types of Substituted Phosphanes $PR^1R^2R^3$

By *Max Schmidt* and *Wolf-Rainer Neeff*[*]

Issleib and *Krech*[1] have recently investigated the nucleophilic cleavage of "phenylphosphorus" with phenyllithium and, on the basis of their findings, quite justifiably postulated the existence of an analogy between elemental sulfur $(-S-)_x$, and cyclopolyphosphanes $(-PR-)_x$. Such a working hypothesis served as a starting point for investigations which we have been carrying out for some time now[2] on the degradation reactions of cyclopolyphosphanes with Lewis bases as a parallel to the many examples already known in the case of sulfur[3]. According to this hypothesis one would expect the cyclic phosphanes $(RP)_n$ to react with organolithium compounds as follows:

$$(R^1P)_n + n\,LiR^2 \rightarrow n\,LiPR^1R^2$$

The lithium phosphides then formed could react with organohalides according to:

$$LiPR^1R^2 + R^3X \rightarrow LiX + PR^1R^2R^3$$

In fact we have been able to show that various types of organophosphanes can be prepared quite easily, and in manageable yields according to this principle in a "single vessel reaction" with exclusion of air and moisture, if solutions of an organolithium compound LiR^2 and an organochloride R^3Cl are added simultaneously to a solution of cyclopolyphosphane $(R^1P)_n$:

$$(R^1P)_n + n\,LiR^2 + n\,R^3Cl \rightarrow n\,PR^1R^2R^3 + n\,LiCl$$

The phosphanes thus obtained react as expected with methyl iodide to give the corresponding phosphonium salts (with R^1, R^2, and $R^3 \neq CH_3$, completely unsymmetrical). If triorgano-silyl, -germyl, or -stannyl chlorides are used instead of RCl the analogous phosphanes containing P—Si, P—Ge, or P—Sn bonds respectively are obtained.

Obvious side reactions, which lower the yields of the mononuclear phosphanes (some of which – depending on the substituents are difficult to handle and occasionally ignite

spontaneously in air) in this apparently general method of synthesis will not be considered here. The limitations of the method become apparent when bifunctional halogenoalkanes are used; the above mentioned side reactions then predominate and as a result the isolation of homogeneous reaction products is made impossible.

We have successfully coupled to phosphorus various combinations of the same or different residues R where R is: CH_3, C_2H_5, C_3H_7, *n*-C_4H_9, *t*-C_4H_9, C_6H_5, $(CH_3)_3Si$, $(CH_3)_3Ge$, and $(CH_3)_3Sn$.

Typical procedure:

Solutions of LiC_4H_9 (0.64 g, 10 mmoles) and C_3H_7Cl (0.79 g, 10 mmoles) in pentane (10 ml) are added dropwise and simultaneously to a solution of $(C_2H_5P)_4$ (0.6 g; 2.5 mmoles) in boiling pentane (50 ml) with exclusion of oxygen and moisture. The resulting yellow mixture is heated under reflux for 12 h and then stirred for a further 48 h at room temperature. The yellow color vanishes, and a white precipitate (LiCl) separates out. Fractional distillation at 58—59 °C/1 torr yields colorless ethylpropylbutylphosphane $P(C_2H_5)(n\text{-}C_3H_7)(n\text{-}C_4H_9)$. On treatment with methyl iodide in ether it is converted into methylethylpropylbutylphosphonium iodide $[(CH_3)(C_2H_5)(C_3H_7)(C_4H_9)P]I$.

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[1] *K. Issleib* and *F. Krech*, Z. anorg. allg. Chem. *372*, 65 (1970).
[2] *W. R. Neeff*, Dissertation, Universität Würzburg 1969.
[3] *M. Schmidt*, Österr. Chemiker-Ztg. *64*, 236 (1963).

Iodophosphanes PH_2I and PHI_2

By *Max Schmidt* and *Helmut H. J. Schröder* [*]

Between phosphane, PH_3 and the four phosphorus trihalides, PX_3 (X = F, Cl, Br, I), there are, in principle, eight possible halogenophosphanes PH_2X and PHX_2, of which only the difluorophosphane PHF_2 has, as yet, been characterized [1]. However, in view of the drastic difference between fluorine on the one hand and the heavier halogens on the other this compound can hardly be compared with the other formally possible halogenophosphanes.

Alkyl and aryl iodophosphanes, RPI_2 and R_2PI, have been known for some time. We set out to isolate the formal fundamental members of this class of compounds, HPI_2 and H_2PI. We were able to detect them for the first time as intermediates in the electrophilic degradation of white phosphorus, P_4, with anhydrous hydriodic acid, which led to P_2I_4 and PH_3 [2]. We have now been able to synthesize the new iodophosphanes PH_2I and PHI_2 by hydrogen-iodine exchange reactions of phosphane with PI_3, P_2I_4 or I_2:

$$PH_3 + 2\,PI_3 \rightleftharpoons 3\,PHI_2$$
$$2\,PH_3 + PI_3 \rightleftharpoons 3\,PH_2I$$
$$PH_4I + P_2I_4 \rightleftharpoons 2\,PHI_2 + PH_2I$$
$$PH_3 + 2\,I_2 \rightleftharpoons PHI_2 + 2\,HI$$
$$PH_3 + I_2 \rightleftharpoons PH_2I + HI$$

In anhydrous solvents such as CS_2, the products are stable only in equilibrium with the reactants and with hydriodic acid. All attempts at isolating them failed since HI cleavage takes place, the final products being PI_3 and P_2I_4.

^{1}H-NMR spectrum (TMS, internal): PHI_2 in CS_2: doublet −5.03 ppm, J_{P-H} = 145 Hz; PH_2I in CS_2: doublet −2.95 ppm, J_{P-H} = 168 Hz; PHI_2 in C_6D_6: doublet −3.40 ppm, J_{P-H} = 147 Hz; PH_2I in C_6D_6: doublet −1.42 ppm, J_{P-H} = 171 Hz.

^{31}P-NMR spectrum (85 % H_3PO_4, external): PHI_2 in CS_2: doublet +9 ppm, J_{P-H} = 145 Hz, PH_2I in CS_2: triplet +156 ppm, J_{P-H} = 168 Hz.

These NMR data can be attributed to a transition from p to sp^3 orbitals for the bonds along the series $PH_3 \rightarrow PH_2I \rightarrow PHI_2 \rightarrow PI_3$.

On the basis of the IR spectra (4000—260 cm^{-1}) of the solutions obtained in CS_2 in the above mentioned reactions the following frequencies can be assigned to PHI_2: νPH 2260—2270, δPH 781—782, ν_{as}PI 327—329, ν_sPI 320—322 cm^{-1}; and to PH_2I: νPH 2360, δPH 750 cm^{-1}.

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German version: Angew. Chem. *82*, 808 (1970)

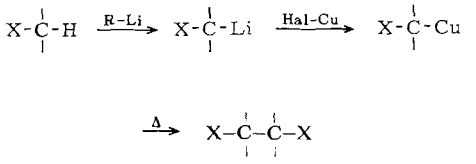
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[1] *R. W. Rudolph* and *R. W. Parry*, Inorg. Chem. *4*, 1339 (1965).
[2] *M. Schmidt* and *H. H. J. Schröder*, Z. anorg. allg. Chem., in press.

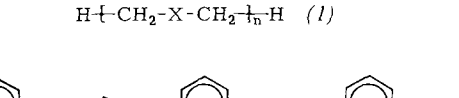
Selective Metalation of 1,2-Bis(6-methyl-2-pyridyl)-ethane and its Preparative Uses [1] [**]

By *Thomas Kauffmann, Gerhard Beissner, Wilfried Sahm,* and *Annegret Woltermann* [*]

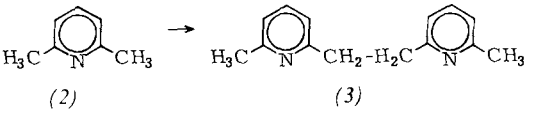
The coupling of organic ligands bound to mono- or divalent copper is a convenient method for linking sp^3 C atoms if an activating group X is present which permits direct alkali metalation (hydrogen-metal exchange) and subsequent introduction of copper by transmetalation [2].



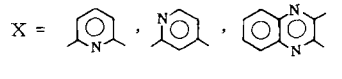
If X is bound, as in *(2)*, to two methyl groups, this ligand coupling leads to formation of the second member (n = 2) of the homologous series *(1)* containing the given group X [3, 5].

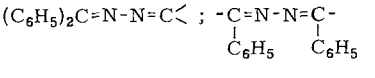


(1)



(2) *(3)*

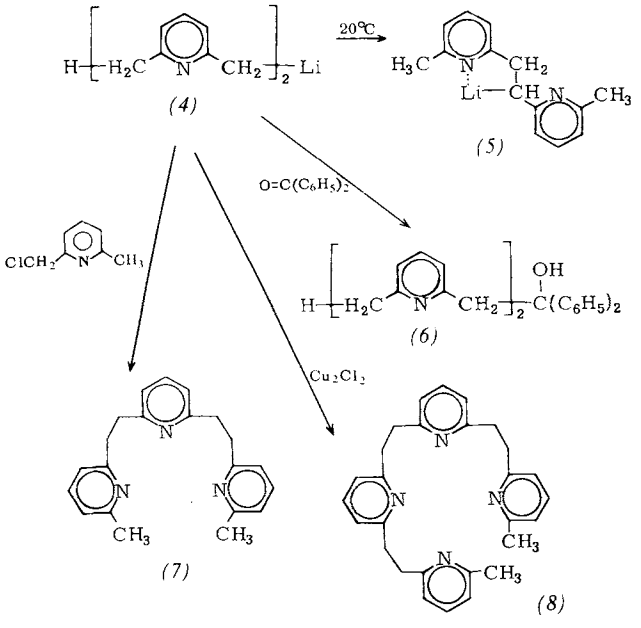




A selective metalation at the methyl groups of the second member would prove advantageous for the preparation of higher members. We have succeeded in carrying out such a metalation in the case of compound *(3)*: On reacting 1,2-bis(6-methyl-2-pyridyl)ethane *(3)* in THF/*n*-hexane (*ca.*

10:1) at −70 °C (≙ "standard conditions") with *n*-butyllithium in the molar ratio 1:1 or 1:2 the methyl/methylene metalation ratio was 83/17 in each case (NMR analysis of D_2O-hydrolysis product). The monolithium compound *(4)* obtained as main product (yield 62%) in the solution after reaction with one molar equivalent of *n*-butyllithium rearranges irreversibly on warming at +20 °C to the methylene metalation product *(5)*, whose higher thermodynamic stability can be explained by the given chelate structure[6].

Reaction of *(4)* under "standard conditions" (see above) with 2-chloromethyl-6-methylpyridine[7] or $CuCl_2$[8] (in the molar ratio 1:1 in each case) leads to the formation of 2,6-bis[2-(6-methyl-2-pyridylethyl]pyridine *(7)* (60%; m.p. 108 °C)[9] or 1,2-bis{6-[2-(6-methyl-2-pyridyl)ethyl]-2-pyridyl}ethane *(8)* (48%; m.p. 145 °C), the third and fourth members respectively of the homologous series *(1)* (X = 2,6-pyridinediyl). The corresponding reaction with benzophenone leads to the alcohol *(6)* (61%, m.p. 95 °C)[10].



(4) *(5)* *(6)* *(7)* *(8)*

The dilithium compound *(9)*, which is obtained in 82% yield by reaction of *(3)* with two mol. equiv. of *n*-butyllithium, reacts with Cu_2Cl_2 (2 mol. equiv.) under standard conditions[8] to give the previously reported[11] pyridinophanes *(11)* and *(12)* in 1% and 4% yields respectively; application of the dilution principle does not increase the yields. Mass spectrometric analysis of the reaction products revealed the presence — in addition to that of *(11)* and *(12)* — of the cyclic dehydrohexamer of *(2)* and to the open-chain dehydropolymer having 4,6,8, and 10 pyridine nuclei.

Compound *(9)* reacts with 2 mol. equiv. of 2-chloromethyl-6-methylpyridine or benzophenone to give *(8)* (67%) or *(10)* (79%, m.p. 244 °C) respectively.

Unlike compound *(3)*, the higher homologs *(7)* and *(8)* do not undergo selective metalation at the methyl groups on reaction with *n*-butyllithium (under standard conditions with 2 moles of butyllithium, ratio of methyl/methylene metalation ≈ 55/45 and 19/81 resp.). The low methyl metalation in the case of *(8)* cannot be explained only as being due to the unfavorable ratio of methyl/methylene protons (33/67).

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[1] Activation of organic compounds by introduction of transition metal atoms, Part 8: — Part 7: [2].

[2] *Th. Kauffmann* and *M. Schönfelder*, Liebigs Ann. Chem. *731*, 37 (1970).

[3] Cf. [2] and [4] and literature cited therein.

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[6] That N atoms in the γ-position exert a directing influence in hydrogen-metal exchange by development of a coordinate bond to the metal has been observed on many occasions. Cf. *e.g. R. L. Vaux, W. M. Puterbaugh*, and *C. R. Hauser*, J. inorg. Chem. *29*, 3514 (1964); *G. Wittig* and *H. Reiff*, Angew. Chem. *80*, 8 (1968); Angew. Chem. internat. Edit. *7*, 7 (1968).

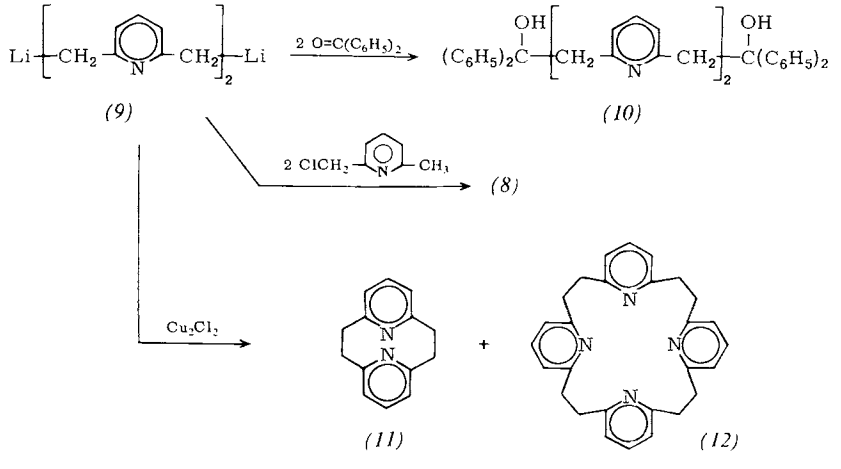
[7] *W. Mathes* and *H. Schüly*, Angew. Chem. *75*, 235 (1963); Angew. Chem. internat. Edit. *2*, 144 (1963).

[8] In the reaction with Cu_2Cl_2, the reaction mixture was finally heated to +60 °C.

[9] Yields based on *(3)*. The structures of the new compounds (characterized by m.p. values) are established by elemental analysis, molecular weight determinations, and NMR, IR, and mass spectrometry.

[10] In the reaction of *(4)* with benzophenone and with 2-chloromethyl-6-methylpyridine the disubstitution products *(10)* and *(8)* respectively are formed alongside the monosubstitution products *(6)* and *(7)* (7% and 5% yields resp.) since the monolithium compound *(4)* is in equilibrium with the dilithium- *(9)* and non-metalated compound *(3)* [ratio of *(4)*/*(9)* *ca.* 8:1].

[11] *W. Backer, K. M. Buggle, J. F. W. McOmie*, and *D. A. M. Watkins*, J. chem. Soc. *1958*, 3594; *W. Jenny* and *H. Holzrichter*, Chimia *22*, 306 (1968).



(9) *(10)* *(8)* *(11)* *(12)*

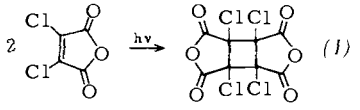
[1,2,3,4-Tetrakis(methoxycarbonyl)cyclobutadiene]-tetracarbonylmolybdenum[**]

By *H. D. Scharf* and *K. R. Stahlke*[*]

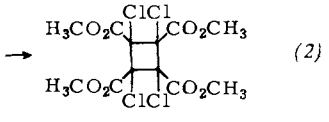
In a previous communication we reported on the photochemical (2+2)-cyclodimerization of dichloro- and dibromomaleimides in dioxane[1]. No dimerization products were formed on photolysis of solutions of the corresponding maleic anhydrides at the same concentrations (0.2 M solutions).

We have now found that irradiation of a concentrated solution of dichloromaleic anhydride in acetone (optimum concentration 2.5—3.0 moles/l) at room temperature with light of wavelength $\lambda > 290$ nm[2] yields a dimeric dichloromaleic anhydride *(1)*; m.p. 280 °C (dioxane)[3], IR spectrum: $\tilde{\nu}$ = 1800 (C=O), 1880 (C=O), 785 cm^{-1} (C—Cl).

Since the reaction is not quenched by triplet quenchers and since only one isomer of *(1)* is formed, we assume that a singlet reaction is involved, probably *via* an excimer mechanism. Because of the very short lifetime of singlet excited molecules it is reasonable that dimerization is to be observed only in concentrated solutions.



(1)

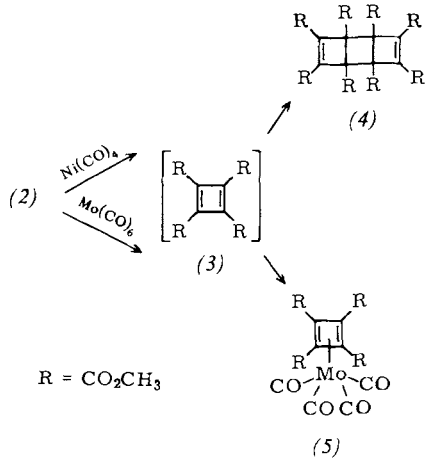


(2)

Reaction of *(1)* with diazomethane yields the tetramethyl ester *(2)* [m.p. 106 °C (methanol); IR spectrum: $\tilde{\nu}$ = 2840 (methyl stretching vibration); 1750 (C=O); 1250 (C—O—C), 710 cm^{-1} (C—Cl); ^{1}H-NMR spectrum: τ = 6.15 (s)[4]].

It was of interest to examine the influence of electronegative substituents[5], in this case of the ester group, on the stability of the cyclobutadiene system. Only the tricyclic compound *(4)* [m.p. 158 °C (methanol); IR spectrum: $\tilde{\nu}$ = 1730 (C=O), 1630 cm^{-1} (C=C); ^{1}H-NMR spectrum: τ = 6.14 (12 H/s), 6.30 (12 H/s)] could be obtained on dehalogenation of *(2)* with $Ni(CO)_4$.

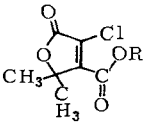
However, in the dehalogenation of *(2)* with $Mo(CO)_6$ the tetrakis(methoxycarbonyl)cyclobutadiene *(3)* could be isolated in small amounts as the tetracarbonylmolybdenum complex *(5)* along with the tricyclic compound *(4)*. The deep red square crystals melt at 180—182 °C (methanol); IR spectrum: $\tilde{\nu}$ = 1910 and 1990 cm^{-1} (symmetric and antisymmetric CO vibration)[6]; ^{1}H-NMR spectrum: τ = 6.5 (s).



(4)

(5)

On the basis of spectroscopic data[7] we assign the α-chlorodehydroterebic acid structure to the secondary product *(6)* [m.p. 104—105 °C (CCl_4)] formed in the prolonged irradiation of dichloromaleic anhydride. The acid *(6)* can be esterified to *(7)* by reaction with diazomethane. The mode of formation of *(6)* is reminiscent of the synthesis of terebic acid from isopropanol and maleic acid[8] under similar conditions.



(6), R = H
(7), R = CH_3

1,2,3,4-Tetrachlorocyclobutanetetracarboxylic dianhydride (1)

A solution of dichloromaleic anhydride (52 g, multisublimed) in anhydrous acetone (100 ml) is irradiated for three days[2]; the dimer *(1)* formed is filtered off and recrystallized from anhydrous dioxane. The yield of *(1)* can be increased to 6 g (12%) by further irradiation of the filtrate for 200 h. The yield is very much dependent on the purity of the dichloromaleic anhydride.

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[**] This work was supported by the Fonds der chemischen Industrie.

[1] *H. D. Scharf* and *F. Korte*, Chem. Ber. *98*, 764 (1965).

[2] High-pressure Hg vapor lamp HPK 125 Philips, pyrex filter.

[3] The elemental analyses of compounds *(1)*—*(7)* are consistent with the given structures.

[4] Varian A 60 spectrometer; solvent: CCl_4 or $CHCl_3$; TMS as internal standard.

[5] See also *R. Criegee* and *R. Huber*, Chem. Ber. *103*, 1862 (1970).

[6] *R. A. Friedel* and *J. Wender*, J. Amer. chem. Soc. *77*, 3951 (1955).

[7] Both substances given M—CO as the basic mass in the mass spectrum. We thank Dr. *A. W. Fehlhaber*, Bonn, for recording the spectra.

[8] *G. O. Schenk* and *G. Koltzenburg*, Angew. Chem. *69*, 177 (1957).

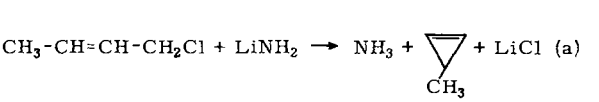
3-Methylcyclopropene from 1-Chloro-2-butenes

By *Roland Köster*, *Someshwar Arora*, and *Paul Binger*[*]

We have devised a simple method for the preparation of pure 3-methylcyclopropene *(1)* in yields of up to *ca.* 35% from 1-chloro-2-butenes (*cis*- and *trans*-crotyl chloride)[2] (cf.[1]). Compound *(1)* had been previously prepared in only 2% yields from 1-chloro-*trans*-2-butene and sodium amide in tetrahydrofuran[3].

Dropwise addition of crotyl chloride[2] to a suspension of lithium amide in boiling dioxane leads to the formation of *(1)* in *ca.* 35% yield. Up to 80% of the calculated amount [eq. (a)] of ammonia is liberated as gas along with *(1)*. From this gas mixture *(1)* (IR[4], mass, and ^{1}H-NMR spectra[4]) is recovered in 30% yield and 98% purity. It is essential that the suspension contain traces of water or alternatively small amounts of LiOH.

The use of sodium amide in different ethers results in varying yields of *(1)* (diethyl ether 11%, diethylene glycol di-



(1)

methyl ether 21%, dioxane 34%). 1,3-Butadiene and 1-methylcyclopropene are the usual by-products and therefore it has never been possible to achieve higher than 90% purity. Potassium amide cleaves boiling dioxane and is therefore not suitable for this synthesis.

A particular advantage of the $LiNH_2$ method is that the thermally unstable *(1)* is immediately formed in a very pure form. Even at 0 °C the exothermic oligomerization of *(1)* results in numerous hydrocarbons $(C_4H_6)_n$ where $n = 2$ ($\geq$2 isomers), $n = 3$ ($\geq$6 isomers), and $n = 4$ ($\geq$7 isomers), which can be detected by a combination of GC—MS. On the other hand, dropwise addition of a pre-cooled (—78 °C) 3—4 M solution of *(1)* in pentane to ethyldiborane at —5 °C leads to high yields of ethyl-(2-methylcyclopropyl)boranes whose retention times in the gas chromatogram are identical with those of the ethyl-(*trans*-2-methylcyclopropyl)boranes formed from 1-methylcyclopropene[5]. Oligomerization of *(1)* during hydroboration occurs only up to a maximum of 20%.

The $LiNH_2$ method is also superior to the $NaNH_2$ method in tetrahydrofuran[6] or in dioxane[7] for the preparation of 1-methylcyclopropene from 3-chloro-2-methylpropene (methallyl chloride) (yield *ca.* 40%; 97% purity). The experimental procedure is entirely analogous to that described below.

3-Methylcyclopropene (1)

1-Chloro-2-butene[2] (118 g, 1.3 moles) is added dropwise over a period of 6 hours to a well stirred suspension of $LiNH_2$ (30 g, 1.31 moles) in boiling dioxane (140 ml) containing about 0.6 g H_2O. The resulting gas mixture is carried in a stream of argon, bubbled through 5 N H_2SO_4 (300 ml), and trapped at —78 °C.

Compound *(1)* is obtained in 30% yield (21.5 g; 98% purity) along with traces (GC) of 1,3-butadiene and some unidentified compounds (1.5%); b.p. —4 °C (unstable). — Mass spectrum: 54 (50) ($M^{\oplus}$) with fragment ions (rel. intensity), 53 (43.5), 39 (100), 28 (45.8), 27 (61.8), and 26 (30.1). — ^{1}H-NMR spectrum (—40 °C, neat): τ = 2.82 (d, $J \approx 1$ Hz), 8.54 (m), and 9.03 ppm (d, $J = 5$ Hz) in the ratio 1.9:1.2:2.9 (calc. 2:1:3).

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[1] *R. Köster, S. Arora,* and *P. Binger,* Angew. Chem. *81*, 186 (1969); Angew. Chem. internat. Edit. *8*, 205 (1969).

[2] "*trans*-Crotyl chloride" (Chemische Werke Hüls AG) contains 22.3% *cis*- and 77.7% *trans*-isomer (GC); cf. also *R. M. Magid* and *R. D. Gandour,* J. org. Chem. *35*, 269 (1970).

[3] *S. Wawzonek, B. J. Studnicka,* and *A. R. Zigman,* J. org. Chem. *34*, 1316 (1969).

[4] *G. L. Closs, L. E. Closs,* and *W. A. Böll,* J. Amer. chem. Soc. *85*, 3796 (1963).

[5] *R. Köster, S. Arora,* and *P. Binger,* Angew. Chem. *81*, 185 (1969); Angew. Chem. internat. Edit. *8*, 205 (1969).

[6] *F. Fisher* and *D. E. Applequist,* J. org. Chem. *30*, 2089 (1965); *I. S. Krull* and *D. R. Arnold,* Org. Preparations and Procedures *1*, 283 (1969).

[7] Cf. [1], there footnote [9].

Sodium Dimethyldithioarsinate, a New Complexing Agent

By *Malte Förster, Herwig Hertel,* and *Wilhelm Kuchen*[*]

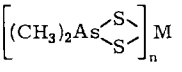
In contrast to the extensively investigated metal complexes $[R_2PS_2]_nM$ of dithiophosphinic acids the corresponding compounds of dithioarsinic acids have, to the best of our knowledge, not previously been reported[**].

By passing hydrogen sulfide into a boiling ethanolic solution of sodium dimethylarsinate *(1)* we have been able to prepare sodium dimethyldithioarsinate *(2)* and to isolate

$$(CH_3)_2As(O)ONa + 2\ H_2S \rightleftharpoons (CH_3)_2As(S)SNa + 2\ H_2O$$
(1) *(2)*

it in almost quantitative yield as the dihydrate (stable, colorless crystals, m.p. 181—182 °C).

In water/ethanol this compound reacts with numerous metal ions to give complexes of the type *(3)*, most of which are intensely colored.



(3)

(3), M	Color	M.p. (°C)	Magnetic moment (B.M.)
Cr(III)	dark blue	223—225 (dec.)	3.90 (298 °K)
Ni(II)	brown-violet	145—146 (dec.)	diamagnetic
Co(II)	green	decomp. above 200	4.40 (298 °K)
Zn(II)	colorless	decomp. above 200	—
Cd(II)	colorless	decomp. above 200	—

The complexes are insoluble in water. Only the octahedral Cr(III) and the planar Ni(II) complexes dissolve in benzene, carbon tetrachloride, chloroform, or methylene chloride. According to osmometric measurements the Cr(III) complex is present as the monomer in chloroform. The magnetic moment found for the Co(II) complex corresponds to a tetrahedral environment of the metal, as is also to be expected for the Zn and Cd complexes. We explain the insolubility of the tetrahedral complexes as being due to association *via* ligand bridges as have been detected in the analogous dithiophosphinato complexes[1] and which according to model considerations ought to be more likely in the arsinato complexes[2].

The electron spectrum of the Cr(III) complex yielded the ligand field parameters $\Delta = 13740\ cm^{-1}$ and $\beta = 0.455$ ($B_0 = 918\ cm^{-1}$). Consequently, the ligand $(CH_3)_2As(S)S^-$ can be placed in the spectrochemical series as follows,

$$I^- < Br^- < (CH_3)_2P(S)S^- < (CH_3)_2As(S)S^- < Cl^- < dtp^-\ [3] < F^-$$

while in the nephelauxetic series it occupies the position shown below:

$$F^- < H_2O < NH_3 < Cl^- < Br^- < (CH_3)_2P(S)S^-\ [4] < (CH_3)_2As(S)S^- < dtp^-$$

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[**] Shortly after translation of the present communication into English, a publication entitled "Synthesis and Infrared Spectra of Some Dithiocacodylate Complexes" by *A. T. Casey, N. S. Ham, D. J. Mackey,* and *R. L. Martin,* Australian J. Chem. *23*, 1117 (1970), came to our notice, which reports *inter alia* the preparation of sodium dimethyldithioarsinate and most of the complexes described here.

[1] *M. Calligaris, G. Nardin,* and *A. Ripamonti,* J. chem. Soc. (A) (London) *1970*, 714.

[2] Cf. a) *H. Hertel,* Dissertation, Technische Hochschule Aachen 1967; b) *W. Kuchen* and *H. Hertel,* Chem. Ber. *101*, 1991 (1968).

[3] $dtp^- = (C_2H_5O)_2P(S)S^-$.

[4] The values found for $[(CH_3)_2P(S)S]_3Cr$ were $\Delta = 13700\ cm^{-1}$ and $\beta = 0.473$; *K. Diemert, H. Hertel,* and *W. Kuchen,* unpublished.

Electrophilic Cyclodimerization of *tert*-Butylacetylene with Hydrogen Chloride[1]

By *Karl Griesbaum*, *Zillur Rehman*, and *Uwe-Ingomar Záhorszky*[*]

Reaction of *tert*-butylacetylene *(1)* with anhydrous hydrogen chloride at room temperature[2] leads to the normal adducts *(3)* and *(4)*, and to the adducts *(6)* and *(7)*, which are formed by a 1,2-methyl shift to the vinyl cation *(2)*. Besides these, the gas chromatogram of the crude adduct mixture showed the presence of a few additional components, but only in the amount of or less than 1% each.

Two of these unknown components, having higher retention times in the gas chromatogram than either of the diadducts *(4)*, *(6)*, or *(7)*, were of interest from the point of view of a possible cyclodimerization. We have been able to isolate both components as crystalline, colorless substances by a combination of fractional distillation and preparative gas chromatography (3 m Carbowax-20M column).

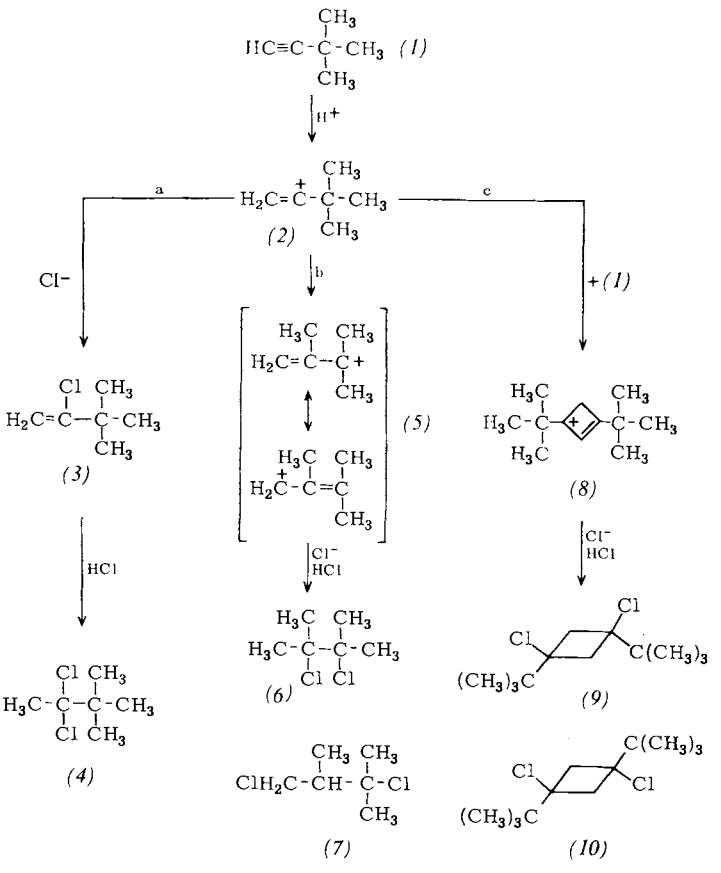
The substance having the higher retention time (67 min) has a m.p. 175—177 °C and its mass spectrum contains a molecular ion triplet typical of dichloro compounds at m/e = 236, 238, 240 corresponding to the empirical formula $C_{12}H_{22}Cl_2$, *i.e.* to an adduct of two molecules of HCl and two molecules of *tert*-butylacetylene. An intense doublet at m/e = 118, 120 (M/2) indicates ready splitting of the molecule into two equal fragments and thus to the presence of a symmetrical cyclic structure. Further typical fragment ions occur at m/e = 200, 202 (M — HCl), m/e = 185, 187 (M — CH_3 — HCl), m/e = 165 (M — HCl — Cl), m/e = 103, 105 (M/2 — CH_3), m/e = 57 (*tert*-butyl), and m/e = 56 (isobutene).

The NMR spectrum (CCl_4) showed a singlet at δ = 1.02 ppm and a four-line pattern centered at 2.79 ppm in the intensity ratio 9:2. The four-line pattern is obviously due to a AA'BB' system (J_{AB} = 13 Hz), whose individual signals are further split by a small — presumably diagonal — coupling of *ca.* 3 Hz.

This data is in accord with the structure of a *cis*-1,3-di-*tert*-butyl-1,3-dichlorocyclobutane *(9)*, which was supported by comparison of the NMR spectrum with that of the corresponding *cis*-1,3-dichloro-1,3-dimethylcyclobutane[3].

The second component, *i.e.* the substance having the lower retention time (48 min), has a m.p. 115—118 °C and shows the same signals in the mass spectrum as *(9)* although with different relative intensities. The NMR spectrum showed only two singlets at δ = 1.12 ppm and δ = 3.01 ppm in the intensity ratio 9:2. This data is consistent with the structure of the *trans*-compound *(10)* which is isomeric with *(9)*.

These investigations indicate that three reaction routes are open to the vinyl cation *(2)*: a) simple combination with Cl^- ions or with Cl^- and HCl to give the normal adducts *(3)* and *(4)*; b) rearrangement to the resonance-stabilized allyl cation *(5)*[4]; and c) cycloaddition to form the allyl cation *(8)* with subsequent formation of *(9)* and *(10)*.



To the best of our knowledge, the synthesis of *(9)* and *(10)* represents the first case of a merely acid-catalyzed cyclodimerization *via* vinyl cations, in which no isomerization of the acetylenic substrate to allenic structures can occur.

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[1] This work was supported by the Deutsche Forschungsgemeinschaft and the Badische Anilin- und Soda-Fabrik, Ludwigshafen/Rh.

[2] *K. Griesbaum* and *Z. Rehman*, J. Amer. chem. Soc. *92*, 1416 (1970).

[3] *K. Griesbaum*, *W. Naegele*, and *G. G. Wanless*, J. Amer. chem. Soc. *87*, 3151 (1965).

[4] In the meantime this rearrangement has also been observed at a vinyl cation of structure *(2)* generated by solvolysis: *H. G. Martinez*, *M. Hanack*, *R. H. Summerville*, *P. v. R. Schleyer*, and *P. Stang*, Angew. Chem. *82*, 323 (1970); Angew. Chem. internat. Edit. *9*, 302 (1970).

Azapeptides, A Novel Class of Peptide Analogs

By *Joachim Gante*[*]

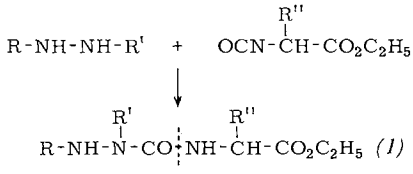
In the "azapeptides", a novel system of compounds analogous to the peptides, a few of the α-CH groups of the amino acid esters of the peptide chain are replaced by N-atoms:



peptide chain azapeptide chain

The side-chain R remains unchanged.

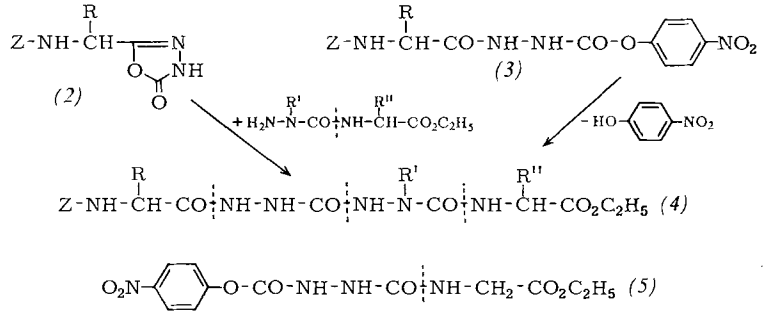
Various new synthetic routes for these compounds have been developed in our laboratories[1]. For example, hydrazine hydrate and alkyl- and acylhydrazines are added to ethyl α-isocyanatocarboxylates to give "alternating" products *(1)* (containing alternately azaamino acid and amino acid residues).



R = H, benzyloxycarbonyl (Z), tosyl (Tos)
R′ = R″ = H, alkyl

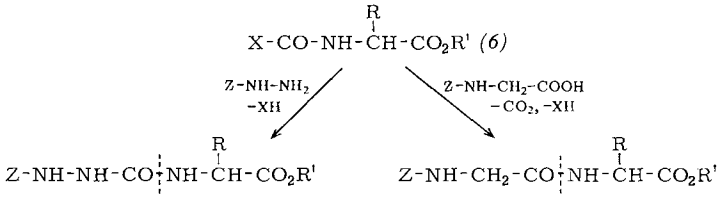
Long-chain peptide analogs can be prepared by alternate reaction of *N*-protected azapeptide esters with hydrazines and isocyanato fatty acids.

2-(Benzyloxycarbonylaminoalkyl)-1,3,4-oxadiazol-5-ones *(2)* and "activated" benzyloxycarbonylaminoacylazaglycyl-*p*-nitrophenyl esters *(3)* react with azapeptides unprotected on the amino group to give higher peptide analogs *(4)* having directly coupled azaamino acid residues.



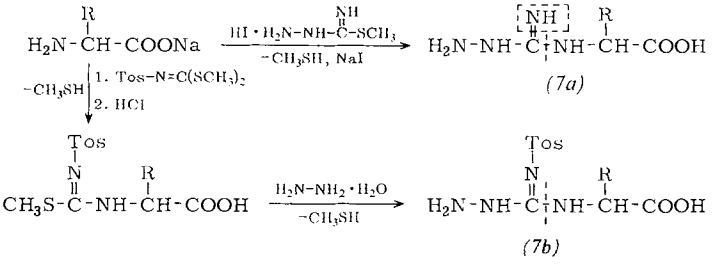
The azapeptide *(5)*, which is activated on the amino group correspondingly reacts with lengthening of the chain at the amino end.

The *N*-activated amino acid esters *(6a)*[2], *(6b)*[3], and *(6c)*[4] can be used for both azapeptide and peptide synthesis with chain lengthening at the amino end.



(6a), X = 2,4-dinitrophenoxy-; *(6b)* X = 1-imidazolyl-;
(6c), X = 1,2,4-triazol-1-yl.

Reaction of sodium salts of amino acids with *S*-methylisothiosemicarbazide hydrogen iodide leads to unprotected "azaimidopeptides" *(7a)*, a further class of azapeptide analogs, in which the carbonyl oxygen of an azaamino acid ester is replaced by NR[5].



Reaction of sodium salts of amino acids with dimethyl tosyl iminodithiocarbonate and subsequent reaction of the (isolable) intermediates with hydrazine hydrate yields azaimidopeptides *(7b)* having tosyl-protected imino groups[5].

The properties of the new peptide analogs closely resemble those of the peptides. The reactions commonly used in the synthesis of peptides — *e.g.* cleavage of the *N*-protecting group, hydrolysis of the ester, coupling of fragments to yield large molecules by well known methods — can also be used in the case of the azapeptides.

Lecture at Clausthal-Zellerfeld July 14, 1970 [VB 249 IE]
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[1] *J. Gante*, Fortschr. chem. Forsch. *6*, 358 (1966).
[2] *J. Gante*, Chem. Ber. *99*, 1576 (1966).
[3] *J. Gante*, Chem. Ber. *99*, 2521 (1966).
[4] *J. Gante*, Angew. Chem. *78*, 602 (1966); Angew. Chem. internat. Edit. *5*, 593 (1966).
[5] *J. Gante*, Chem. Ber. *101*, 1195 (1968).

Biochemistry of the Central Nervous System. Some Observations on Mass Transport

By *Eberhard Riedel*[*]

The biochemical reactions occurring in the central nervous system are closely related to neurophysiologically measurable processes and cannot be fully understood without consideration of neuroanatomical features of brain structure. In the central nervous system particular attention attaches to membrane structures of the cell and vessel walls and to the transport occurring there. Apart from physical transport, active transport plays an especially important role in the central nervous system. In addition, barrier systems (blood-brain barrier, liquor-brain barrier) make for a strict selection in exchange processes with the supply system of the blood circulation. Physical transport with

pore-free membranes (solution diffusion) and with membranes containing pores were discussed. In order to investigate such processes we developed new methods of determining permeation using capacitative, conductometric, and other detectors (gas chromatography) and have been able to detect not only solution diffusion but also pore diffusion (model studies) on synthetic high polymers (polyesters, low-pressure polyethylenes). Facilitated diffusion (*Danielli*) represents a special case and cannot properly be termed activated diffusion.

The morphology of the cellular elements of the central nervous system is of importance to the biochemist with regard to membrane structure and membrane transport. Information transfer in the central nervous system is by electrical impulses within a widely branched neuron network (10^9 neurons in the human brain) which is nourished by the neuroglia, a supply and support tissue system exhibiting an extremely high degree of metabolic activity.

Of the various theories of the active K—Na transport (K—Na pump), which is of great significance for the transport of electrical signals, the assumption of a redox pump must apparently be ruled out since ion transport is not blocked by respiratory inhibitors (cyanide). The carrier theory (*Hodgkin, Whitman*) provides satisfactory explanations. *Hokin* also mentioned K/Na-active phospholipid systems. It appears that a symporter mechanism (*Mitchell*) is mainly responsible for the transport of amino acids, glucose *etc.*

Work in our laboratories is concerned with the susceptibility of the central nervous system to convulsive seizures. In the brains of experimentally epileptic animals (Kopeloff method) we have been able to observe changes in the K and Na content which are dependent on the development of an attack and which have to be interpreted in terms of the phenomena mentioned above.

Lecture at Bielefeld on June 1, 1970 [VB 250 IE]
German version: Angew. Chem. *82* 816 (1970)

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Charge Distribution in Ionic Crystals

By *Alarich Weiss* [*]

Various methods are used for the determination of the charge distribution in crystals. The earliest experiment was the probing of a crystal with fast charged particles *e.g.* protons. When the crystals are available as thin films, channels of low charge density can be recognized in the crystal lattice from the intensity distribution in the proton beam.

The most important method for the study of charge distribution is the diffraction of X-rays in the crystal lattice. It can be concluded from the few quantitative results reported that in the simplest cases, such as the alkali halides, practically spherical ions are present in the lattice. The radii determined from the electron density distribution differ considerably from the Goldschmidt radii, but are in good agreement with the radii calculated by *Tosi* on the basis of the Madelung-Born-Mayer model. The surprising fact that the cations in the alkali halides are larger than the "free" ions, while the anions are smaller, appears reasonable from quantum-mechanical model calculations. The wave functions obtained from such model lattice calculations can be used for the calculation of physical properties such as the diamagnetic susceptibility and the dipole polarizability. The resulting values agree better with the experimental values than when the radii of the "free" ions are used.

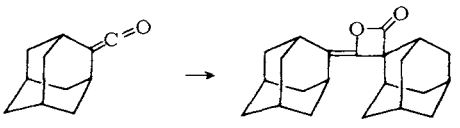
Studies of the nuclear magnetic resonance spectrum of some ions in simple crystals can also furnish information about the charge distribution in crystals. The charge distribution must be deduced from the nuclear magnetic resonance spectra by means of model calculations. Such models of charge distribution can be based upon a simple point charge model. The multipole moments induced in the ions in the lattice, particularly dipole and quadrupole moments, demand careful attention, as is shown by model calculations on simple lattices. Moreover, valuable information about the charge distribution in ionic crystals can be obtained from Mössbauer spectroscopy and from the longwave IR spectra.

Lecture at Göttingen on April 23, 1970 [VB 251 IE]
German version: Angew. Chem. *82*, 843 (1970)

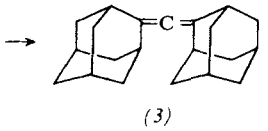
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SELECTED ABSTRACTS

Bis(adamantylidene)methane *(3)*, an allene of theoretical interest, has been synthesized by *J. Strating, A. H. Alberts,* and *H. Wynberg.* In the presence of catalytic amounts of $AlCl_3$ in boiling ether, the ketene *(1)* dimerizes directly to the



(1) *(2)*



(3)

β-lactone *(2)* in 50 % yield. Pyrolysis of *(2)* at 260 °C affords *(3)*, m.p. 224—116 °C, 95 % yield, with liberation of CO_2. The IR and NMR spectra are in accord with the allene structure. / Chem. Commun. *1970*, 818 / —Ma. [Rd 226 IE]

The ESR spectrum of triplet methylene was measured for the first time by *R. A. Bernheim, H. W. Bernard, P. S. Wang, L. S. Wood,* and *P. S. Skell.* Methylene was generated by photolysis of diazirine in a xenon matrix (proportion *ca.* 1 : 10^4) at 4.2 °K. The ESR data show that triplet methylene is slightly bent under these conditions. The signal is constant for several hours at 4.2 °K; therefore the triplet state should be the electronic ground state. On warming to 20 °K and cooling back to 4.2 °K the spectrum does not change. After warming to 77 °K, however, it disappears irreversibly. / J. chem. Physics *53*, 1280 (1970) / —Hz. [Rd 234 IE]

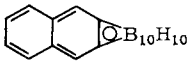
Simultaneous excitation of two absorbing centers by one photon is postulated by *H. J. Schugar, G. R. Rossman, J. Thibeault,* and *H. B. Gray* for the interpretation of the electronic spectra of some binuclear iron(III) complexes. As the most important example, the spectrum of $[(HEDTAFe)_2O]^{2-}$ (ethylenediammonium salt in aqueous solution) is analyzed; HEDTA stands for the pentadentate ligand $R'RNCH_2CH_2NR_2$ with $R=CH_2COO^-$ and $R'=CH_2CH_2OH$. The four transitions at the longest wavelengths (11—24 × 10^3 cm^{-1}) are essentially the same as those of a mononuclear

octahedral high-spin iron(III) complex. At shorter wavelengths a group of bands follows which is not encountered in mononuclear complexes as $[HEDTAFeOH]^-$ or $[HEDTAFeOH_2]$. The energies of these bands are all readily displayed as the energy sums of two of the long-wavelength bands. This could mean that excitation of both metal ions is effected by absorption of one photon. This phenomenon was known hitherto only with crystals, and is now demonstrated for the first time on a discrete complex. / Chem. Physics Letters *6*, 26 (1970) / --Hz. [Rd 227 IE]

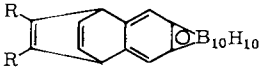
Electron-transfer bands between unlike transition-metal ions in the UV spectra of perovskites are discussed by *J. Ferguson* and *H. J. Guggenheim*. Crystals of the compositions $KMn_xNi_{1-x}F_3$ and $KZn_{1-x-y}Mn_xNi_yF_3$ show an intense ultraviolet band ($\tilde{\nu}_{max} > 50000\ cm^{-1}$). As the absorption of crystals containing Ni and Mn exceeds the absorption of those containing only one metal the absorption is ascribed to the excitation of the chromophore $Mn^{2+} \cdot\cdot F^- \cdot\cdot Ni^{2+}$ to $Mn^{1+} \cdot\cdot F^- \cdot\cdot Ni^{3+}$. Polarization data on $BaMn_{0.5}Ni_{0.5}F_4$ with a similar structure, corroborate this suggestion. On substitution of Cu^{2+} and Mn^{2+} into $KZnF_3$ crystals, a broad structured band with $\tilde{\nu}_{max} = 41500\ cm^{-1}$ is observed the intensity of which increases on cooling. All these features can be rationalized with the transition $Mn^{2+}(3d^5)$, $Cu^{2+}(3d^9)$ to $Mn^{1+}(3d^54s)$, $Cu^{3+}(3d^8)$. In addition, the magnetic properties of these types of crystals can be interpreted on the basis of the energy level diagrams derived. / Phys. Rev. [3] *B 1*, 4223 (1970) / —Hz. [Rd 235 IE]

Chromosome damage in lead workers is the subject of a report by *G. Schwanitz*, *G. Lehnert*, and *E. Gebhart*. The authors found a higher proportion of mitoses with secondary chromosome aberrations than in a control group. Not only chromosome breaks and translocations but also spiralization defects, adhesion, and pulverization were observed. These effects could also be produced *in vitro* by 10^{-4}—10^{-6} M lead acetate solutions; the number of defective mitoses appeared substantially independent of the lead concentration. / Dtsch. Med. Wschr. *95*, 1636 (1970) / —Kr. [Rd 236 IE]

Naphtho[2,3-*a*]-*o*-carborane *(1)* has been synthesized by *D. S. Matteson* and *R. A. Davis* from α,α'-dibromo-*o*-xylene and dilithio-*o*-carborane. The resulting dihydronaphthocarborane could be dibrominated with *N*-bromosuccinimide and was converted into *(1)* by treatment with sodium iodide (58% yield). Compound *(1)*, fluorescent yellow crystals, melts at 152—159 °C in a sealed tube. The NMR



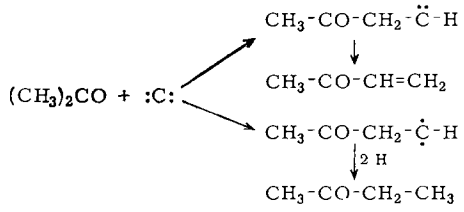
(1)



(2), R = CH_3OCO

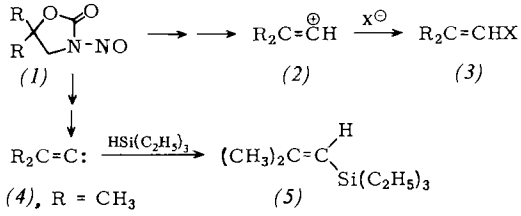
spectrum suggests weakly aromatic character. Bromine adds to the inner ring, and the action of atmospheric oxygen leads to formation of polymeric peroxides. For steric reasons, dienophiles are able to attack only the outer naphthalene ring to form, *e.g.*, *(2)* or its analog with maleic anhydride. Tetracyanoethylene does not react. / Chem. Commun. *1970*, 669 / —Kr. [Rd 237 IE]

Insertion of atomic carbon (^3P) into C—H bonds was studied by *P. S. Skell*, *J. H. Plonka*, and *L. S. Wood*. For instance, acetaldehyde and carbon vapor form acetone (consumption of two H atoms, yield 5% based on C). Pure acetone is converted into 3-buten-2-one and 2-butanone (yields 2.5



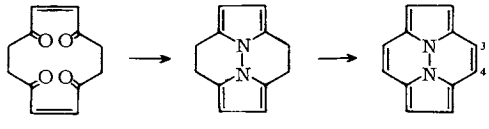
and 3.0%, respectively). Addition of butadiene lowers the yield of 2-butanone to 1%, this being interpreted in terms of the intermediacy of singlet and triplet acetonylcarbene. / Chem. Commun. *1970*, 710 / —Kr. [Rd 238 IE]

New syntheses of vinyl halides and vinylsilanes, *(3)* and *(5)*, respectively, are described by *M. S. Newman* and *C. D. Beard*. These authors treated 5,5-dialkyl-*N*-nitrosooxazolidone *(1)* with lithium 2-methoxyethoxide and NaI, LiBr, or LiCl in 2-methoxyethanol to give the vinyl halides *(3)*



(yields about 80%). The reactions proceed *via* the unsaturated cations *(2)*. Hardly any vinyl ethers are formed. Reaction of *(1)*, R = CH_3, with alkoxide in benzene containing triethylsilane gives the triethyl(2-methyl-1-propenyl)silane *(5)* in 61% yield. The unsaturated carbene *(4)* occurs as intermediate. / J. Amer. Chem. Soc. *92*, 4309 (1970) / —Kr. [Rd 239 IE]

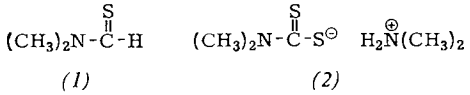
A nitrogen-bridged [12]annulene *(3)* [8b,8c-diazacyclopent-[*fg*]acenaphthylene] has been synthesized by *W. W. Paudler* and *E. A. Stephan*. Reaction of the tetraone *(1)* with hydrazine in the presence of oxygen afforded the tetracyclic compound *(2)*, which can be reduced to *(3)* with *e.g.* dichlorodicyanobenzoquinone. While the 3,4-dihydro derivative of *(3)* must be regarded as aromatic on the basis of its



(1) *(2)* *(3)*

NMR spectrum, the NMR spectrum of *(3)* shows a considerable weakening of the ring current. The substance possibly exists in the form of the isomeric tricyclic compound having no N—N bond, or the two forms may be in valence-tautomeric equilibrium. / J. Amer. Chem. Soc. *92*, 4468 (1970) / —Kr. [Rd 240 IE]

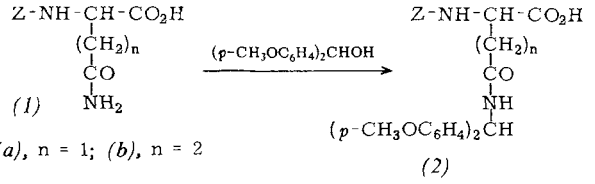
Thioformamides and dithiocarbamates have been obtained by *L. Maier* by heating of a mixture of sulfur, formaldehyde, and amines in ethanol/water to 80 °C. Dimethylamine yields mainly dimethylthioformamide *(1)* and di-



(1) *(2)*

methylammonium dimethylthiocarbamate *(2)*, alongside a very small amount of dimethylformamide. The yields of *(1)* and *(2)* depend on the molar ratio of the reactants and the solvent. Diethylamine gives the analogs of *(1)* and *(2)* as well as $(C_2H_5)_2NSOH \cdot 1/2\ H_2O$, which is the first stable derivative of an *N*-sulfenic acid (m.p. 132—135 °C, decomp.). Primary amines afford only thioformamides. / Helv. Chim. Acta *53*, 1216 (1970) / —Kr. [Rd 241 IE]

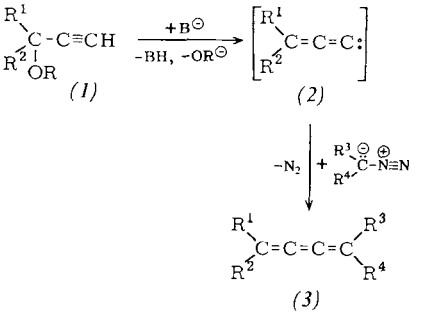
A new amide protecting group for the synthesis of peptides with amides such as asparagine and glutamine is the subject of a report by *W. König* and *R. Geiger*. The authors have shown that the 4,4-dimethoxybenzhydryl group proves to be a useful protecting group in such syntheses; it can be introduced into the system almost as easily as can the xanthenyl residue. 4,4'-Dimethoxybenzhydrol, which can be readily obtained from the ketone by reduction with $NaBH_4$, reacts with benzoyloxycarbonylglutamine *(1a)*



(1) *(a)*, n = 1; *(b)*, n = 2 *(2)*

and -asparagine *(1b)* in glacial acetic acid under acid catalysis to give the protected amides *(2a)* and *(2b)* resp. Unsubstituted amides and peptides themselves can also be protected in this way. 4,4'-Dimethoxybenzhydrylamides are stable towards catalytic hydrogenation. *(2a)* and *(2b)* can be converted to peptides by the usual methods. The protecting group can be cleaved with trifluoroacetic acid/anisole. / Chem. Ber. *103*, 2041 (1970) / —Kr. [Rd 243 IE]

A new method for the synthesis of cumulenes has been described by *H. Reimlinger* and *R. Paulissen*. α-Ethynyl alcohols *(1)* are converted by bases into the vinylidenecarbenes *(2)*, which, in the presence of diazo compounds, yield the cumulenes *(3)*. This method is suitable only for



(1) *(2)* *(3)*

the preparation of butatriene derivatives. For example: $R^1 + R^2$ = *o,o'*-biphenylylene, $R^3 = R^4 = C_6H_5$, yield 26%; $R^1 = R^2 = (CH_3)_2CH$, $R^3 + R^4$ = *o,o'*-biphenylylene, yield 5%. / Tetrahedron Lett. *1970*, 3143 / —Kr. [Rd 244 IE]

BOOK REVIEWS

Introduction to the Chemical Analysis of Plastics. By *A. Krause* and *A. Lange*. Iliffe Books Ltd., London 1969. 1st ed., 326 pp., numerous tables, 60 s.

This is an English translation of the first German edition of "Kunststoff-Bestimmungsmöglichkeiten" [1], which was published in 1965. The book contains a large number of well-tried simple tests for the identification of unknown plastics, *e.g.* by solubility tests, color reactions, combustion tests, *etc.* Most of the book is devoted to collections of test methods for the various classes of plastics; additives and aids for the processing and use of plastics, *e.g.* stabilizers, plasticizers, and fillers, are dealt with relatively briefly. The book ends with a list of standard (mostly DIN) methods for the quality and input control of industrial polymers and recommendations of the Commission for the Assessment of Plastics in connection with the food law. The book contains a bibliography and an index, though the latter does not make up for the very brief list of contents, which offers little assistance to the user. A very detailed list of contents would be a desirable feature in any future edition.

The book, which has already proved its worth in the German edition, will undoubtedly also have a wide circle of users in the English version, though it must be pointed out that there is always a danger, in the choice of simple methods of analysis, that the inexpert reader will reach the wrong conclusions. Advice on this point would be very useful.

Dietrich Braun [NB 884 IE]

Electrochemistry at Solid Electrodes. Monographs in Electroanalytical Chemistry and Electrochemistry. By *R. N. Adams*. Marcel Dekker, Inc., New York 1969. 1st Edit., xiii + 402 pp., numerous figures, bound $ 18.75.

The content of this book does not justify the comprehensiveness of its title. What the author has compiled is essentially confined to a narrow segment of the electrochemistry with solid electrodes, namely the application of the latter to *voltammetric* investigations of *organic* compounds. Considered in the light of this more restrictive title, the book offers experimenters some useful information concerning work with solid electrodes, although it must be said that a more systematic approach would not have been out of place.

In the first part of the book the author seeks to impart to the reader the indispensable theoretical background. His selection of the by now well known fundamentals seems to the reviewer to be highly arbitrary, especially as regards the electrode-kinetic relationships. Reference should have been made at this point to corrosive effects and to the influence of mixed potentials.

The treatment of diffusion processes is very detailed, if highly idealized. Adsorption phenomena are not discussed. The terse statement in the foreword, to the effect that adsorption would not be considered since it did not constitute the most important part of an electrode reaction, strikes one as a rather weak argument.

The second part of the book is concerned mainly with experimental work and applications. Here, at any rate, the author is able to display the extent of his experience, giving the reader a valuable, self-contained section which for the first time presents data on the available investigations on organic compounds. Less commendable are the occasionally incomprehensible circuit diagrams accompanying the text on instrumentation, and also one or two electrode arrangements which are clearly taken from the author's sketchbook. The author might have demonstrated his originality in other ways, by appropriate treatment of the subject-matter.

Rolf Bertram [NB 888 IE]

[1] Cf. Angew. Chem. internat. Edit. *5*, 619 (1966).

Advances in Structure Research by Diffraction Methods Vol.3. – Fortschritte der Strukturforschung mit Beugungsmethoden, Bd. 3. Edited by *R. Brill* and *R. Mason*. Friedr. Vieweg u. Sohn, Braunschweig 1970. 1st Edit., iii, 251 pp., 77 figures, linen DM 48.—.

Like the first two volumes[1], the present third volume again contains contributions by well-known authors. The four articles are written in English by French, German, and Russian authors.

A. Authier presents a 50-page treatment of "Ewald Waves in Theory and Experiment (Dynamical Theory of X-Ray Diffraction)". The counterpart of this in some sense is an article (48 pp) on "Dynamical Theory of Electron Diffraction" by *K. Kambe* and *K. Molière*.

R. Hosemann, A. Schönfeld, and *W. Wilke* write in 72 pages on "Small Angle Scattering". The particularly extensive bibliography here follows on that given by *Yudowitch* in the book by *Guinier* and *Fournet* on the same subject, and covers the period from 1955 to 1967 "as fully as possible" with 530 references.

The fourth and last contribution (75 pp.) is an article by *A. I. Kitajgorodskij* entitled "General View on Molecular Packing".

The articles are aimed at readers who have had contact in their work with the material in question. They should be of great value to such readers. On the other hand, they are probably too difficult for the interested non-specialist, for whom they are not really intended in any case.

Dietrich Mootz [NB 895 IE]

Kunststoff-Handbuch. Aufbau, Verarbeitung, Eigenschaften und Anwendung der synthetischen Werkstoffe. Bd. V: Polystyrol. (Plastics Handbook. Structure, Processing, Properties, and Uses of Synthetic Materials. Vol. V. Polystyrene). Edited by *R. Vieweg* and *G. Daumiller*. Carl Hanser Verlag, München 1969. 1st Edit., xxi, 876 pp., 675 figures, 126 tables, linen DM 234.—.

The present volume[2] on polystyrene, which occupies the third place in economic importance among plastics, is particularly successful, since the contributions on its production, processing, properties, and uses are well matched both in size and in content. So much is known about this plastic that the collation of the various contributions from outstanding specialists into a coherent chapter is in itself a creative process, in which the editors have been very successful. The arrangement of the material is systematic and clear; the references and the subject index make it easy to find one's way around, and the text is well supported by tables and by good illustrations.

An introduction describing the history and the economic importance of polystyrene is followed by sections on its polymerization and processing, in which considerable space is devoted to rheology. In addition to injection molding, extrusion, deep drawing, compression molding, and sintering, further processing, such as the joining of polystyrene moldings by cementing and welding, as well as metalizing and printing (in an appendix), is also described. The section on properties, in which copolymers and high-impact modified polystyrenes are also discussed, covers the mechanical, thermal, electrical, and aging behavior of this group of plastics. Two outstanding and excellently illustrated sections are devoted to the use of polystyrene and polystyrene foams.

The authors of the various chapters, who are carefully selected experts in their fields, have brought together a wealth of experience that provides the user of the volume with a coherent, valuable, and rapid source of information.

The volume can be warmly recommended to processors, engineers, chemists, physicists, and students who wish information on special problems in connection with polystyrene.

Otto Horn [NB 896 IE]

[1] Cf. Angew. Chem. internat. Edit. *6*, 474 (1967).

[2] Cf. Angew. Chem. internat. Edit. *8*, 994 (1969).

The Chemistry of Fluorine and its Compounds. By *H. J. Emeléus*, Academic Press, New York-London 1969. 1st Edit., ix, 133 pp., numerous formulas, bound 65 s.

This monograph is not intended to present every individual item of knowledge about fluorine and its compounds. The author's intention is merely to provide a brief survey of the very extensive chemistry of fluorine. Instead of trying to present exhaustive information, he tries above all to demonstrate the shortage of physical data and to point out unsolved problems of fluorine chemistry in order to attract young scientists to this field.

The fluorine chemistry of the elements of the main groups of the periodic table is discussed chapter by chapter in a very informative manner, and great attention is given to unsolved problems. Short, clear summaries of the chemistry of hypofluorites, perfluoro organometallic compounds, perfluoro aromatic compounds, and fluoroalkyl and fluoroaryl derivatives of the transition metals form a logical supplement. A brief introduction is devoted to the properties of fluorine and deals with all the peculiarities that give fluorine a special place among the halogens and make it so interesting to chemists in all fields.

The presentation and print are very pleasing, and the book is written in a flowing and lucid manner and is free from printing errors. The arrangement and the choice of material show that the author, who has greatly enriched the chemistry of fluorine and paved the way for new developments over the past 30 years by his own scientific work, has a complete picture of the subject matter. The book can be wholeheartedly recommended to all chemists, and particularly to all undergraduates, graduate students, and chemistry lecturers.

Alois Haas [NB 897 IE]

Reagents for Organic Synthesis. Vol. 2. By *Mary Fieser* and *L. F. Fieser*. Wiley-Interscience, New York-London-Sydney-Toronto 1969. 1st Edit., 538 pp., bound DM 72.—.

The first volume of this handbook[1] has proved an indispensable aid in the reviewer's laboratory. It is now undoubtedly one of the standard works for the organic chemistry laboratory. The present second volume covers the literature of the next $2^1/_2$ years up to January 1969. It contains 1320 further references on 320 reagents that were discussed in the first volume, as well as 550 references on 226 reagents that are mentioned in the book for the first time. The alphabetic arrangement and the well-proven plan of the text on the individual reagents have been retained. This second part is again liberally provided with structural formulas to explain the examples of applications, and this makes for greater ease of scanning.

Special attention is paid in this volume to the organometallic reagents, as befits their steadily growing importance. European companies are now also listed among the suppliers. The positive impression of the first volume can also be claimed unreservedly for the second. If any criticism is necessary, it relates only to the organization of the book and not to its content.

In our opinion, the decision to update the handbook by supplementary volumes, though convenient, is rather shortsighted. If a supplementary volume of about 500 pages is required to cover the literature of only $2^1/_2$ years, it can be seen that this work will lose the character of a laboratory handbook in a short time. Moreover, the ease of scanning will certainly not be helped by the addition of a large number of supplementary volumes.

We feel that it would have been much better to revise and expand the main volume at short intervals. This would preserve its character as a laboratory handbook, and would also have the advantage that the authors would constantly be forced to deal with the reagents and examples in accordance

[1] Cf. Angew. Chem. internat. Edit. *8*, 398 (1969).

with their true importance. Many reagents that were highly praised by their discoverers have subsequently fallen short of expectations. Similarly, many examples of special applications may be omitted if they should later show little scope for generalization. The actual value of this book would undoubtedly be greatly increased by such periodic revisions and expansions.

Hermann Stetter [NB 900 IE]

The Biochemistry of the Nucleic Acids. By *J. N. Davidson.* Methuen & Co. Ltd., London 1969. 6th Edit., xvi, 352 pp., numerous illustrations, bound 50 s.

The latest edition of the present book is intended by the author as an introduction to the biochemistry of nucleic acids for students of biochemistry and chemistry. The book justifies this claim in full, since it not only presents the established results in this field skillfully, accurately, and in an understandable manner, but also describes the aims and problems of current research in the biochemistry of the nucleic acids. This introduction has been written in the style of a monograph, and the reader is accordingly not entirely dependent on the author's authority. More than two thousand literature references enable the reader to acquire a deeper understanding of important relations and problems by reading the original literature. Another pleasing feature is that the reader is not confronted with religious, philosophical, and ethical speculations on questions of molecular biology. It is to be hoped that this book will be made available to a wider circle of students of biology, biochemistry, and chemistry by translation into German.

Karl-Heinz Scheit [NB 901 IE]

Anorganische Chemie. Eine grundlegende Betrachtung (Inorganic Chemistry — A Fundamental Approach). By *Z. G. Szabó.* From the Heidelberger Taschenbücher series, Vol. 63. Springer Verlag, Berlin-Heidelberg-New York 1969. 1st Edit. VIII, 159 pp., 16 figures, 20 tables, bound, DM 14.80.

"The sole aim of a modern lecture on inorganic chemistry must be to offer such a selection of fundamental data as will permit a whole range of technical aspects to be derived". The present book follows this principle, which is enunciated in the foreword. All the fundamentals of general chemistry are discussed, for example the periodic system, structure of the electron shells, chemical bonding, electronegativity, polymorphism, physical properties of the elements, acids and bases, kinetics and energetics of chemical reactions, solubility, complexes, and redox processes.

The physical properties of the elements are given starting with hydrogen, followed by the noble gases, then the other nonmetallic elements, finally the semimetals, the alkali metals and alkaline earth metals, other metals, the transition metals, the lanthanoids, and the actinoids. The author describes in turn the hydrides, halides, oxides, hydroxides, sulfides, oxo-acids, peroxides, and complexes. The last few chapters are devoted to the biological importance, the geochemical occurrence and the abundance of elements, and to the preparation and utilization of elements and compounds.

All this material is presented in a highly compressed form. To benefit from reading it the beginner must simultaneously study a comprehensive textbook. One would hope to find a number of improvements in a later edition. The sections on chemical bonding, including special cases such as boron hydrides and complexes, should be modernized. The properties of acids and bases are best discussed on the basis of Brønstedt's definition. Redox reactions with normal potentials belong in the initial chapters and not at the end of the book; only then will the reader understand reactions such as

$$Cl_2 + 2Br^- \rightarrow Br_2 + 2Cl^-.$$

Some reworking is also called for in the section on compounds. Examples of nonexistent compounds are NiH_2, Ni_2O_3, CuOH, $Pb(OH)_4$, $(NH_4)_2S$ in water. On the other hand, HCl_2^-, more than six boranes, *etc.*, do exist. Anyone lecturing in inorganic chemistry will find it worth his while to read this book.

Oskar Glemser [NB 904 IE]

Die Acidität der CH-Säuren (The Acidity of CH Acids). By *H. F. Ebel.* Georg Thieme Verlag, Stuttgart 1969. 1st Edit., iv, 100 pp., 8 tables, board, DM 21.—.

The first one-third of the book contains a comprehensive summary of the various possible methods of measuring acidity, particularly detailed attention being given to the generally less familiar techniques for determining very low acidities (*e.g.* from the rates of metalation reactions, base-catalyzed halogenation, or base-catalyzed H/D exchange). The main section of the book offers the reader a tabulated survey of the acidities of approximately 200 CH acids measured in aqueous solution, in polar protonic or aprotic solvents, and finally also in relatively or completely nonpolar aprotic media. The pK values varied over the extremely broad range from <-11 (pentacyanocyclopentadiene) to $+37$ (isopropylbenzene). Finally, the last and shortest part is devoted to a discussion of the importance of the various intermolecular effects (in particular the inductive and conjugation effects, and also, to a smaller extent, hybridization) capable of giving rise to the appearance of CH acidity.

All in all, this little book contains so much useful information, presented in some cases with a novel approach, that it will quickly be found indispensable by everyone in any way concerned with the problems of CH acidity.

Friedrich Klages [NB 908 IE]

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Metal-Boron Compounds – Problems and Perspectives

By Günter Schmid [*]

"True" metal-boron compounds have been known for about ten years. The bonding between the metal and boron atoms can vary widely in nature: Not only simple covalent bonds are encountered but also coordinate bonds and boron-metal multicenter bonds. Furthermore, π complexes of transition metals with boron-nitrogen systems and metal complexes containing boron(I) compounds as ligands have recently also been prepared.

1. Introduction

It is remarkable that until a few years ago only nonmetallic and metalloidal elements were to be found as ligands in boron compounds. Thus, with the exception of the metal borides [**], which have been known for a comparatively long time, no compounds of boron with metals were known up to about 1960. Although various reports of such compounds had appeared previously, present knowledge shows that the substances so described cannot be regarded as true metal-boron compounds since they contain no direct bonds between the metal and boron. As examples we can name the alkali-metal adducts of arylboranes such as $(C_6H_5)_3BNa$, which was reported by *Krause* [1] as long ago as 1924. This species should, however, be looked upon as $Na_2[(C_6H_5)_3B-C_6H_4-B(C_6H_5)_3]$, which contains no metal-boron bonds [2]. Similar problems occur with "dibutylboronpotassium" $(n\text{-}C_4H_9)_2BK$ [3–5]; all that we can say with certainty about this compound is that it can transfer dibutylboryl on to various reactants; this led *inter alia* to the discovery of boryl ketones $(n\text{-}C_4H_9)_2B-CO-R$ [4].

The past decade has seen the discovery of a wealth of "true" metal-boron compounds characterized by a wide variety of bonds between boron and metal atoms. In view of the many boron-nonmetal compounds this is hardly surprising, particularly as there is no fundamental distinction, but only one of degree, between *e.g.* a covalent bond between boron and carbon and one between boron and metal. In fact, it is precisely the electronegativity difference between metals and boron that would indicate the possibility of stable bonds between these elements.

2. Coordinate Metal-Boron Bonds

In most of its compounds boron is in a trigonal-planar ligand environment and is therefore assigned an sp^2 configuration. It can assume sp^3 character on rehybridization, which entails a gain in energy; in the process, its coordination number increases to 4, the L shell being fully occupied by an octet of electrons. Rehybridization of this kind is promoted by adduct formation with electron donors.

$$D: + BR_3 \rightarrow \overset{\delta+}{D}:\rightarrow\overset{\delta-}{B}R_3 \qquad (1)$$

(D = donor)

The stability of donor-acceptor bonds naturally depends on the donor and acceptor strengths of the components. For instance, as strong Lewis acids boron halides form stable addition compounds with amines, phosphanes, ethers, or sulfides.

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[**] Polymeric metal borides are not considered in this article, which is restricted mainly to metal-boron compounds of low molecular weight.

[1] *E. Krause* and *A. v. Grosse*: Die Chemie der metallorganischen Verbindungen. Bornträger, Berlin 1937.

[2] *R. Köster* u. *H. Polychronou*, Advan. Organometal. Chem. *2*, 257 (1964).

[3] *R. W. Auten* and *Ch. A. Kraus*, J. Amer. Chem. Soc. *74*, 3398 (1952).

[4] *G. Schmid* and *H. Nöth*, Chem. Ber. *101*, 2502 (1968).

[5] *G. Schmid*, Dissertation, Universität München 1965.

Many metal complexes have lone pairs of electrons and therefore behave as Lewis bases. Addition of such bases to the Lewis acids BR_3 affords coordinate metal-boron bonds, provided that the borane does not attack another part of the molecule. The cyclopentadienyl hydrides of molybdenum, tungsten, and rhenium represent typical metallic bases. Group B metals in complex anions are also endowed with lone pairs. Thus the very first synthesis of a metal-boron compound having a coordinate bond was accomplished with triphenylgermanate(II) as the base component [6].

$$LiGe(C_6H_5)_3 + B(C_6H_5)_3 \rightarrow Li[(C_6H_5)_3Ge{-}B(C_6H_5)_3] \quad (2)$$

Further compounds of this kind have since been discovered; they are best prepared directly from tetraphenylarsonium salts $[(C_6H_5)_4As]MX_3$ and borane derivatives BR_3 [7,8]:

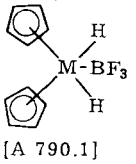
$$[(C_6H_5)_4As]MCl_3 + BF_3 \rightarrow [(C_6H_5)_4As][Cl_3M{-}BF_3] \quad (3)$$
$M = Ge, Sn$

Borane adducts of transition metal complexes have been studied much more thoroughly. The carbonylmetalate ions of manganese, rhenium, and cobalt equilibrate with diborane-6 [9]:

$$(BH_3)_2 + 2\,[M(CO)_nL]^- \rightleftharpoons 2\,[H_3B{-}M(CO)_nL]^- \quad (4)$$
$M = Mn, Re, Co;\quad L = CO, P(C_6H_5)_3;\quad n = 3,4$

Whereas one mol. equiv. $[Re(CO)_5]^-$ in tetrahydrofuran consumes two of BH_3, the equilibrium lies far to the left-hand side for M = Co. Above −25 °C, $[H_3B{-}Mn(CO)_5]^-$ also liberates diborane. Replacement of one CO group by phosphane effects such a profound increase in the basicity of the metal atom that for M = Mn and L = $P(C_6H_5)_3$ the equilibrium (4) is shifted largely to the right.

Johnson and *Shriver* [10,11] first exploited the basic character of cyclopentadienylmetal hydrides to promote their addition to boranes BR_3. Thus $(\pi\text{-}C_5H_5)_2MoH_2$, $(\pi\text{-}C_5H_5)_2WH_2$, and $(\pi\text{-}C_5H_5)_2ReH$ react with BF_3 and BCl_3 to give 1:1 adducts having a metal-boron coordinate bond (see Fig. 1).



[A 790.1]

Fig. 1. Proposed structure of $(\pi\text{-}C_5H_5)_2MH_2 \cdot BF_3$.

Surprisingly, BH_3 does not form corresponding stable adducts although the acidity towards amines follows the series $BH_3 > BF_3$. According to *Pearson* [12] this is explained by the fact that the metal hydrides are "hard" bases and therefore react preferentially with the "hard" acids BF_3 and BCl_3; BH_3 is a "soft" acid.

Square-planar d^8 complexes also have lone pairs in the d_{z^2} orbital. For instance, $L_2Ir(CO)X$ and $L_2Rh(CO)X$ (L = $P(C_6H_5)_3$, $As(C_6H_5)_3$; X = halogen) readily undergo "oxidative addition reactions" with HCl [13,14], CH_3I [15], halogen [16], Cl_3SiH [17], and even H_2 [18], to give octahedral d^6 complexes. However, if $[(C_6H_5)_3P]_2Rh(CO)X$ is treated with boron halides in benzene, the reaction

$$[(C_6H_5)_3P]_2(CO)RhX + BX'_3 \rightarrow [(C_6H_5)_3P]_2(CO)Rh(X)BX'_3 \quad (5)$$
$X,X' = Cl, Br$

takes place with formation of pentacoordinated Rh^I complexes [19]; "reductive" cleavage of a boron-halogen bond does not occur. With complexes containing different halogens (X = X'), partial halogen exchange takes place leading to mixtures of isomers. The νCO bands in the IR spectra of the adducts are shifted by 20 to 70 cm^{-1} towards shorter wavelengths compared with those of the boron-free rhodium compounds, corresponding to an increased partial positive charge on the metal atom. Confirmation of a direct Rh–B bond is provided by the ^{11}B-NMR spectra, which display Rh–B coupling (J_{Rh-B} = 145–146 Hz).

3. Covalent Metal-Boron Bonds

Covalent bonds between boron and metals and boron and non-metals are similar in character. Compounds in which an sp^2-hybridized boron atom is linked directly to a metal atom or metal ion can also be regarded as simple derivatives of borane R_2BM, where M denotes a coordinately saturated metal atom.

The stability of the metal-boron bond depends primarily upon the other ligands attached to B and M. The empty boron p_z orbital can interact with the ligands R provided that they can engage in back-donation. Should this not be the case (the ligands then exerting an electron-withdrawing effect), the metal must be able to satisfy the electron requirements of the boron atom. This can be done by interaction between the d

[6] *D. Seyferth, G. Raab,* and *O. S. Grimme,* J. Org. Chem. *26,* 3034 (1961).

[7] *M. P. Johnson, D. F. Shriver,* and *S. A. Shriver,* J. Amer. Chem. Soc. *88,* 1588 (1966).

[8] *D. F. Shriver,* Lecture at IX. Int. Congr. Coordinat. Chem., St. Moritz 1966.

[9] *G. W. Parshall,* J. Amer. Chem. Soc. *86,* 361 (1964).

[10] *M. P. Johnson* and *D. F. Shriver,* J. Amer. Chem. Soc. *88,* 301 (1966).

[11] *D. F. Shriver,* J. Amer. Chem. Soc. *85,* 3509 (1963).

[12] *R. G. Pearson,* J. Amer. Chem. Soc. *85,* 3533 (1963).

[13] *L. Vaska* and *J. W. Diluzio,* J. Amer. Chem. Soc. *83,* 2784 (1961).

[14] *L. Vaska* and *J. W. Diluzio,* J. Amer. Chem. Soc. *84,* 679 (1962).

[15] *R. F. Heck.,* J. Amer. Chem. Soc. *86,* 2796 (1964).

[16] *L. Vallarino,* Inorg. Nucl. Chem. *8,* 288 (1958).

[17] *A. J. Chalk* and *J. F. Harrod,* J. Amer. Chem. Soc. *87,* 16 (1965).

[18] *L. Vaska* and *R. E. Rhodes,* J. Amer. Chem. Soc. *87,* 4970 (1965).

[19] *P. Powell* and *H. Nöth,* Chem. Commun. *1966,* 637.

electrons of the metal and the empty p_z orbital. A metal-boron linkage of this kind resembles the covalent metal-metal bonds or metal-metalloid bonds frequently met in practice. The $(d\rightarrow d)\pi$ contributions that determine the character of a metal-metal bond are replaced by $(d\rightarrow p)\pi$ contributions in the metal-boron bond; however, the less favorable degree of overlapping of the participating atomic orbitals renders the metal-boron bond much less stable.

3.1. Borylcarbonylmetal Compounds

Carbonylmetal complexes and their phosphane or cyclopentadienyl derivatives are particularly suitable as starting materials for the synthesis of covalent boron-metal compounds. Since stable coordination is usually encountered, ligand exchange reactions and rearrangements can most probably be ruled out.

3.1.1. Preparation

Introduction of a boryl group into carbonylmetal complexes is readily accomplished by reaction of haloboranes with alkali-metal carbonylmetalates in ethers at room temperature.

$$R_{3-n}BX_n + n\ Na[M(CO)_m] \rightarrow R_{3-n}B[M(CO)_m]_n + n\ NaX \quad (6)$$

Cleavage of metal-metal bonds by haloboranes also leads to metal-boron compounds, although the reaction is of a less general nature.

$$[(CH_3)_2N]_2BCl + Co_2(CO)_8 \rightarrow [(CH_3)_2N]_2B{-}Co(CO)_4 + ClCo(CO)_4 \quad (7)$$

Phosphane- and cyclopentadienyl-substituted borylcarbonylmetal compounds are also obtainable by analogy with eq. (6) and according to eq. (8). The phosphane complexes are far more stable than the pure carbonylmetal derivatives.

$$R_{3-n}BX_n + n\ Na[M(CO)_{m-1}L] \rightarrow R_{3-n}B[M(CO)_{m-1}L]_n + n\ NaX \quad (8)$$

$L = PR'_3,\ \pi\text{-}C_5H_5$

A number of complexes prepared according to eq. (6) to (8) are listed in Table 1.

Table 1. Typical borylcarbonylmetal compounds.

	Color	M.p. (°C)	Ref.
$[(CH_3)_2N]_2B{-}Mn(CO)_5$	orange-red	60 (decomp.)	[20, 21]
$(CH_3)_2NB[Mn(CO)_5]_2$	orange-red	85 (decomp.)	[5]
$[(CH_3)_2N]_2B{-}Re(CO)_5$	yellow	60–65	[22]
$Cl_2B{-}Co(CO)_4$	brown	slow decomp.	[22]
$(C_6H_5)_2B{-}Co(CO)_4$	brown	47 (decomp.)	[22]
$(C_6H_5)_2B{-}Mn(CO)_4P(C_6H_5)_3$	yellow	120	[23]
$(C_6F_5)_2B{-}Mn(CO)_4P(C_6H_5)_3$	yellow	60–65	[22]
$(n\text{-}C_4H_9)_2B{-}Mn(CO)_4P(C_6H_5)_3$	yellow	100 (decomp.)	[23]
$ClB[Mn(CO)_4P(C_6H_5)_3]_2$	yellow	65	[22]
$[(CH_3)_2N]_2B{-}Co(CO)_3P(C_6H_5)_3$	brown	155 (decomp.)	[22]
$(C_6H_5)_2B{-}Co(CO)_3P(n\text{-}C_4H_9)_3$	brown	72 (decomp.)	[22]
$Cl_2B{-}Fe(CO)_2(\pi\text{-}C_5H_5)$	beige	113–116	[20]
$Cl_2B{-}Mo(CO)_3(\pi\text{-}C_5H_5)$	brown	85 (decomp.)	[24]
$(C_6H_5)_2B{-}W(CO)_3(\pi\text{-}C_5H_5)$	brown	75–80 (decomp.)	[24]

3.1.2. Chemical Properties

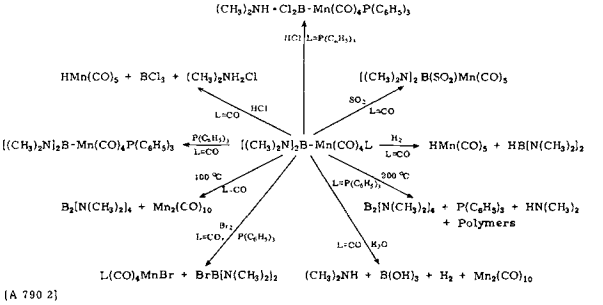
It is generally possible to distinguish three potential sites of reaction responsible for the chemical properties of the borylcarbonylmetal compounds:

a) The boron-metal bond.

b) The ligands attached to boron.

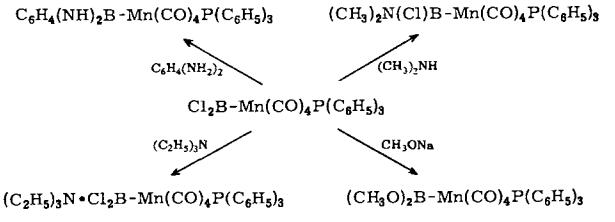
c) The ligands attached to the metal.

While the boron-metal bond proves reactive in almost every case, the reactivity of the *B*- and *M*-ligands depends upon their nature. The schemes depicted in Figures 2 and 3 illustrate the most important reactions of Mn–B compounds of this kind [21, 23].



[A 790.2]

Fig. 2. Reactions of $[(CH_3)_2N]_2B{-}Mn(CO)_4L$.



[A 790.3]

Fig. 3. Reactions of $Cl_2B{-}Mn(CO)_4P(C_6H_5)_3$.

3.1.3. Bonding and Structure

An insight into the bonding and structure of borylcarbonylmetal compounds is afforded by IR and ^{11}B-NMR spectroscopy.

The CO stretching vibrations of these molecules are very sensitive to ligand effects leading to changes in bond order between the C and the O atom. An effect of this kind is known to occur on replacement of CO ligands in carbonylmetal complexes by phosphanes [25–27]; frequency shifts towards small wave

[20] *H. Nöth* and *G. Schmid*, Angew. Chem. *75*, 861 (1963); Angew. Chem. internat. Edit. *2*, 623 (1963).

[21] *H. Nöth* and *G. Schmid*, J. Organometal. Chem. *5*, 109 (1966).

[22] *H. Nöth* and *G. Schmid*, Allg. Prakt. Chem. *17*, 610 (1966).

[23] *H. Nöth* and *G. Schmid*, Z. Anorg. Allg. Chem. *345*, 69 (1966).

[24] *G. Schmid* and *H. Nöth*, J. Organometal. Chem. *7*, 129 (1967).

[25] *M. Bigorgne* and *J. Benard*, Rev. Chim. Minerale *3*, 831 (1966).

[26] *A. Reckziegel* and *M. Bigorgne*, J. Organometal. Chem. *3*, 341 (1965).

[27] *M. Pankowski* and *M. Bigorgne*, C. R. Acad. Sci. Paris *264*, 1382 (1967).

numbers are always observed. The phenomenon is due to an increase in the relative negative charge on the metal atom caused by the new ligand, and is readily appreciated on consideration of the resonance structures:

$$\ddot{M}\leftarrow C\equiv O: \longleftrightarrow M \rightleftarrows C=\ddot{O}$$

As expected, borylcarbonylmetal compounds behave similarly. The influence of the R_2B groups on the CO bond order warrant more interest. The combined inductive and resonance effects of the ligand R affect the frequency of the CO vibrations in the same way as is observed on introduction of phosphane groups. This affords proof of π-bonding contributions to the metal-boron bond.

It may be seen from Fig. 4 that there is a linear relationship between the inductive effect of the R_2B group and the positions of the νCO frequencies in the IR spectrum: Plots of *e.g.*, the Taft constants σ^* for R in $R_2B-Mn(CO)_4P(C_6H_5)_3$ *vs.* the three strongest νCO bands (a–c), or *vs.* the two strongest (a and b) in the case of $R_2B-Co(CO)_4$, turn out to be straight lines.

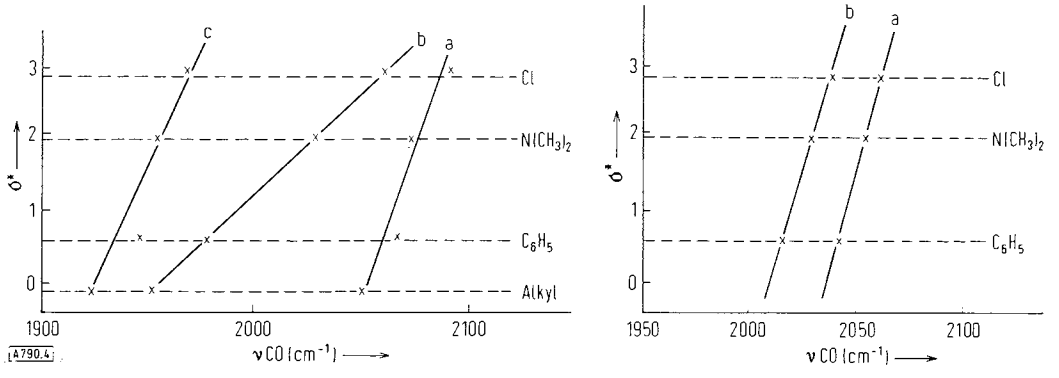


Fig. 4. Plot of the linear relationship between σ^* for R and νCO of compounds $R_2B-Mn(CO)_4P(C_6H_5)_3$ (left) and $R_2B-Co(CO)_4$ (right).

The σ^* values for R=Cl, C_6H_5, and alkyl are those given by *Taft*[28] while for R=$N(CH_3)_2$ σ^* was determined from the position of νCO (in the cases given the values determined in this way are in good agreement). *Bigorgne* found the same relation ship between σ^* and νCO for the compounds $R_3Si-Co(CO)_4$[25].

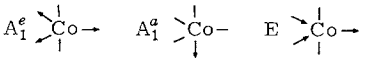
A further criterion for the correlation between σ^* and the CO bond order comes from a comparison of σ^* with the valence force constants of the CO bond. According to *Cotton* and *Kraihanzel*[29], and to *McDiarmid et al.*[30,31] the force constants k_e (for equatorial CO groups) and k_a (for axial CO groups) can be expressed in the forms

$$k_e = \mu(\lambda_{A_1^e} + 2\,\lambda_E)/3$$

and

$$k_a = \mu\lambda_{A_1^a},$$

where λ = wavelength[*]; μ = reduced mass; and A_1^e, A_1^a, and E correspond to the vibrational modes:



A plot of 10^2 (k_e-k_a) *vs.* σ^* for $R_2B-Co(CO)_4$ is also a straight line.

The relationships between the inductive effect of the R_2B group and the positions of the CO bands in the IR spectrum provide only limited information about the electronic environment of the boron atom, a feature of particular interest. We can, however, glean valuable evidence from ^{11}B-NMR spectroscopy. Owing to the considerable role played by resonance effects, the electron density on the boron atom is not necessarily reduced by the increasing electronegativity of its ligands. It may even be that the third ligand, the metal group, is able to compensate for the lack of back-donation by the other ligands. Indeed, it is reasonable to expect that the electron-donation by the metal to the boron-metal bond will increase with increasing acceptor character of these ligands. Table 2 compares the chemical shifts of a number of borylcarbonylmetals with those of the corresponding haloboranes.

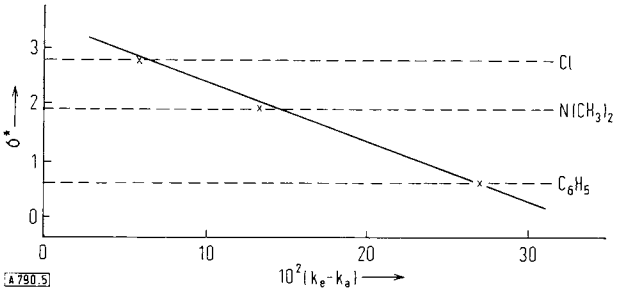


Fig. 5. Plot of the linear relationship between σ^* for R and $10^2(k_e-k_a)$ of $R_2B-Co(CO)_4$ (k values in mdyne/Å).

[*] $\lambda = 0.588851 \times 10^{-6}\,\nu^2$.

[28] *R. W. Taft* in *M. S. Newman*: Steric Effects in Organic Chemistry. Wiley, New York 1956.

[29] *F. A. Cotton* and *C. S. Kraihanzel*, J. Amer. Chem. Soc. *84*, 4432 (1962).

[30] *A. P. Hagen* and *A. G. McDiarmid*, Inorg. Chem. *6*, 686 (1967).

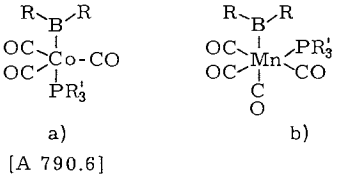
[31] *A. P. Hagen* and *A. G. McDiarmid*, Inorg. Chem. *6*, 1942 (1967).

Table 2. ^{11}B-NMR data for compounds $R_2B-Mn(CO)_4L$ and $R_2B-Co(CO)_3L$ and for the corresponding chloroboranes R_2BCl [external standard: $BF_3 \cdot O(C_2H_5)_2$].

	δ (ppm)		δ (ppm)
$Cl_2B-Mn(CO)_4B(C_6H_5)_3$	−16.0	Cl_2BCl	−56.8
$Cl_2B-Co(CO)_4$	−20.6		
$Cl_2B-Co(CO)_3P(C_6H_5)_3$	−17.3		
$Cl_2B-Co(CO)_3As(C_6H_5)_3$	−17.5		
$[(CH_3)_2N]_2B-Mn(CO)_5$	−27.1	$[(CH_3)_2N]_2BCl$	−27.5
$[(CH_3)_2N]_2B-Mn(CO)_4P(C_6H_5)_3$	−20.0		
$[(CH_3)_2N]_2B-Co(CO)_4$	−25.5		
$[(CH_3)_2N]_2B-Co(CO)_3P(C_6H_5)_3$	−26.9		
$(C_6H_5)_2B-Mn(CO)_5$	−42.8	$(C_6H_5)_2BCl$	−58.6
$(C_6H_5)_2B-Co(CO)_4$	−34.2		
$(C_6H_5)_2B-Co(CO)_3P(OC_6H_5)_3$	−42.5		
$(C_6H_5)_2B-Co(CO)_3P(C_4H_9)_3$	−42.7		
$(C_6H_5)_2B-Co(CO)_3As(C_6H_5)_3$	−42.8		

Apart from the bis(dimethylamino)boranes, some considerable discrepancies are apparent between the chemical shifts of the boron-metal compounds and those of their chloro analogs. The chloro derivatives R_2BCl exhibit an increasing downfield shift along the series $R = N(CH_3)_2 < Cl < C_6H_5$. On replacement of Cl by the metallic group $Mn(CO)_4L$ or $Co(CO)_3L$ the order changes to $Cl < N(CH_3)_2 < C_6H_5$. If it is assumed, as is perfectly reasonable, that the neighboring-group anisotropic effects of the ligands of a given type of compound remain unaltered, this finding is best interpreted in terms of an increased π-bonding contribution to the boron-metal bond, which is attributable to the metal.

The most reliable structural information so far has been obtained for $R_2B-Co(CO)_3PR'_3$ and $R_2B-Mn(CO)_4PR'_3$ [5, 21, 23]. The two strong CO bands (A_1 and E respectively) found for the phosphane-substituted boron-cobalt compounds suggest a *trans* bipyramidal structure of C_{3v} symmetry. The three or four strong CO bands in boron-manganese compounds of this type would indicate an octahedral *cis* configuration of the ligands surrounding the Mn atom.



[A 790.6]

Fig. 6. Proposed structure of the compounds $R_2B-Co(CO)_3PR'_3$ (a) and $R_2B-Mn(CO)_4PR'_3$ (b).

3.2. Borylphosphanemetal Compounds

Complexes in which a metal atom bonded to a boryl group completes its coordination sphere with phosphane ligands are particularly stable. Organophosphanes are more effective donors than carbon monoxide and thus render the metal atom more strongly negative. In contrast, the acceptor properties predominate in the case of PF_3, thus leading to a pronounced positive charge on the metal.

3.2.1. Preparation

The routes available for the synthesis of borylphosphanemetal complexes are depicted by equations (9) to (12).

$$(R'_3P)_nM + R_2BX \rightarrow (R'_3P)_{n-m}M(X)BR_2 + m\ PR'_3 \quad (9)$$

$$(R'_3P)_nM-H + R_2BX \rightarrow (R'_3P)_nM-BR_2 + HX \quad (10)$$

$$(R'_3P)_nM-M' + R_2BX \rightarrow (R'_3P)_nM-BR_2 + M'X \quad (11)$$

M′ = alkali metal

$$2\ (PP)_2M-H + R_2BX \rightarrow (PP)_2MX_2 + (PP)_2M(BR_2)_2 + H_2 \quad (12)$$

PP = diphosphine

Platinum and cobalt complexes are obtained particularly readily by "oxidative addition" as shown in eq. (9) [32]. Tetrakis(triphenylphosphane)platinum(0) reacts, *e.g.* with diphenylchloroborane, diphenylbromoborane, or tribromoborane in cyclohexane to give the compounds *cis*-$[(C_6H_5)_3P]_2Pt(X)BR_2$ (X = Cl, Br; R = C_6H_5, Br). Two $P(C_6H_5)_3$ ligands can be replaced by $(C_6H_5)_2P-CH_2-CH_2-P(C_6H_5)_2$ (TPE). According to the same principle, *cis*-$(TPE)_2Co(X)BR_2$ (X = Cl, Br, I; R = C_6H_5, Br, I) is formed from $(TPE)_2Co$ and R_2BX in boiling benzene [32].

Reactions between metal hydrides and haloboranes in accordance with eq. (10) are known in the case of platinum and iridium complexes. The pale yellow compound $[(C_6H_5)_3P]_2ClPt-B(C_6H_5)_2$ is formed by elimination of HCl from $(C_6H_5)_2BCl$ and $[(C_2H_5)_3P]_2Pt(Cl)H$ in boiling xylene, and the beige compound $[(C_6H_5)_3P]_3Cl_2Ir-B(C_6H_5)_2$ is formed similarly on addition of triethylamine.

Reaction (11), which can be regarded as a variant of (10), has hitherto only been used for the preparation of boryltrifluorophosphanecobalt compounds: The compound $(F_3P)_4Co-K$ synthesized by *Kruck* [33] reacts in ether with the haloboranes $[(CH_3)_2N]_2BCl$, $C_{12}H_8BCl$ ($C_{12}H_8B$ = borafluorenyl), and $(C_6H_5)_2BCl$ to give $[(CH_3)_2N]_2B-Co(PF_3)_4$, $C_{12}H_8B-Co(PF_3)_4$, and $(C_6H_5)_2B-Co(PF_3)_4$, respectively, which are crystalline, yellow to brown products with covalent cobalt-boron bonds [22, 34].

The greatest interest attaches to reaction (12) although it has hitherto been limited to only one type of complex: (TPE)Co−H reacts with R_2BX (X = Cl, Br, I; R = Br, I, C_6H_5; BR_2 = borafluorenyl) in boiling benzene or xylene to give complexes $(TPE)_2Co(BR_2)_2$ containing two Co−B bonds [35–37]. Both the unexpected reaction course, with liberation of molecular hydrogen, and certain peculiarities in the behavior of the compounds attract attention.

[32] *G. Schmid, W. Petz, W. Arloth,* and *H. Nöth,* Angew. Chem. *79,* 683 (1967); Angew. Chem. internat. Edit. *6,* 696 (1967).

[33] *Th. Kruck* and *W. Lang,* Z. Anorg. Allg. Chem. *343,* 181 (1966).

[34] *G. Schmid,* unpublished.

[35] *G. Schmid* and *H. Nöth,* Z. Naturforsch. *20b,* 1008 (1965).

[36] *G. Schmid* and *H. Nöth,* Chem. Ber. *100,* 2899 (1967).

[37] *G. Schmid,* Chem. Ber. *102,* 191 (1969).

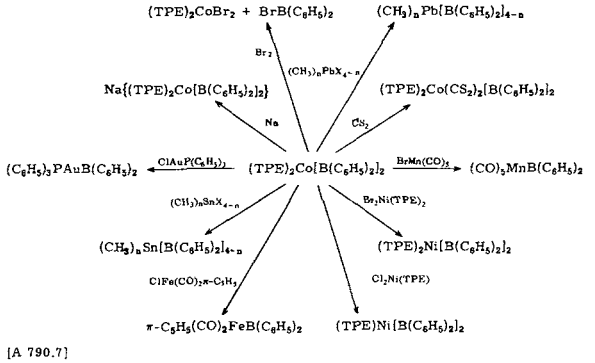
3.2.2. Chemical Properties

The covalent boron-metal bonds in the borylplatinum and boryliridium complexes mentioned above differ from those in the borylcarbonylmetal complexes (Section 3.1.2) in their greatly enhanced stability. For instance, they are much more resistant to oxygen. However, even these bonds are cleaved by strong oxidizing agents such as bromine [35]:

$$(R_3P)_2Pt(Cl)B(C_6H_5)_2 + Br_2 \rightarrow (R_3P)_2Pt(Cl)Br + (C_6H_5)_2BBr \quad (13)$$

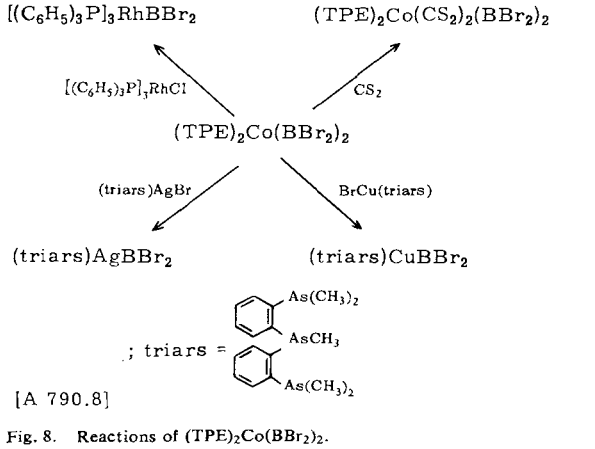
$(TPE)_2Co(BR_2)_2$ behaves somewhat differently. The extreme sensitivity of the Co–B bond is revealed by, among other things, its spontaneous oxidation by atmospheric oxygen. The magnetic moment of $(TPE)_2Co[B(C_6H_5)_2]_2$, $\mu = 2.84\,\mu_B$, is consistent only with a paramagnetic d^7 low-spin complex. However, this moment is much too high for an unpaired electron and thus indicates a large orbital contribution to the total moment, as has been observed with square-planar Co^{II} complexes [38]. Accordingly, the compound is easily reduced to diamagnetic $Na[(TPE)_2Co[B(C_6H_5)_2]_2$ by sodium [36]. The R_2B group in $(TPE)_2Co(BR_2)_2$ can be exchanged for other metal complexes [36].

$$(TPE)_2Co(BR_2)_2 + 2\,L_nM{-}Hal \rightarrow (TPE)_2CoHal_2 + 2\,L_nM{-}BR_2 \quad (14)$$



[A 790.7]

Fig. 7. Reactions of $(TPE)_2Co[B(C_6H_5)_2]_2$.



[A 790.8]

Fig. 8. Reactions of $(TPE)_2Co(BBr_2)_2$.

[38] *F. A. Cotton* and *R. H. Holm*, J. Amer. Chem. Soc. *82*, 2983 (1960).

This reaction can be used for the synthesis of new metal-boron compounds $L_nM{-}BR_2$ (L = ligand) that are inaccessible by other routes (cf. Figures 7 and 8).

By this method, we prepared the first molecules containing covalent boron-copper, boron-silver, boron-gold, boron-nickel, boron-rhodium, and boron-lead bonds [36, 37, 39]. Boron-tin derivatives were formerly prepared by eq. (15) [40].

$$(R_2N)_2BCl + LiSnR'_3 \rightarrow (R_2N)_2B{-}SnR'_3 + LiCl \quad (15)$$

However, it proves impossible to introduce arylboryl groups by this method, whereas no difficulties are encountered in reaction (14) [41]. Even the hitherto unknown borylplumbanes can be prepared by this technique [39].

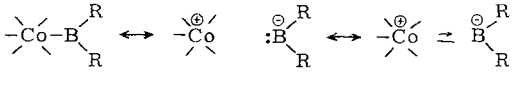
3.2.3. Bonding and Structure

The chemical peculiarities of the complexes $(TPE)_2Co(BR_2)_2$ stem from the nature of their Co–B bond. This is illustrated most vividly by the chemical shifts $\delta^{11}B$. While the borylcarbonylmetals, like the borylphosphaneplatinum and borylphosphaneiridium compounds give normal ^{11}B-NMR spectra, *i.e.* behave as molecules with typical trivalent boron atoms, the first-named complexes differ considerably. The δ values observed, ranging from +15.0 to +23.5 ppm, are very similar to those measured for molecules having tetravalent boron atoms [42].

Table 3. ^{11}B-NMR data for compounds $(PP)_2Co(BR_2)_2$ [external standard: $BF_3 \cdot O(C_2H_5)_2$].

	δ (ppm)
$(TPE)_2Co[B(C_6H_5)_2]_2$	+23.0
$(TPE)_2Co(BBr_2)_2$	+23.0
$\{C_6H_4[P(CH_3)_2]_2\}_2Co[B(C_6H_5)_2]_2$	+23.5
$\{C_6H_4[P(CH_3)_2]_2\}_2Co(BC_{12}H_8)_2$	+15.0

If these findings are interpreted solely in terms of the increase in negative charge on the boron atom with neglect of any possible paramagnetic contact shift, each boron atom carries a unit negative charge. The likely bonding is illustrated by the following resonance structures:



Since the central form can be regarded as a pseudocarbene, such complexes are often designated "borene-metal complexes". Such an interpretation assists our understanding of not only the ligand-exchange reactions and the presence of Co^{II} in the complexes, but also the results of magnetic measure-

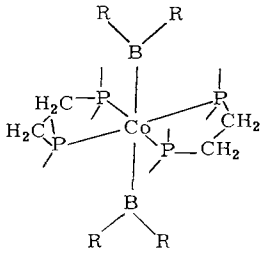
[39] *H. Schäfer*, Dissertation, Universität Marburg 1969.

[40] *H. Nöth* and *K. H. Hermannsdörfer*, Angew. Chem. *76*, 377 (1964); Angew. Chem. internat. Edit. *3*, 377 (1964).

[41] *H. Nöth*, *H. Schäfer*, and *G. Schmid*, Angew. Chem. *81*, 530 (1969); Angew. Chem. internat. Edit. *8*, 515 (1969).

[42] *H. Nöth* and *H. Vahrenkamp*, Chem. Ber. *99*, 1049 (1966).

ments that suggest a tetragonal-bipyramidal structure with the two R_2B groups separated by a relatively large distance and *trans* to each other (Jahn-Teller distortion of octahedral d^7 complexes).

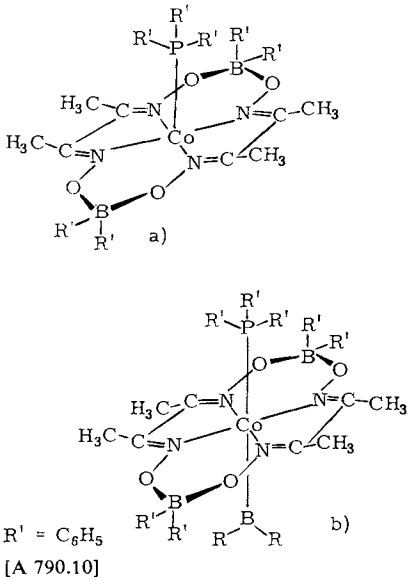


[A 790.9]

Fig. 9. Proposed structure of the compounds $(PP)_2Co(BR_2)_2$

3.3. Bis(2,3-butanedionedioximato)cobalt-Boron Compounds[43]

The compound bis(2,3-butanedionedioximato)chlorotriphenylphosphanecobalt(III), which is formulated as $(C_6H_5)_3P(DMGH)_2CoCl$[*] and was described by *Tschugaeff*[44] in 1907, can be used for the preparation of compounds $(C_6H_5)_3P(DMGBR'_2)_2Co-BR_2$ containing covalent metal-boron bonds. Reduction with potassium in tetrahydrofuran and reaction with diphenylchloroborane initially leads to bridged $(C_6H_5)_3P[DMGB(C_6H_5)_2]_2Co$ (Fig. 10a). Repeated alkali-metal reduction leading to formation of $(C_6H_5)_3P[DMGB(C_6H_5)_2]_2Co-K$ followed by treatment with R_2BCl finally affords compounds having the structure shown in Fig. 10b (R = C_6H_5, $N(CH_3)_2$, Cl or R_2B = borafluorenyl).



$R' = C_6H_5$

[A 790.10]

Fig. 10. Proposed structure of compounds $(C_6H_5)_3P[DMGB(C_6H_5)_2]_2Co$ (a) and $(C_6H_5)_3P(DGMB(C_6H_5)_2]_2Co-BR_2$ (b).

[43] *G. Schmid, P. Powell,* and *H. Nöth,* Chem. Ber. *101,* 1205 (1968).

[*] DMGH = $\begin{matrix} H_3C-C=NO^- \\ | \\ H_3C-C=NOH \end{matrix}$.

[44] *L. Tschugaeff,* Ber. Dtsch. Chem. Ges. *40,* 3498 (1907).

Like the complexes $(TPE)_2Co(BR_2)_2$ (see Section 3.2), these complexes can also undergo ligand exchange; similar bonding therefore appears probable.

$$(C_6H_5)_3P[DMGB(C_6H_5)_2]_2Co-BR_2 + L_nM\text{-}Hal \rightarrow (C_6H_5)_3P[DMGB(C_6H_5)_2]_2Co-Hal + L_nM-BR_2 \quad (16)$$

Interestingly, the metal-boron stretching frequency at 530–540 cm^{-1} was first assigned with a high degree of certainty in the IR spectrum of these complexes.

4. Cage Compounds Containing Boron and Metal Atoms

closo and *nido* compounds of boron have been known for some time. Higher boranes and the carboranes have been the focal points of many intense studies in recent years[45–52]. Alongside the usual covalent B–H and B–B bonds, they contain characteristic multicenter bonds. Metal atoms having vacant d orbitals can also participate in such electron-deficient bonds, especially when in their higher oxidation states since the number of vacant d orbitals is then larger.

4.1. Dicarbollyl Derivatives of Transition Metals[*]

Since the carbollylmetal complexes closely resemble the metallocenes and their derivatives, they were designated π-carbollylmetal complexes by their discoverer *Hawthorne*, although there are actually fundamental differences in bonding between the two types. Classification of these complexes as compounds containing multicenter bonds appears more reasonable.

In 1965[51] *Hawthorne et al.* succeeded in preparing undecahydrodicarba-*nido*-undecaborate(2-). This species can exist in two isomeric forms, namely (3)-1,2- and (3)-1,7-$B_9C_2H_{11}^{2-}$ [**] (Fig. 11).

The isomeric, singly protonated "dicarbollide" ions (3)-1,2-$B_9C_2H_{12}^-$ and (3)-1,7-$B_9C_2H_{12}^-$, which yield

[45] *R. E. Williams, C. D. Good,* and *J. Shapiro,* 140th Meeting Amer Chem. Soc. 1961, Abstr. 14 N, 36.

[46] *T. L. Haying, J. W. Ager jr., S. L. Clark, D. J. Mangold, H. L. Goldstein, M. Hillman, R. J. Polak,* and *J. W. Saymanski,* Inorg. Chem. *2,* 1089 (1963).

[47] *M. M. Fein, J. Bobinsky, N. Mayes, N. Schwartz,* and *M. S. Cohen,* Inorg. Chem. *2,* 1111 (1963).

[48] *W. N. Lipscomb,* Proc. Nat. Acad. Sci. U.S. *47,* 1791 (1961).

[49] *K. Issleib, R. Lindner,* and *A. Tzschach,* Z. Chem. *6,* 1 (1967).

[50] *R. Köster* and *M. A. Grassberger,* Angew. Chem. *79,* 197 (1967); Angew. Chem. internat. Edit. *6,* 218 (1967).

[51] *M. F. Hawthorne* and *R. L. Pilling,* J. Amer. Chem. Soc. *87,* 3987 (1965).

[52] *W. N. Lipscomb*: Boron Hydrides. W. A. Benjamin, New York 1963.

[*] The suffix "ollyl" in the trivial names for carbaborate ligands and "ollide" for the corresponding anions are derived from the Spanish word "*olla*" meaning basket.

[**] See [53] and Inorg. Chem. *7,* 1945 (1968) for the nomenclature of this system.

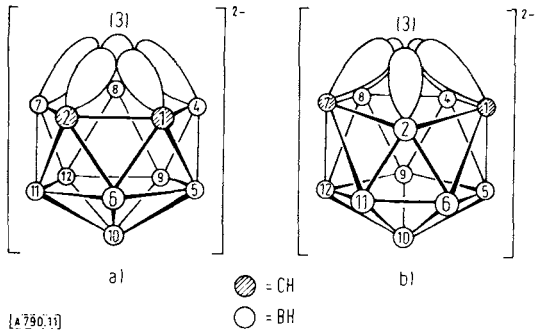


Fig. 11. Structures of the isomers (3)-1,2-$B_9C_2H_{11}^{2-}$ (a) and (3)-1,7-$B_9C_2H_{11}^{2-}$ (b).

the dianions according to eq. (17), contain a hydrogen atom attached to an icosahedral apex [53] which is replaced by a metal atom in the dicarbollyl complexes.

$$B_9C_2H_{12}^- + NaH \rightarrow Na^+ + B_9C_2H_{11}^{2-} + H_2 \quad (17)$$

4.1.1. Preparation

Of the many dicarbollyl complexes of metals known at present we shall now consider a few selected examples.

$FeCl_2$ reacts with (3)-1,2-$B_9C_2H_{11}^{2-}$ to give the ferrocene analog $[Fe((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{2-}$ [54] which can be isolated as the tetramethylammonium salt. *C*-Substituted derivatives can also be synthesized by the same technique. The reddish-brown Fe^{II} complex is readily oxidized on exposure to air to the red anion $[Fe((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^-$:

$$2\,(3)\text{-}1,2\text{-}B_9C_2H_{11}^{2-} + FeCl_2 \rightarrow [Fe((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{2-} + 2\,Cl^- \quad (18)$$

$$[Fe((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{2-} \rightarrow e^- + [Fe((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^- \quad (19)$$

The cyclopentadienyl-like properties of (3)-1,2-$B_9C_2H_{11}^{2-}$ are again apparent in the Fe^{III} complex $[(\pi\text{-}C_5H_5)Fe((3)\text{-}1,2\text{-}B_9C_2H_{11})]$ [55], whose synthesis proceeds as shown in eq. (20). Eq. (21) and (22) represent the formation of tricarbonyl-manganese and -rhenium derivatives [56a]:

$$C_5H_5^- + (3)\text{-}1,2\text{-}B_9C_2H_{11}^{2-} + FeCl_2 \rightarrow [(\pi\text{-}C_5H_5)Fe((3)\text{-}1,2\text{-}B_9C_2H_{11})] + 2\,Cl^- + e^- \quad (20)$$

$$(3)\text{-}1,2\text{-}B_9C_2H_{11}^{2-} + BrM(CO)_5 \rightarrow [((3)\text{-}1,2\text{-}B_9C_2H_{11})M(CO)_5]^- + Br^- \quad (21)$$

$$[((3)\text{-}1,2\text{-}B_9C_2H_{11})M(CO)_5]^- \rightarrow [((3)\text{-}1,2\text{-}B_9C_2H_{11})M(CO)_3]^- + 2\,CO \quad (22)$$

M = Mn, Re

[53] *M. F. Hawthorne, D. C. Young, T. D. Andrews, D. V. Howe, R. L. Pilling, A. D. Pitts, M. Reintjes, L. F. Warren,* and *P. A. Wegner,* J. Amer. Chem. Soc. *90,* 879 (1968).

[54] *M. F. Hawthorne, D. C. Young,* and *P. A. Wegner,* J. Amer. Chem. Soc. *87,* 1818 (1965).

[55] *M. F. Hawthorne* and *R. L. Pilling,* J. Amer. Chem. Soc. *87,* 3987 (1965).

[56] a) *M. F. Hawthorne* and *T. D. Andrews,* J. Amer. Chem. Soc. *87,* 2496 (1965); b) Chem. Commun. *1965,* 443.

$CoCl_2$ reacts similarly to $FeCl_2$ with (3)-1,2-$B_9C_2H_{11}^{2-}$ to give $[Co((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^-$ containing Co^{III} [56b] The cesium and tetramethylammonium salts of this complex are readily reduced to the red cobaltocene analog $[Co((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{2-}$, the Co^{III} complex being regenerated on exposure to atmospheric oxygen.

Nickel and palladium exist in a great variety of oxidation states in carbollyl complexes [53,57]. The compounds $[M^{n+}((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{n-4}$ (M = Ni, Pd) and their *C*-substituted derivatives can contain the metal atoms in the formal oxidation states +2, +3, and +4. The compound $[Ni((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{2-}$ is formed, *e.g.*, from $NiCl_2$ and (3)-1,2-$B_9C_2H_{11}^{2-}$; $[Pd((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{2-}$ is formed similarly. The M^{IV} complex can be attained by reaction of the metal acetylacetonates with dicarbollide ions. Comproportionation of the M^{II} and M^{IV} complexes gives compounds containing M^{III}.

$[\pi\text{-}(C_6H_5)_4C_4]Pd((3)\text{-}1,2\text{-}B_9C_2H_{11})$, which is prepared according to eq. (23), may be cited as an example of a palladium complex with mixed ligands:

$$2\,Na_2((3)\text{-}1,2\text{-}B_9C_2H_{11}) + [\pi\text{-}(C_6H_5)_4C_4PdCl_2]_2 \rightarrow 2\,[\pi\text{-}(C_6H_5)_4C_4]Pd((3)\text{-}1,2\text{-}B_9C_2H_{11}) + 4\,NaCl \quad (23)$$

The first dicarbollyl derivative of platinum (1,5-C_8H_{12})Pt((3)-1,2-$B_9C_2H_{11}$) was prepared recently [57b]. There is also a large number of chromium, molybdenum, and tungsten complexes. It will suffice here to mention $[Cr((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^-$ [58], $[((3)\text{-}1,2\text{-}B_9C_2H_{11})Mo(W)(CO)_3]^{2-}$, $[((3)\text{-}1,2\text{-}BC_2H_{11})W_2(CO)_8]^{2-}$, or $[((3)\text{-}1,2\text{-}B_9C_2H_{11})MoW(CO)_8]^{2-}$, which are obtained from $CrCl_3$ and $Mo(CO)_6$ or/and $W(CO)_6$ by reaction with the dicarbollide ion [53].

Copper and gold are also represented in the series of carbollyl complexes, in the form of $[M((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{2-}$ (M = Cu, Au) [59,60].

In 1967, *Hawthorne* described the carbollide ion undecahydrodicarba-*nido*-nonaborate(2-), $B_7C_2H_{11}^{2-}$ [61], which seems quite as suitable as the $B_9C_2H_{11}^{2-}$ system for carbollyl complex formation. Reaction (24) yields 3,3′-*commo*-bis[nonahydro-1,2-dicarba-3-cobalta-*closo*-decaborate](2-), which is oxidized by an excess of $CoCl_2$ in tetrahydrofuran [62,63]:

$$2\,B_7C_2H_{11}^{2-} + CoCl_2 \rightarrow 2\,H_2 + [Co(B_7C_2H_9)_2]^{2-} + 2\,Cl^- \quad (24)$$

[57] a) *L. F. Warren jr.* and *M. F. Hawthorne,* J. Amer. Chem. Soc. *89,* 476 (1967); b) *ibid. 92,* 1157 (1970).

[58] *M. F. Hawthorne,* Lecture at Int. Sympos. on Organometallic Chemistry, München 1967; *M. F. Hawthorne* and *H. W. Ruhle,* Inorg. Chem. *8,* 176 (1969).

[59] *R. M. Wing,* J. Amer. Chem. Soc. *89,* 5599 (1967).

[60] *L. F. Warren jr.* and *M. F. Hawthorne,* J. Amer. Chem. Soc. *90,* 4823 (1968).

[61] *M. F. Hawthorne* and *T. A. George,* J. Amer. Chem. Soc. *89,* 7114 (1967).

[62] *T. A. George* and *M. F. Hawthorne,* J. Amer. Chem. Soc. *90,* 1661 (1968); *91,* 5475 (1969).

[63] *M. F. Hawthorne* and *A. D. Pitts,* J. Amer. Chem. Soc. *89,* 7115 (1966).

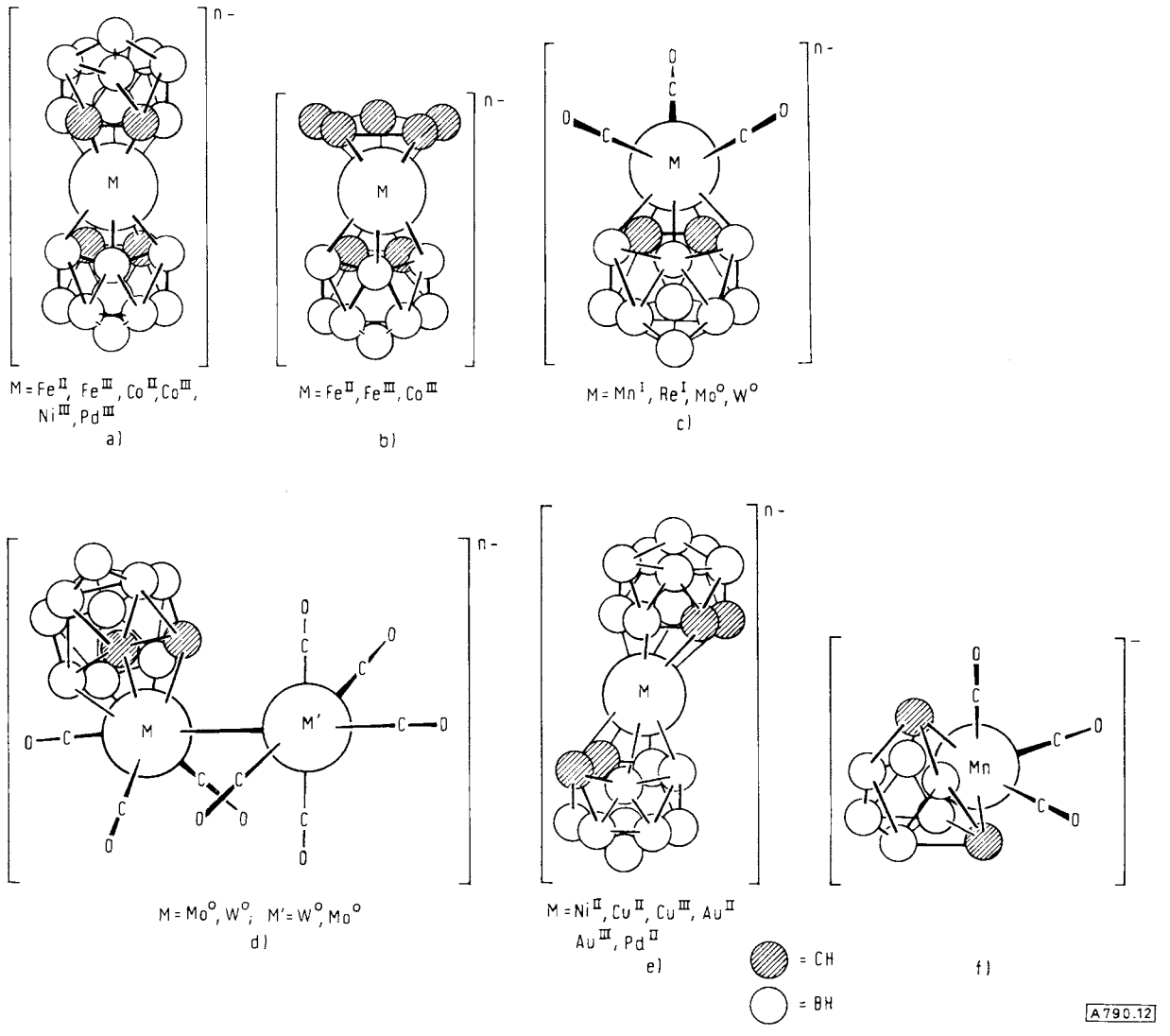


Fig. 12. Structures of dicarbollylmetal complexes: $[M((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{n-}$ (a), $[(\pi\text{-}C_5H_5)M((3)\text{-}1,2\text{-}B_9C_2H_{11})]^{n-}$ (b), $[((3)\text{-}1,2\text{-}B_9C_2H_{11})M(CO)_3]^{n-}$ (c), $[((3)\text{-}1,2\text{-}B_9C_2H_{11})MM'(CO)_8]^{n-}$ (d), $[M((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{n-}$ (e), $[(B_6C_2H_8)Mn(CO)_3]^-$ (f).

$$[Co(B_7C_2H_9)_2]^{2-} + 1/2\ CoCl_2 \rightarrow 1/2\ Co + Cl^- + [(B_7C_2H_9)_2Co]^- \quad (25)$$

A metal atom is readily incorporated into a carborane skeleton on reaction of $B_7C_2H_{11}^{2-}$ with $BrMn(CO)_5$: $[(B_6C_2H_8)Mn(CO)_3]^-$ (Fig. 12f) is formed in boiling tetrahydrofuran [63].

4.1.2. Structure

The structures of a number of characteristic dicarbollylmetal complexes, most of which were determined by X-ray studies [57b,64–67], are depicted in Fig. 12a–f.

4.2. Phosphacarbollylmetal Complexes

(3)-1,2- and (3)-1,7-phosphacarbollides also prove suitable for complex formation with metal ions. Thus *Todd et al.* were able to prepare the first complexes $[M((3)\text{-}1,7\text{-}B_9H_9CHPCH_3)_2]$ and $[M((3)\text{-}1,2\text{-}B_9H_9CHPCH_3)_2]$ (M = Fe, Co, Ni) and to determine their structures [68a, b], which were found to resemble those of the dicarbollyl complexes. Replacement of a phosphacarbollyl ligand by allyl, cyclopropenyl, or nitrosyl has recently been accomplished [68c].

4.3. Gallacarboranes

Although carboranes form cage-like structures with a wide variety of transition metals, a carborane structure containing a Group IIIB metal was only

[64] *A. Zalkin, D. H. Templeton,* and *T. E. Hopkins,* J. Amer. Chem. Soc. *87,* 3988 (1965).

[65] *A. Zalkin, T. E. Hopkins,* and *D. H. Templeton,* Inorg. Chem. *5,* 1189 (1966).

[66] *A. Zalkin, T. E. Hopkins,* and *D. H. Templeton,* Inorg. Chem. *6,* 1911 (1967).

[67] a) *R. M. Wing,* J. Amer. Chem. Soc. *90,* 4828 (1968); *92,* 1187 (1970); b) *D. St. Clair, A. Zalkin,* and *D. H. Templeton, ibid. 92,* 1173 (1970); c) *M. R. Churchill* and *K. Gold, ibid. 92,* 1180 (1970).

[68] a) *L. J. Todd, J. C. Paul, J. L. Little, P. S. Welcker,* and *C. R. Peterson,* J. Amer. Chem. Soc. *90,* 4489 (1968); b) *J. L. Little, P. S. Welcker, N. J. Loy,* and *L. J. Todd,* Inorg. Chem. *9,* 63 (1970); c) *P. S. Welcker* and *L. J. Todd, ibid. 9,* 286 (1970). d) *R. N. Grimes* and *W. J. Rademaker,* J. Amer. Chem. Soc. *91,* 6498 (1970).

discovered very recently. However, there is every reason to believe that such complexes will become available in large numbers.

Trimethylgallium reacts *e.g.* with 2,3-dicarbahexaborane-8, $C_2B_4H_8$, in the gaseous state at 215 °C to give 1-methyl-1-galla-2,3-dicarba-*closo*-heptaborane-7, $CH_3GaC_2B_4H_6$ [68d], which is assigned the structure shown in Fig. 13 on the basis of its ^{1}H-NMR, ^{11}B-NMR, IR, and mass spectra.

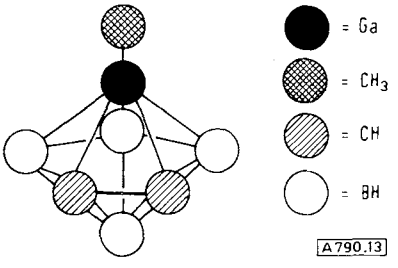


Fig. 13. Proposed structure for $CH_3GaC_2B_4H_6$.

4.4. Thiaboratometal Complexes

The assumption that the carbollylmetal complexes are not classical π-complexes but boron-metal multicenter complexes leads to the conclusion that the existence of such compounds cannot be limited to carborane systems.

The first thiaborane complexes were reported by *Muetterties et al.* [69]: The readily accessible anion $B_{10}H_{10}S^{2-}$ reacts with transition metal ions to give complexes of the kind $[M(B_{10}H_{10}S)_2]^{n-}$ (M = Fe^{II}, Fe^{III}, or Co^{II}). Structural analogies exist between these complexes and the system $[M((3)\text{-}1,2\text{-}B_9C_2H_{11})_2]^{n-}$. The compounds $(B_{10}H_{10}S)Pt[P(C_2H_5)_3]_2$ and $[(B_{10}H_{10}S)Re(CO)_3]^-$ are also examples taken from a new branch of complex chemistry that is still in its infancy.

4.5. Decaboranemetal Complexes

Finally, mention should be made of a class of metal-boron cage compounds that can be derived from pure boron hydrides without any hetero atoms. *Greenwood et al.* succeeded in preparing the first complexes [70, 71] $[B_{10}H_{12}AlH_2]^- \cdot nO(C_2H_5)_2$ and $[B_{10}H_{12}GaH_2]^-$ by reaction of $(CH_3)_3NAlH_3$, $(CH_3)_3NAlH_2Cl$, and $(CH_3)_3NGaH_3$, respectively, with $B_{10}H_{14}$. In the same way, $B_{10}H_{14}$ reacts with alkyl derivatives of zinc, cadmium, and mercury to give products of composition $B_{10}H_{12}M \cdot nS$ [72–75] (S = solvent). Treatment of $(C_5H_5N)_4FeBr_2$ with $B_{10}H_{14}$ in benzene or tetrahydrofuran furnishes the tetrahedral high-spin complex $[Br_2Fe(B_{10}H_{13})(NC_5H_5)]$ [76].

The scope of the reaction was extended by *Muetterties et al.*, who were also able to throw some light on the hitherto unsolved structural problems [77].

$$4\ B_{10}H_{13}^- + [(C_6H_5)_3P]_2NiCl_2 \rightarrow [Ni(B_{10}H_{12})_2]^{2-} + 2\ B_{10}H_{14} + 2\ (C_6H_5)_3P + 2\ Cl^- \quad (26)$$

$$2\ B_{10}H_{13}^- + [(C_2H_5)_3P]_2PtCl_2 \rightarrow [(C_2H_5)_3P]_2Pt(B_{10}H_{12}) + B_{10}H_{14} + 2\ Cl^- \quad (27)$$

$$2\ B_{10}H_{13}^- + [(C_6H_5)_3P]_2(CO)IrCl \rightarrow \{[(C_6H_5)_3P]_2(CO)Ir(B_{10}H_{12})\}^- + B_{10}H_{14} + Cl^- \quad (28)$$

Reactions (26)–(28) represent a series of simple preparations from the readily accessible $B_{10}H_{13}^-$ ion. The yellow to red crystalline complexes exhibit remarkable thermal stability, some of them not decomposing below 300 °C.

The structures proposed are based on the assumption that instead of fulfilling a 6,9 bridging function (Fig. 14a), as was initially supposed, the metal atom occupies the open plane formed by four boron atoms (in positions 5, 6, 9, 10) to give an icosahedral fragment. Its stability is apparent from the foregoing discussion. Thus the $B_{10}H_{12}^{2-}$ ligand conforms to the systems $B_9C_2H_{11}^{-2}$, $B_{10}CH_{11}^{3-}$ [78, 79], or $B_{10}SH_{10}^{2-}$.

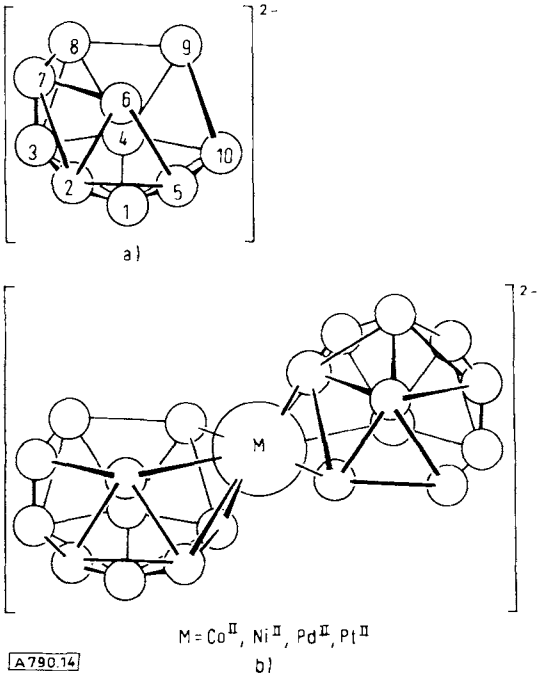


Fig. 14. Proposed structure for the ion $(B_{10}H_{12})^{2-}$ (a) and for the complexes $[M(B_{10}H_{12})_2]^{2-}$ (b).

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[70] *N. N. Greenwood* and *J. A. McGinnety*, Chem. Commun. *1965*, 331.

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[73] *N. N. Greenwood* and *N. F. Travers*, J. Chem. Soc. *1967*, 880.

[74] *N. N. Greenwood* and *N. F. Travers*, J. Chem. Soc. *1968*, 15.

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[76] *N. N. Greenwood* and *H. Schick*, Chem. Commun. *1969*, 935.

[77] *F. Klanberg, P. A. Wegner, G. W. Parshall*, and *E. L. Muetterties*, Inorg. Chem. *7*, 2072 (1968).

[78] *D. E. Hyatt, J. L. Little, J. T. Moran, F. R. Scholer*, and *L. J. Todd*, J. Amer. Chem. Soc. *89*, 3342 (1967).

[79] *W. H. Knoth*, J. Amer. Chem. Soc. *89*, 3342 (1967).

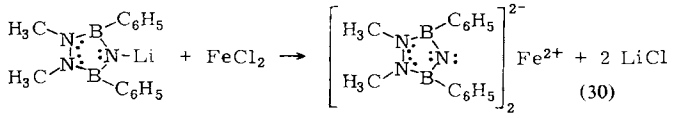
5. Aminoboranes as Ligands in Metal Complexes

Boron-nitrogen chemistry and carbon chemistry have many common features as a result of isosteric relationships. The benzene-borazole analogy [80] is probably one of the best known. Nevertheless, all the other boron-nitrogen systems resemble the corresponding carbon compounds within certain limits. One of the most significant features was discovered only comparatively recently, *i.e.* the ability of B=N double bond systems to form π-complexes analogous to those of C=C compounds. In 1967, hexamethylborazine $(CH_3)_6B_3N_3$ was successfully used as a π-complex ligand in $(CO)_3Cr[B_3N_3(CH_3)_6]$ [81,82]. Many chemical and physical properties of this complex, which may be prepared in accordance with eq. (29), are analogous to those of $[(CH_3)_6C_6]Cr(CO)_3$:

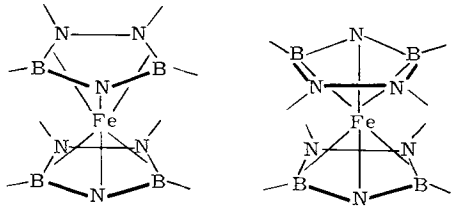
$$(CH_3CN)_3Cr(CO)_3 + B_3N_3(CH_3)_6 \rightarrow [B_3N_3(CH_3)_6]Cr(CO)_3 + 3\ CH_3CN \quad (29)$$

It forms orange-red crystals that sublime above 90 °C in a high vacuum. The IR spectra resemble each other, as do also the ^{1}H-NMR spectra [82]. The chemical shifts $\delta^{11}B$ and $\delta^{15}N$, which appear 8.2 and 47 ppm farther upfield in $[(CH_3)_6B_3N_3]Cr(CO)_3$ than in free borazine, provide additional evidence for the presence of B=N-metal π bonds. The shift of the νCO bands towards shorter wavelengths compared with $Cr(CO)_6$ rules out a pure acceptor function of borazole and shows it instead to be a typical donor-acceptor ligand.

The complex prepared by eq. (30) can be viewed as a ferrocene analog whose possible structures are shown in Fig. 15 [83].



(30)



[A 790.15]

Fig. 15. Possible structures of $Fe[(CH_3)_2N_3B_2(C_6H_5)_2]_2$.

This compound also shows a positive shift of the ^{11}B-resonance signal, thus indicating a bonding similar to that in the borazine complex.

That the boron-nitrogen system is, in principle, able to form π-complexes is apparent from the addition of simple acyclic aminoboranes to transition metals.

$$(CH_3CN)_3M(CO)_3 + [(CH_3)_2N]_3B \rightarrow [(CH_3)_2N]_3BM(CO)_3 + 3\ CH_3CN \quad (31)$$

M = Cr, W

According to eq (31) tris(acetonitrile)tricarbonylchromium(tungsten) reacts [84] with tris(dimethylamino)borane to give yellow, readily sublimable crystalline products that are clearly seen to be π complexes from their properties.

The same is true of the compounds $(CO)_3Fe[(CH_3)_2N]_2BCH_3$ [85a], $Cl_2Pd[(CH_3)_2N]_2BCH_3$, $Cl_2Pd[(CH_3)_2N]_2BCl$ [85b], $(CO)_3Fe[CH_2=CH-B(Br)N(CH_3)_2]$, and $(\pi\text{-}C_3H_5)Ni[(CH_3)_2B-N(CH_3)_2]_2$ [85a]. In the complex $(CO)_3Fe[(CH_3)_2N]_2BCH_3$, formed as orange crystals in accordance with eq. (32), as well as in the Pd^{II} complexes, bis(dimethylamino)borane acts as a

$$Fe_2(CO)_9 + [(CH_3)_2N]_2BCH_3 \rightarrow (CO)_3Fe[(CH_3)_2N]_2BCH_3 + Fe(CO)_5 + CO \quad (32)$$

bidentate ligand that can replace, *e.g.*, two CO groups in $Fe(CO)_5$. In $(\pi\text{-}C_3H_5)Ni[(CH_3)_2B-N(CH_3)_2]_2$, one allyl group of $Ni(\pi\text{-}C_3H_5)_2$ has formally been replaced by two substituents analogous to ethylene.

6. The :B–X Group as a Ligand in Metal Complexes

Our discussion would not be complete without a brief mention of a new, little-studied class of compounds containing a :B–X moiety coordinated to the metal by way of the lone pair on the monovalent boron atom. It behaves as a neutral substituent analogous to CO or PR_3 : $L_nM \leftarrow B-X$ [86]. X must be a strongly electron-repelling group that can satisfy the electronic requirements of the boron atom. So far, reaction (33) has been used to prepare a dimethylaminoborylene derivative of pentacarbonyliron(0) which closely resembles the parent compound in its

$$Fe_2(CO)_9 + Br_2BN(CH_3)_2 \rightarrow FeBr_2 + 5\ CO + (CO)_4Fe \leftarrow BN(CH_3)_2 \quad (33)$$

physical properties (state of aggregation, vapor pressure); however, it differs from $Fe(CO)_5$ in its extreme sensitivity to air oxidation, which is attributable to the presence of Fe–B bonds. The borylene complex is formed in only low yield along with a

[80] *E. Wiberg* and *A. Bolz*, Ber. Dtsch. Chem. Ges. *73*, 209 (1940).

[81] *R. Prinz* and *H. Werner*, Angew. Chem. *79*, 63 (1967); Angew. Chem. internat. Edit. *6*, 91 (1967).

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number of by-products not shown in eq. (33). It is the first representative of a class of compounds that could be of great interest in connection with the stabilization of short-lived molecules other than :B–X, such as carbenes [87–89].

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The author's own work described in this paper was performed in collaboration with J. Deberitz, K. Maier, W. Petz, P. Powell, H. Schäfer, and L. Weber. I wish to express my gratitude to Professor H. Nöth for his interest in this work. Thanks are also due to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

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Relations Between Structure and Reactivity in Free-Radical Chemistry[1]

By Christoph Rüchardt [*]

An analysis of the relations between structure and reactivity in free-radical chemistry has shown that the usual interpretation of reactivities by means of the stability of the radicals involved is greatly simplified and often incorrect. The C–X bond energies of the alkanes and simple alkyl derivatives can be explained qualitatively by strain effects in the ground state on the basis of the VSEPR theory and nonbonding interactions. To be able to explain reactivities in free-radical chemistry, it is necessary to deduce information about the geometry of the transition states during free-radical formation from experimental measurements. The relations between structure and reactivity in free-radical chemistry are interpreted in terms of bond dissociation energies, as well as polar and steric effects.

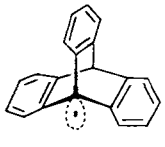
1. Introduction

The chemistry of free radicals [2] has developed into an important section of organic chemistry since the discovery of the triphenylmethyl radical by *Gomberg* [3] in 1900. Free radicals are involved in well-known industrial syntheses such as polymerization, air oxidations, cracking processes, and chlorinations. Interest in the knowledge of the relations between structure and reactivity in the chemistry of free radicals is therefore not confined to chemists who are concerned with reaction mechanisms or engaged in preparative work.

Before the problems encountered are defined, a brief mention of the stereochemistry of free radicals is necessary. The preferred geometry of tricoordinated carbon radicals is now well known from their spectra [4]. Skillfully designed experiments have made it possible to record the ESR spectra of short-lived free radicals. A planar or nearly planar preferred configuration has been deduced from the β-C–H and ^{13}C coupling constants of simple alkyl radicals. The vacuum UV spectrum of the methyl radical led to the same result [4a]. Quantum-chemical calculations are also compatible with the assumption of planar radicals [4a, 5]. Other experimental observations indicate, however, that free radicals are not so strictly bound to the planar configuration as *e.g.* carbonium ions, *i.e.* they accept an angular deformation more



(1)



(2)

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[1] Based on a lecture to the Ludwigshafen-Mannheim branch of the GDCh on November 13, 1968, and a plenary lecture to the General Meeting of the GDCh in Hamburg, September 15–20, 1969.

[2] Reviews: a) *C. Walling*: Free Radicals in Solution. Wiley, New York 1957; b) *W. A. Pryor*: Free Radicals, McGraw-Hill, New York 1966; c) *G. Sosnovsky*: Free Radical Reactions in Preparative Organic Chemistry. MacMillan, New York 1964; d) *C. J. M. Stirling*: Radicals in Organic Chemistry. Oldbourne Press, London 1965; e) *W. A. Pryor*: Introduction to Free Radical Chemistry. Prentice-Hall, Englewood Cliffs. N.J. 1967; f) *C. Rüchardt* and *I. Mayer-Ruthardt*, Chemie in unserer Zeit *3*, 40 (1969).

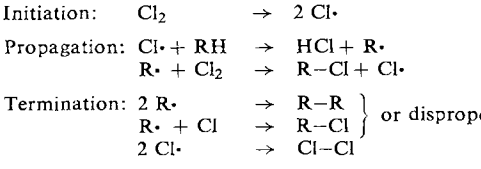
[3] See ref. [2a], pp. 1–7, for an historical survey.

[4] For reviews, see: a) *R. C. Fort* and *P. v. R. Schleyer*, Advan. Free-Radical Chem. *1*, 284 (1966); b) *R. O. C. Norman* and *B. C. Gilbert*, Advan. Phys. Org. Chem. *5*, 53 (1967); c) *A. Liberles*: Introduction to Theoretical Organic Chemistry. MacMillan, New York 1968; d) *J. K. Kochi* and *P. J. Krusic*, J. Amer. Chem. Soc. *90*, 7157 (1968), and literature cited therein; e) *B. Mile*, Angew. Chem. *80*, 519 (1968); Angew. Chem. internat. Edit. *7*, 507 (1968); *M. C. R. Symons*, Nature *222*, 1123 (1969).

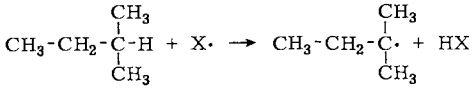
[5] *M. J. S. Dewar* and *M. Shanshal*, J. Amer. Chem. Soc. *91*, 3654 (1969); see also *V. Buss*, *P. v. R. Schleyer*, and *L. C. Allen*, J. Amer. Chem. Soc., in press.

readily than the latter [4a, 5]. Thus nonplanar bridgehead radicals such as the 1-norbornyl *(1)* or the 9-triptycyl radical *(2)* can be produced under comparatively mild conditions [4a].

Free-radical reactions usually proceed as radical chains [2]. These consist of chain initiation, the propagation steps which determine the conversion, and the chain termination reactions, as illustrated for the chlorination of alkanes.

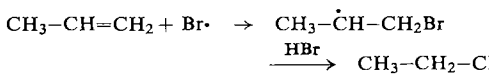


Most propagation steps are exothermic. It is understandable [6] that only very fast reactions, *i.e.* exothermic reactions, can compete with the extremely fast bimolecular chain termination reactions of dimerization and disproportionation [2, 7]. Dimerizations and disproportionations have to overcome only very low activation barriers, usually lower than 1 kcal/mole [2, 7]. The first propagation step, in which an alkyl radical is formed, determines the product distribution of the reaction. Thus in free-radical substitutions, *e.g.* the chlorination (X = Cl·) or autoxidation (X = ROO·) of 2-methylbutane *(3)*, the tertiary hydrogen is substituted in preference to the secondary or primary hydrogens.

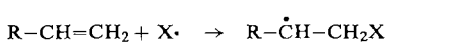


(3)

The orientation in free-radical additions [2, 8] is contrary to *Markownikoff*'s rule. The peroxide-initiated addition of HBr to propylene leads to 1-bromopropane



and the addition to vinyl monomers in polymerization is almost exclusively terminal.

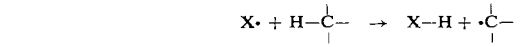


It is clear from these results that radicals with the smallest possible number of hydrogen atoms at the radical center are formed preferentially. This difference in the formation tendency of primary, secondary, and tertiary radicals, as well as radicals substituted in the α-position, is the decisive phenomenon in the discussion of the relations between structure and reactivity in free-radical chemistry. Highly alkylated radicals and radicals with phenyl or vinyl groups or with hetero atoms in the α-position have the greatest formation tendency. Aryl radicals do not occur as chain carriers in substitutions and additions. The following discussion will be concerned mainly with simple alkyl radicals.

2. The Different Formation Tendencies of Alkyl Radicals

A quantitative analysis of the formation tendencies of various radicals forms the basis of the understanding of the relation between their structure and their reactivity. However, it is relatively difficult to follow the kinetics of radical formation directly in the extremely fast propagation steps [9]. Reactivities are therefore generally compared by determining the relative extents to which competing reaction paths are followed. The statistically corrected competition constants found in this way for substitution express *e.g.* the ratio in which radicals X· attack tertiary, secondary, and primary C–H bonds (for examples, see Table 1 [10]).

Table 1. Relative reactivities (per H atom) of C–H bonds in free-radical substitutions [10]. R = Alkyl.



X	H–Ċ–			D_{H-X} [a] (kcal/mole)
	R–CH_3	R–CH_2–R	R_3CH	
F	≡ 1.0	1.2	1.4	136
Cl	≡ 1.0	4.7	9.8	103
$(CH_3)_3CO\cdot$	≡ 1.0	10	44	102
C_6H_5	≡ 1.0	9.3	44	103
Br	≡ 1.0	250	6300	87

[a] Bond dissociation energy of H–X [11].

The higher formation tendency of tertiary radicals as compared with primary or secondary radicals is independent of the attacking agent. However, the various substitutions described differ greatly in their *selectivity*. The greater the bond energy of the new H–X bond, the less selective is the attack of X·.

According to the Hammond principle [12], there is only a weak H–X bond in the transition state for the exothermic propagation steps of Table 1. The more strongly exothermic the reaction is, the earlier is the position of the transition state on the reaction coordinate, the smaller is the extent to which the C–H bond is broken in the transition state, and the less selective is the reaction. An intuitive explanation is provided in Sections 4 and 6.

[6] See ref. [2a], pp. 37ff.

[7] See, *e.g. S. J. Lapporte*, Angew. Chem. *72*, 759 (1960); *S. A. Weiner* and *G. S. Hammond*, J. Amer. Chem. Soc. *91*, 986 (1969).

[8] For a review, see *C. Walling* and *E. S. Huyser*, Org. Reactions *13*, 91 (1963); *F. W. Stacey* and *J. F. Harris*, *ibid. 13*, 150 (1963).

[9] See, *e.g.* ref. [2b], p. 240; *J. A. Howard*, *W. J. Schwalm*, and *K. U. Ingold*, Advan. Chem. Ser. *75*, 6 (1968).

[10] *A. F. Trotman-Dickenson*, Advan. Free-Radical Chem. *1*, 1, (1965).

[11] *S. W. Benson*, J. Chem. Educ. *42*, 502 (1965).

[12] *G. S. Hammond*, J. Amer. Chem. Soc. *77*, 334 (1955).

The formation tendencies of radicals can also be compared directly on the basis of the kinetics of the thermolysis of free-radical initiators, as is illustrated by a number of decomposition constants of peroxy esters and azoalkanes in Table 2 [13, 14].

Table 2. Rates of formation of radicals from simple peroxy esters (1) and azoalkanes (b) [13, 14]. $t_{1/2}$ (rel.) = relative half-life of the radical formation.

$$R{-}COO{-}OC(CH_3)_3 \rightarrow R\cdot + CO_2 + \cdot OC(CH_3)_3 \quad (a)$$

$$R{-}N{=}N{-}R \rightarrow R\cdot + N_2 + \cdot R \quad (b)$$

R	(a) $t_{1/2}$ (rel.) at 60 °C	(b) $t_{1/2}$ (rel.) at 300 °C
CH_3	(1670)	13000
$CH_3{-}CH_2$	(700)	1170
$(CH_3)_2CH$	333	117
$(CH_3)_3C$	≡ 1	≡ 1

As far as is known at present, in both reactions of Table 2 the radical R· is formed in the rate-determining step [13, 14]. The rate of formation of this radical may therefore be equated to the rate of decomposition of the initiator. The values in parentheses are not quite comparable, since it is thought that only the peroxide bond is initially broken in these examples [13].

It can be seen from Table 2 that the half-life of radical formation decreases rapidly with increasing alkylation, *i.e.* the formation tendency of the radicals increases as in the propagation steps discussed above. *This result is usually interpreted in the literature as being due to a stabilizing action of α-alkyl groups on the radicals formed* [15].

3. The Transition States of Free-Radical Formation

The interpretation of the radical formation tendency as resulting from specific stabilization of the radical center by substituents has by no means been verified, and is even contradictory, as we shall see. The reaction coordinates of the above-mentioned reactions of free-radical substitution and addition and of the thermolysis of peroxy esters and azoalkanes differ in their shapes.

3.1. The Radical-Forming Propagation Steps

The radical-forming propagation steps of aliphatic substitutions or additions are exothermic to thermoneutral. The removal of the tertiary hydrogen from isobutane by chlorine is exothermic (13 kcal/mole), while the removal by bromine is slightly endothermic (see Fig. 1). According to the Hammond principle [12], therefore, the transition state of the formation of HCl from chlorine and isobutane strongly resembles the starting compound, and even in the almost thermoneutral bromination, there is little stretching of the C–H bond, *i.e.* little free-radical character has developed, in the transition stage.

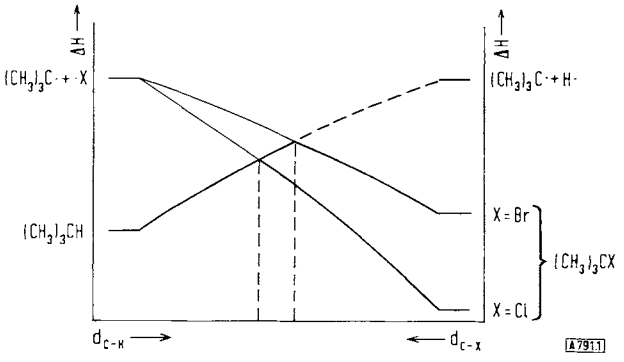
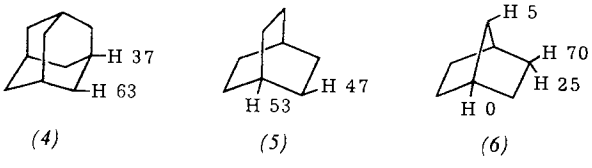


Fig. 1. Reaction coordinate of the free radical aliphatic substitution of isobutane.

$$(CH_3)_3CH + \cdot X \rightarrow (CH_3)_3C\cdot + HX$$

X	ΔH_R (kcal/mole)	E_a (kcal/mole)
Cl	−13	≈1
Br	+ 3	7

This is shown by the ease of chlorination of adamantane *(4)* and bicyclo[2.2.2]octane *(5)* at the bridgehead [4a]. The transition state still resembles the sp^3-hybridized initial state. Only in the highly strained norborane *(6)* is the reactivity of the bridgehead hydrogen so low that its substitution cannot compete with that in other positions (Fig. 2).



(4) *(5)* *(6)*

[A 791.2]

Fig. 2. Product distribution in the chlorination of bicyclic and tricyclic hydrocarbons (values in %).

3.2. The Decomposition of Peroxy Esters

The decomposition of simple peroxy esters *(8)* is endothermic. The homolytic fragmentation [13] of *tert*-butyl peroxypivalate *(7)* has a reaction enthalpy of +10 kcal/mole [16]. The strong influence of the alkyl residue R on the rate of decomposition confirms the assumed course of the fragmentation [13]. The C_α–CO bond is however only slightly stretched in the transition state (see Fig. 3).

[13] For a review, see *C. Rüchardt*, Fortschr. Chem. Forsch. *6*, 251 (1966).

[14] *S. Seltzer*, J. Amer. Chem. Soc. *85*, 14 (1963); *S. Seltzer* and *F. T. Dunne*, *ibid. 87*, 2628 (1965); *S. F. Nelson* and *P. D. Bartlett*, *ibid. 88*, 137 (1966), and literature cited there.

[15] See, *e.g.*, a) *W. Lwowski*, Angew. Chem. *79*, 922 (1967); Angew. Chem. internat. Edit. *6*, 897 (1967); b) *D. S. Breslow*, *E. I. Edwards*, *R. Leone*, and *P. v. R. Schleyer*, J. Amer. Chem. Soc. *90*, 7097 (1968); c) [2b], p. 128; d) [2d], p. 82; e) *R. W. Lenz*: Organic Chemistry of Synthetic High Polymers. Interscience, New York 1967, p. 282; f) [2a], p. 52; g) *N. Isenberg* and *M. Grdinic*, J. Chem. Educ. *46*, 601 (1969).

[16] This is calculated from the activation energy of 38 kcal/mole for O–O thermolysis of *tert*-butyl peracetate [13] (which corresponds to the O–O bond dissociation energy) and the heat of reaction of 20 kcals/mole for the decarboxylation of acetoxy radicals [11], as well as the difference of 8 kcal/mole between the C–C bond energies of ethane and neopentane.

$$(CH_3)_3C{-}COO{-}OC(CH_3)_3 \xrightarrow{60\,^\circ C} (CH_3)_3C\cdot + CO_2 + \cdot OC(CH_3)_3$$

$\Delta H^{\neq} = +31$ kcal/mole; $\Delta S^{\neq} = +13$ e.u.;
$\Delta H_R \approx 10$ kcal/mole.

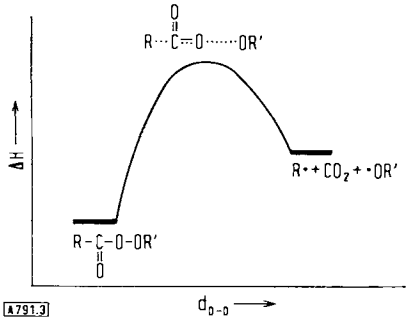


Fig. 3. Reaction coordinate of the decomposition of peroxy esters *(8)*.

$$R{-}COO{-}OR' \rightarrow R\cdot + CO_2 + \cdot OR'$$
(8)

This is clearly illustrated by the relation between the rate of decomposition of esters of cycloalkyl peroxy acids and the ring size[17] (see Fig. 4). The ease of introduction of an sp^2 center into sp^3-hybridized cycloalkyl compounds depends on the ring size[18]. For example, 1-methylcyclopentyl chloride is solvolyzed more rapidly than 1-methylcyclohexyl chloride, since the formation of an sp^2 center leads to a decrease in conformational strain in the case of the five membered ring and to an increase in the case of the six-membered ring. The high solvolysis constants of 1-methylcycloalkyl chlorides with medium-sized rings are also due to the decrease in ring strain on replacement of an sp^3 center ($\sphericalangle \approx 109\,^\circ$) by an sp^2 center ($\sphericalangle \approx 120\,^\circ$)[18].

The rate of formation of carbanions (which are known to have pyramidal structures[4a]) decreases from the three-membered to the twelve-membered ring (see Fig. 4)[19]. According to *Streitwieser*'s investigations, it decreases with decreasing electronegativity of the ring carbon atoms[19].

An entirely different picture is shown by the rate of formation of free radicals from cycloalkyl peroxy esters (see Fig. 4)[17]. The rate of decomposition does not pass through a minimum for the six-membered ring, and the peroxy esters with medium-sized rings are not distinguished by any particular ease of decomposition. The same result was found in the kinetic study of the thermolysis of 1-phenylcycloalkyl peroxy esters[17a], though the decomposition constant of the five-membered peroxy ester is only slightly smaller than that of the six-membered compound in

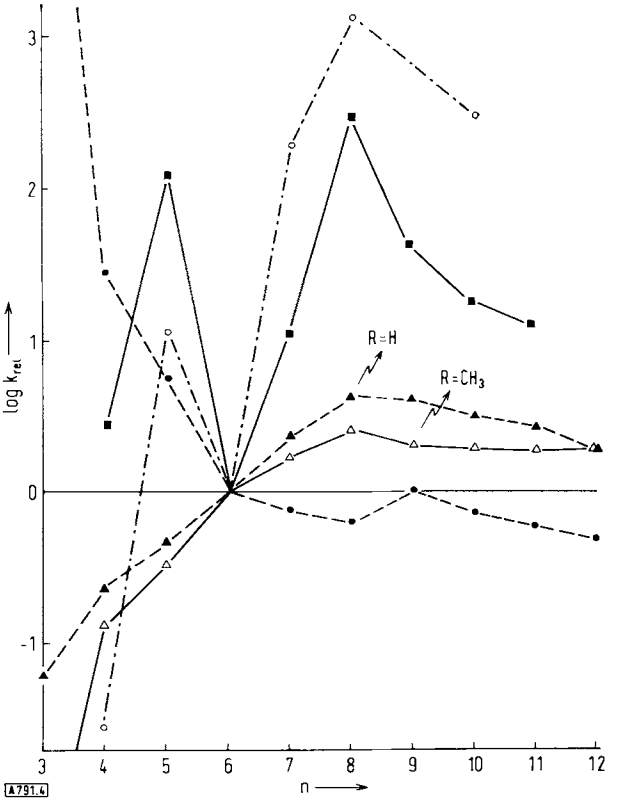
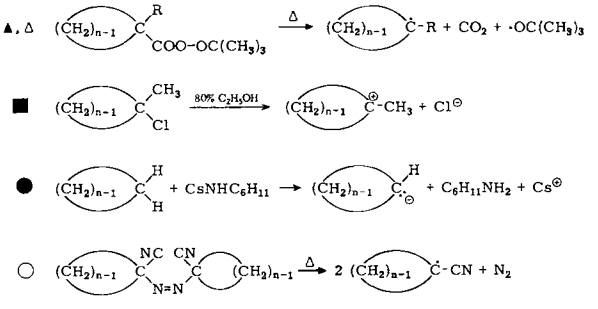


Fig. 4. Dependence of the rate of formation of cyclic carbonium ions, carbanions, and radicals on the ring size.
n = number of ring members.



this example. The rate of homolytic fragmentation of the peroxy esters, on the other hand, decreases roughly as the electronegativity of the ring carbon atoms increases. This is evident from Figure 5, which shows the relation between the decomposition constants and the ^{13}C coupling constants of the corresponding cycloalkanes[17]. The decomposition rate is evidently mainly influenced by a polar effect[13] (see Section 5).

Ring strain effects thus have no appreciable influence on the decomposition of peroxy esters. In the transition state of radical formation, the α-C atom is still substantially pyramidal, and its free-radical character is not yet developed[20].

Kinetic studies on the thermolysis of bridgehead bicycloalkyl and tricycloalkyl peroxy esters point in the same direction[21].

[17] *P. Lorenz, C. Rüchardt,* and *E. Schacht,* Tetrahedron Lett. *1969,* 2787, and literature cited therein.

[17a] *J. Bonnekessel,* Diplomarbeit, Universität Münster 1970.

[18] *H. C. Brown* and *G. Ham,* J. Amer. Chem. Soc. *78,* 2735 (1956); *R. Heck* and *V. Prelog,* Helv. Chim. Acta *38,* 1541 (1955); *H. C. Brown* and *M. Borkowski,* J. Amer. Chem. Soc. *74,* 1894 (1952); *H. C. Brown, R. S. Fletcher,* and *R. B. Johannesen, ibid. 73,* 212 (1951); see also *E. Eliel:* Stereochemistry of Carbon Compounds. McGraw-Hill, New York 1962, p. 268; *H. Tanida* and *T. Tsushima,* J. Amer. Chem. Soc. *92,* 3397 (1970).

[19] *A. Streitwieser, R. A. Caldwell,* and *W. R. Young,* J. Amer. Chem. Soc. *91,* 527 (1969); *A. Streitwieser* and *R. W. Young, ibid. 91,* 529 (1969).

[20] Cyclopentane is also less reactive than cyclohexane in chlorination; see *R. Srinivasan* and *F. I. Sontagg,* Can. J. Chem. *47,* 1627 (1969), and literature cited therein, as well as [17].

[21] a) *J. P. Lorand, S. D. Chodroff,* and *R. W. Wallace,* J. Amer. Chem. Soc. *90,* 5266 (1968); b) *R. C. Fort* and *R. E. Franklin, ibid. 90,* 5267 (1968); c) *L. B. Humphrey, B. Hodgson,* and *R. E. Pincock,* Can. J. Chem. *46,* 3099 (1968); d) *K. Herwig* and *C. Rüchardt,* unpublished results 1970.

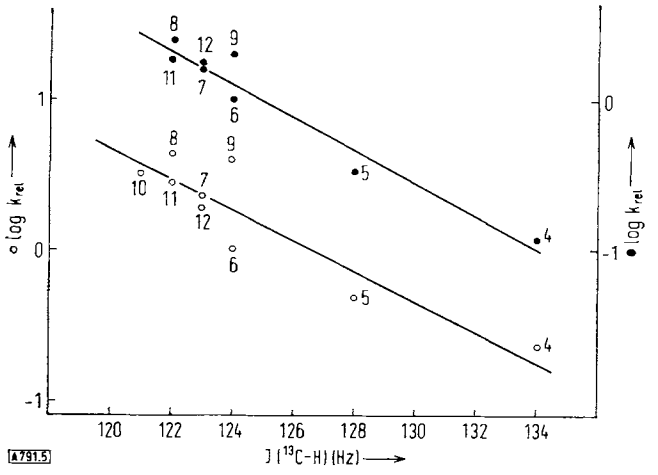
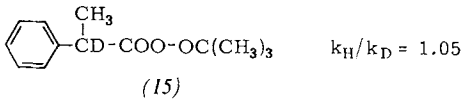


Fig. 5. Relation between the rates of decomposition of *tert*-butyl cycloalkylperoxycarboxylates and the ^{13}C coupling constants of the corresponding cycloalkanes.

○: R=H, ●: R = CH_3.

The numbers denote the number *n* of ring members.

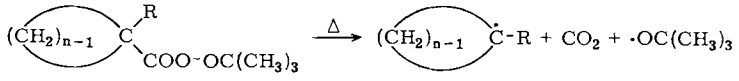
oxy esters, so that (unlike in carbonium-ion formation in solvolysis reactions [4a]) the ring strain, which increases with loosening of the bond, has little effect on the activation energy. It is only in the highly strained norbornane system that any increase in the angle, however small, requires too much energy, so that only the peroxide bond is broken in the initial step. The small secondary kinetic isotope effect in the thermolysis of *tert*-butyl [α-D]-α-phenylperoxypropionate *(15)* also indicates that the transition state of



(15)

the fragmentation of peroxy esters occurs early on the reaction coordinate in relation to the C–C cleavage [23].

There are two possible reasons for the apparent discrepancy of these results with the relatively high



The decomposition constants of compounds *(7)* to *(13)* in Table 3 differ by a factor of only 10 from the thermolysis constant of the peroxypivalic ester *(7)*, which was taken as the reference point. Only the ester of the highly strained 1-norbornaneperoxycarboxylic

Table 3. Thermolysis rates k_1 (rel.) of bridgehead *tert*-butyl esters RCOO–$OC(CH_3)_3$ of bicycloalkyl and tricycloalkyl peroxy acids at 80 °C in aromatic solvents.

Cpd.	R	k_1 (rel.)	Ref.
(7)	$(CH_3)_3C$–	1.0	[21c]
(9)		7.07	[21d]
(10)		1.48	[21c]
(11)		0.103	[21c]
(12)		0.052	[21d]
(13)		0.096	[21d]
(14)		1.57×10^{-3}	[21c]

acid *(14)* is appreciably more stable. It decomposes with cleavage of only the peroxide bond in the rate-determining step [13, 22]. These results also show that the C_α–CO bond is stretched only slightly in the transition state of free-radical formation from per-

activation energy of the decomposition of peroxy esters (see Fig. 3), which, according to the Hammond principle, pointed to a radical-like transition state for the fragmentation of peroxy esters. The peroxide cleavage could be a fast equilibrium step, the subsequent exothermic decarboxylation being rate-determining. It should be possible to establish this by isotope equilibration during the decomposition of peroxy esters specifically labeled with ^{18}O in the carbonyl group [24]. A more probable answer, however, is the assumption [13] of an unsymmetrical peroxy ester fragmentation in which only the weak O–O bond is substantially broken in the transition state, while the stronger C–C bond is only partly broken, so that the α-C atom is still similar to that in the pyramidal state (see Fig. 3). The weaker the C_α–CO bond, the more uniform is the cleavage of both bonds in the fragmentation of *(8)*. This is shown *e.g.* by the influence of α-phenyl substitution on the decomposition constants of cyclic peroxy esters (see above) [17a].

3.3. The Decomposition of Azoalkanes

In contrast with these two reactions, the transition state occurs late on the reaction coordinate in the pyrolysis of azoalkanes. Its geometry is closer to that of the planar radical (see Fig. 6). This can be seen from the pronounced influence of the ring size on the rate of formation of radicals from cycloalkylazo-

[22] *T. G. Traylor*, Intra Sci. Chem. Rep. *3*, 289 (1969).

[23] *T. Koenig* and *R. Cruthoff*, J. Amer. Chem. Soc. *91*, 2562 (1969); *T. Koenig* and *R. Wolf*, *ibid. 91*, 2574 (1969); *T. Koenig*, *J. Huntington*, and *R. Cruthoff*, *ibid. 92*, 5413 (1970).

[24] *M. J. Goldstein* and *H. A. Judson*, J. Amer. Chem. Soc. *92*, 4119 (1970); *P. Lorenz*, Dissertation, Universität Münster 1970; see also *W. A. Pryor* and *K. Smith*, J. Amer. Chem. Soc. *92*, 5403 (1970).

nitriles[25] and 1-methylazocycloalkanes[24a] (see Fig. 4). As in the solvolysis of 1-methylcycloalkyl chlorides, this influence can only be explained by an almost planar transition state. This would also explain the decomposition constants of bridgehead-linked bicycloalkyl and tricycloalkyl azo compounds[26] even allowing for a statistical correction (Table 4). They differ greatly from the decomposition constants of the corresponding peroxy esters (see Table 3). The rate of thermolysis of azoadamantane *(21)* is slower by a factor of 3000, that of azobicyclo-[2.2.2]octane *(20)* by a factor of 20000 [like 1-azobicyclo[3.2.1]octane *(19)* and 1-azotwistane *(18)*], and that of azonorbornane *(17)* by a factor of 500000, than that of azoisobutane *(16)* (see Table 4).

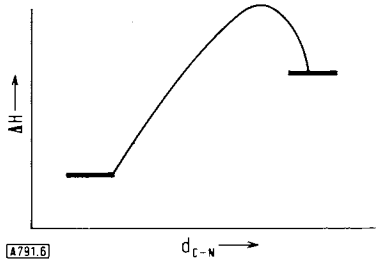


Fig. 6. Reaction coordinate of the decomposition of azoalkanes at 300 °C.

$(CH_3)_3C{-}N{=}N{-}C(CH_3)_3 \rightarrow 2\,(CH_3)_3C\cdot + N_2$

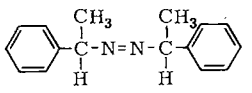
$\Delta H_R \approx 20{-}25$ kcal/mole; $\Delta H^{\neq} = 44$ kcal/mole; $\Delta S^{\neq}$ 17 e.u.

Table 4. Rates of thermolysis of bicycloalkyl and tricycloalkyl azo compounds at 300 °C in C_6H_6.

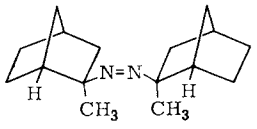
R	R–N=N–R		R–N=N–C(CH$_3$)$_3$	
	No.	k_1 (rel.)	No.	k_1 (rel.)
$(CH_3)_3C$–	*(16)*	≡ 1	*(16)*	≡ 1
	*(17)*	1.98×10^{-6}	*(22)*	4.64×10^{-3}
	*(18)*	3.51×10^{-5}		
	*(19)*	3.67×10^{-5}		
	*(20)*	5.06×10^{-5}	*(23)*	2.04×10^{-2}
	*(21)*	4.02×10^{-4}	*(24)*	4.36×10^{-2}

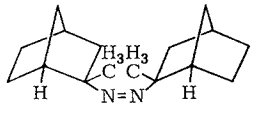
The ring system has less influence on the thermolysis of bicycloalkyl- and tricycloalkylazoisobutanes *(22)* to *(24)*, in agreement with the simultaneous but non-uniform cleavage of both C–N bonds in the course of the thermolysis[27]. The cleavage of the N-*tert*-butyl bond is certainly much farther advanced than that of the other C–N bond in the transition state. This roughly corresponds to the situation in the fragmentation of peroxy esters (see above).

The secondary kinetic isotope effect in the thermolysis of α,α′-dimethyl-α-azotoluene *(25)* also shows that extensive rehybridization of the α-C atom has taken place in the transition state[28].


(25) $k_H/k_D = 1.15$

To check the structure of the transition state in the pyrolysis of azoalkanes, we synthesized and thermolyzed *exo*- and *endo*-2,2′-dimethyl-2-azonorbornane *(26a)* and *(26b)*[29].


(26a)


(26b)

There is no torsional strain barrier to be overcome (hydrogen atom on C-1) to allow the methyl group in *(26a)* to swing into the planar arrangement of the thermolysis transition state, whereas such a barrier is encountered in *(26b)*[30]. In fact, *(26a)* thermolyzes 68 times as rapidly as *(26b)*[29]. The fact that the rates of acetolysis of *exo*- and *endo*-2-norbornyl *p*-toluenesulfonate at 25 °C differ by a factor of 350[30] is probably partly due to a similar steric effect, so that only a smaller factor remains to be explained by neighboring group participation and the formation of the nonclassical norbornyl cation. The rates of decomposition of the *tert*-butyl esters of *exo*- and *endo*-2-norbornaneperoxycarboxylic acids, on the other hand, differ by a factor of only 3–7[31], since torsional strain effects are less active in the pyramidal transition state of the peroxy ester fragmentation. It is not to be expected, however, that torsional strain effects exhibit a linear correlation with the amount of bond stretching[31]. This point can be verified by the study of unsymmetrical azo compounds. The investigation of the rates of formation of other isomeric *exo* and *endo* bicycloalkyl azo compounds

[24a] *J. Hinz* and *C. Rüchardt*, unpublished (1970).

[25] *C. G. Overberger, H. Biletch, A. B. Finestone, J. Lilker*, and *J. Herbert*, J. Amer. Chem. Soc. *75*, 2078 (1953).

[26] *C. Rüchardt* and *A. Oberlinner*, Tetrahedron Lett. *1969*, 4685.

[27] *S. F. Nelson* and *P. D. Bartlett*, J. Amer. Chem. Soc. *88*, 143 (1966); *W. A. Pryor* and *K. Smith*, *ibid.* *89*, 1741 (1967).

[28] *S. Seltzer* and *F. T. Dunne*, J. Amer. Chem. Soc. *87*, 2628 (1965); *S. Seltzer* and *S. G. Mylonakis*, *ibid.* *89*, 6584 (1967).

[29] *J. Hinz*, Diplomarbeit, Universität Münster 1970; *J. Hinz* and *C. Rüchardt*, Tetrahedron Lett. *1970*, 3095. However, when statistical factors are taken into account this difference is less dramatic.

[30] *P. v. R. Schleyer*, J. Amer. Chem. Soc. *89*, 701 (1967), and literature cited therein; *G. D. Sargent*, Quart. Rev. Chem. Soc. *20*, 301 (1966); *P. D. Bartlett*: Nonclassical Ions. W. A. Benjamin, New York 1965. The steric hindrance of the dissociation must naturally also be considered in homolysis, see *e.g. H. C. Brown*, Chem. Brit. *1966*, 199.

[31] *P. D. Bartlett* and *J. M. McBride*, J. Amer. Chem. Soc. *87*, 1727 (1965), and literature cited therein; *W. G. Schindel* and *R. E. Pincock*, J. Org. Chem. *35*, 1789 (1970); *P. D. Bartlett, G. N. Fickes, F. C. Haupt*, and *R. Helgeson*, Accounts Chem. Res. *3*, 177 (1970).

should therefore be of great importance for the estimation of steric effects in solvolysis reactions.

Thus the transition states of the three radical-forming reactions discussed are fundamentally different. The exothermic propagation steps of free-radical substitutions and additions and of the decomposition of peroxy esters pass through transition states in which the C atom is geometrically very close to the initial state. In the endothermic thermolysis of azoalkanes (see Fig. 6), on the other hand, the C–N bonds are already extensively broken and the two planar radicals are already strongly anticipated at the energy peak of the transition state. A blanket explanation of the difference in the formation tendencies of primary, secondary, and tertiary radicals by specific stabilization of the radicals formed by α-alkyl groups is therefore unacceptable. Different rules also apply to carbonium ion formation in endothermic solvolysis reactions and to the exothermic decomposition of aliphatic diazonium ions [32]. For example, bridgehead carbonium ions are formed readily only in exothermic ionization such as the decomposition of diazonium ions [4a], since the bridgehead atom carries very little positive charge in the transition state.

How, then, can we account for the popularity of the explanation of radical formation tendencies by differences in the stability of the radicals formed? In our opinion this is due to the hasty assumption of an analogy between the effects of α-alkylation on the rates of free-radical formation and on the C–H bond energies, which are also decreased by α-substitution.

4. Bond Dissociation Energies [11, 33]

Figure 7a shows the definition of the bond dissociation energy on the basis of reaction coordinates. Bond dissociation does not proceed *via* a transition state with an energy maximum, since the back-reaction corresponds to a dimerization of free radicals. Dimerizations of free radicals have no appreciable activation energy; they are mostly diffusion-controlled [2, 7, 34]. Any specific stabilization of a free-radical C atom by substituents must therefore lead to a decrease in the bond dissociation energy. Figure 7b shows the dissociation energies of C–H bonds in methane and simple alkanes, together with their usual interpretation [35]. As was mentioned earlier, it is assumed that the α-alkylation leads to specific stabilization of the free-radical center without specifically stabilizing or destabilizing the ground state. The agreement of the influence of alkylation on the rate of radical formation (kinetic quantity) and on the bond dissociation energy (thermodynamic quantity) does in fact suggest a common reason for both effects. On the other hand, is this reason the specific stabilization of the radicals?

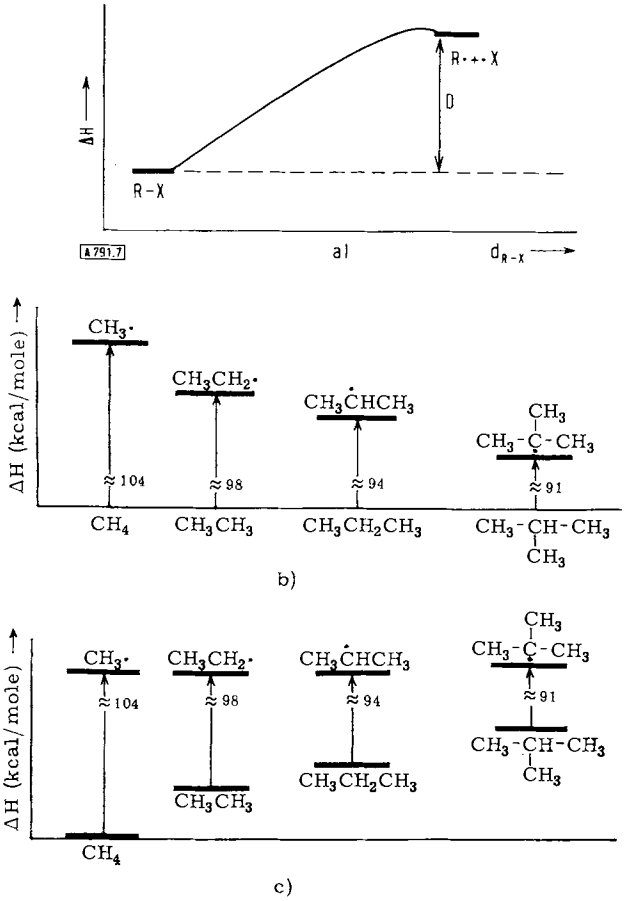


Fig. 7. Dissociation energies *D* of C–X bonds. (a) Definition; (b) usual interpretation [35]; (c) alternative interpretation.

The following arguments oppose this assumption:

It has been deduced from the β-C–H coupling constants of the ESR spectra of short-lived radicals [4] that each methyl group reduces the spin density on the central C atom of the radical by only about 8% [36]. Moreover, the radical is by no means fully developed in the transition state of radical formation. For these two reasons, α-alkyl hyperconjugation should have only a very small effect on the rate of radical formation. Substituents that can enter into resonance with the radical center (as in the benzyl and allyl radicals) should cause a particularly marked increase in the rate of radical formation. The fact that the C–H bonds of cyclohexane are more reactive than the α-C–H bonds of toluene in chlorination [37] shows that even this possibility does not necessarily determine the rate in exothermic free-radical formation. In the other extreme, the bond

[32] *R. Huisgen* and *C. Rüchardt*, Liebigs Ann. Chem. *601*, 1 (1956).

[33] *S. W. Benson, F. R. Cruickshank, D. M. Golden, G. R. Haugen, H. E. O'Neal, A. S. Rodgers, R. Shaw*, and *R. Walsh*, Chem. Rev. *69*, 279 (1969).

[34] See, *e.g.*, *P. D. Bartlett* and *J. M. McBride*: Free Radicals in Solution. Butterworths, London 1967, p. 89; *S. A. Weiner* and *G. S. Hammond*, J. Amer. Chem. Soc. *91*, 986 (1969); *D. J. Carlsson* and *K. U. Ingold*, *ibid. 90*, 7047 (1968).

[35] See, *e.g.*, *R. T. Morrison* and *R. N. Boyd*: Organic Chemistry. Allyn and Bacon, Boston 1966, p. 124; see, however, ref. [2a].

[36] *R. O. C. Norman* and *B. C. Gilbert*, Advan. Phys. Org. Chem. *5*, 98 (1967).

[37] See ref. [2a], p. 360.

dissociation energies could also be explained by a destabilizing effect of higher alkyl substituents in the ground state, as illustrated in Figure 7c, without the need for a specific radical-stabilizing action.

Before any detailed discussion is possible it is necessary to answer the question how one can decide between these two interpretations. If the effect of α-alkylation were mainly or exclusively to stabilize the radical, the difference in the dissociation energy on transition from methyl to ethyl, isopropyl, and *tert*-butyl derivatives would be independent of the eliminated group X, and the gradation of the dissociation energies of C–H bonds in Figure 7 should also be found for C-halogen, C–O, and *e.g.* C–N bonds with practically no change in magnitude.

The validity of this requirement can be seen from bond dissociation energies of benzyl and allyl derivatives, where the radicals are stabilized by resonance with a π-electron system. It can be seen from Table 5 that, irrespective of the eliminated group X, the difference in dissociation energy between the benzyl and methyl compounds and between the allyl and methyl compounds is constant, and correponds roughly to the resonance energy of the benzyl or allyl radical [38].

Table 5. Bond dissociation energies [11] of benzyl and allyl compounds (in kcal/mole).

X =	H	OH	I	CH_3	C_2H_5	*i*-C_3H_7	*t*-C_4H_9	C_6H_5
CH_3–X	104	91	56	88	85	84	80	93
C_6H_5–CH_2–X	85	77	40	72	69	67	64	78
CH_2=CH–CH_2–X	85	77	41	72	69	67	63	77
Δ methyl-benzyl	19	14	16	16	16	17	16	15
Δ methyl-allyl	19	14	15	16	16	17	17	16

Figure 8 shows the bond dissociation energies of several methyl, ethyl, isopropyl, and *tert*-butyl derivatives. It can be seen that the difference in the bond dissociation energies of methyl, ethyl, isopropyl, and *tert*-butyl derivatives is by no means independent of the eliminated group X. On the contrary, the difference between the methyl and *tert*-butyl derivatives varies between 0 and 13 kcal/mole. No relation with the absolute value of the bond dissociation energy can be recognized. It would therefore be contrary to this experimental observation to explain the differences by differences in the degree of stabilization of the radical. Conversely, it may be deduced from the low dependence of the C–F and C–OCH_3 bond dissociation energies on the degree of alkylation that alkyl groups do not appreciably stabilize the radicals. The example of the C–H bond dissociation energy that is always quoted is in fact an extreme case.

To explain the variation of the bond dissociation energies with the degree of alkylation, therefore, it is also necessary to consider the increasing strain in the ground state with increasing alkylation (see Fig. 7c).

[38] See also *A. Streitwieser*: Molecular Orbital Theory for Organic Chemists. Wiley, New York 1961, p. 393; however, see *D. M. Golden, N. A. Gac*, and *S. W. Benson*, J. Amer. Chem. Soc. *91*, 2136 (1969).

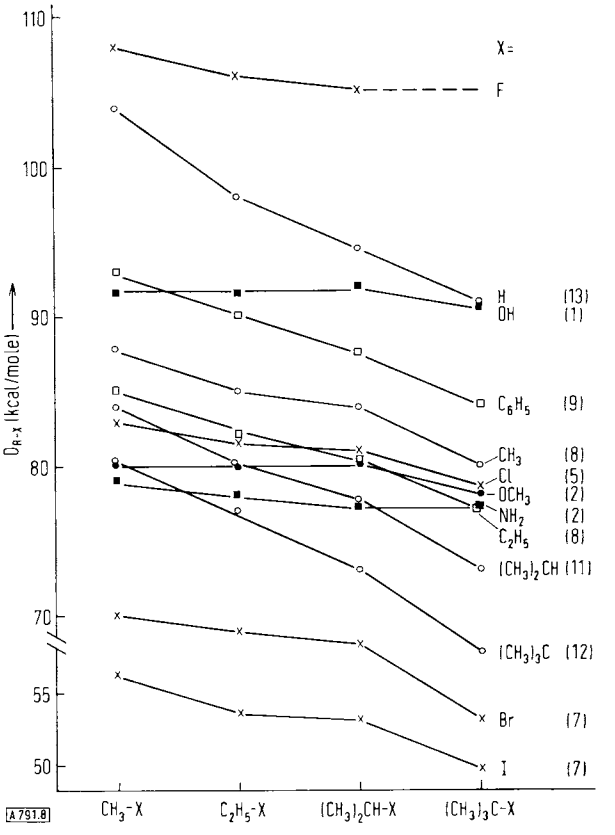


Fig. 8. Bond dissociation energies D_{R-X} of methyl, ethyl, isopropyl, and *tert*-butyl compounds. The numbers in brackets on the right hand edge show the differences in bond dissociation energy (in kcal/mole) between the methyl and *tert*-butyl compounds having the same X.

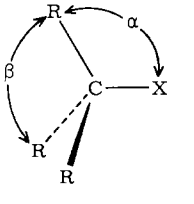
The following discussion is based on the electron pair repulsion model (Valence Shell Electron Pair Repulsion theory, VSEPR) of *Sidgwick, Powell, Gillespie, Nyholm*, and others [39], taking non-bonding interactions [40] into account.

There are three destabilizing factors to be considered in the ground state. These are usually referred to collectively as steric effects:

a) The mutual repulsion of the nuclei.

b) The mutual repulsion of the bonding electrons [39].

c) The repulsion of atoms that are not bound to one another over distances corresponding to the van der Waals radii [40].



(27)

Any influence that tends to reduce the angle between the orbitals or bonds consequently encounters strong resistance [39], whereas an increase in the angle is energetically favored. Since the transition to the planar radical is associated with an increase in the bond angles β, all repulsive effects become smaller.

[39] *R. J. Gillespie*, Angew. Chem. *79*, 885 (1967); Angew. Chem. internat. Edit. *6*, 819 (1967); J. Chem. Educ. *40*, 295 (1963).

[40] *L. S. Bartel*, J. Chem. Educ. *45*, 754 (1968).

The greater the "steric pressure" in the ground state, the more pronounced this phenomenon becomes. This allows a qualitative interpretation of the bond dissociation energies (see Fig. 7c). As can be seen from Figure 8, in almost all examples their differences increase most strongly on transition from the isopropyl to the *tert*-butyl compound, in agreement with the fact that steric repulsion effects usually increase exponentially with the degree of alkylation. If the bond dissociation energies were explained by electronic stabilization of the radicals, the converse would be expected.

The difference in the bond dissociation energies of methyl and *tert*-butyl compounds within a series of similarly substituted compounds increases with the size of the eliminated group X. This is easily recognized in the arrangement of Table 6.

Table 6. Difference in the bond dissociation energies ΔD_{R-X} of CH_3-X and $(CH_3)_3C-X$.

X	ΔD_{R-X} (kcal/mole)	X	ΔD_{R-X} (kcal/mole)
H	13	I	7
$C(CH_3)_3$	12	Br	7
$CH(CH_3)_2$	11	Cl	5
C_6H_5	9	F	(2)
C_2H_5	8	OH	≈ 1–2
CH_3	8	OCH_3	
		NH_2	

It may be assumed that the relaxation of the strain on transition from the tetrahedral C atom to the sp^2-hybridized trigonal center promotes the reaction more strongly for large substituents X than for small substituents. The mutual repulsion of the nuclei or the mutual repulsion of the alkyl groups over distances of the order of the van der Waals radii decreases by the largest amount on dissociation.

Replacement of the H atoms in *(27)*, R=H, by alkyl groups leads to an increase in the angle β (in propane and isopropane, the angle CCC is 111.5° [41]), and hence to a decrease in the angle α. Since the repulsion of the bonding electrons increases exponentially with decreasing α, the reason for the large difference in the C–H bond dissociation energy between butane and isobutane is clear. Besides the bulk of the substituent X, the length of the C–X bond is also important, since this is the only possible explanation why the difference in the bond dissociation energies of the methyl and *tert*-butyl compounds is greatest for the cleavage of the C–H bond (see Fig. 8 and Table 6). The shorter the C–X bond, the higher is the electron density at the bond axis close to the central C atom, and hence the greater is the repulsion between the electrons of the C–X bond and the electrons of the other bonds.

Electronegative groups X such as fluorine, methoxy, and NH_2 strongly attract the bonding electrons away from the central C atom [33]. The electronic repulsion over the angle α in *(27)* is therefore reduced, and the decrease in the angle on introduction of alkyl residues is not accompanied by a large increase in the electronic repulsion.

This approach allows a qualitative interpretation of the differences in the bond dissociation energies.

Can we also explain the acceleration of radical formation by alkyl groups in the examples discussed above, and is this explanation satisfactory even when the transition state of the radical formation occurs early on the reaction coordinate, so that the angles are only slightly increased, as in the decomposition of peroxy esters or in chain chlorination?

The answer to this question is an emphatic "yes" [41a]. Since steric effects, *i.e.* the strain in the ground state, decrease exponentially (see Fig. 9), even a small increase in the angle during radical formation will lead to the elimination of most of the strain of the ground state.

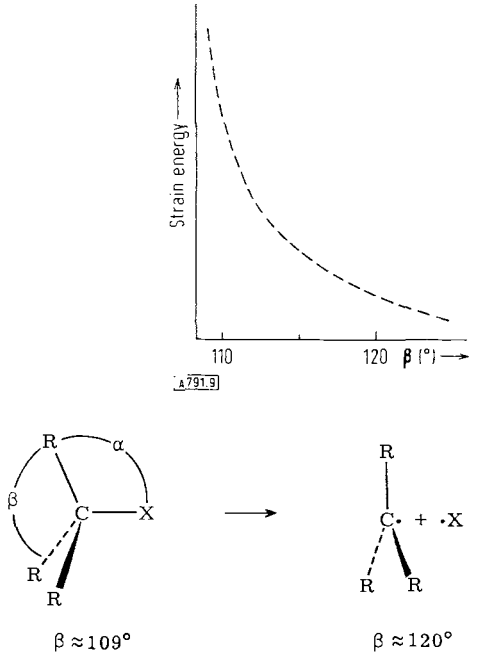


Fig. 9. Decrease in the strain energy on dissociation, expressed as an increase in the angle β.

It is now also possible to understand why the selectivity of free radicals decrease in the order chlorine > *tert*-butoxy > bromine, as shown in Table 1. The transition state of the removal of H by chlorine occurs earliest on the reaction coordinate, since this is the most strongly exothermic process. The increase in the angle in the transition state is therefore smallest in this case, and the difference between *tert*-C–H and CH_3–H cleavage is least.

A refined analysis is now also possible for the difference in the sequence of reactivities of bridgehead peroxy esters and bridgehead azo compounds on thermolysis. Figure 10 shows a logarithmic plot of the decomposition constants against the known solvolysis constants [41b] of the bridgehead bromides in

[41] *Y. Youkawa*: Handbook of Organic Structural Analysis. W. A. Benjamin, New York 1965.

[41a] See also *R. F. Bridger* and *G. A. Russell*, J. Amer. Chem. Soc. *85*, 3754 (1963), particularly p. 3762.

[41b] *G. J. Gleicher* and *P. v. R. Schleyer*, J. Amer. Chem. Soc. *89*, 582 (1967); *P. v. R. Schleyer*, personal communication.

80% ethanol. There are two points of interest here. Firstly, the rates of thermolysis of *tert*-butyl and 1-adamantyl peroxy esters are almost the same, whereas azoisobutane decomposes almost 2500 times as rapidly as 1-azoadamantane. The increase in the angles of the *tert*-butyl group is well advanced in the transition state only for the thermolysis of the azo compound, and not for the peroxy ester fragmentation. In the rigid tricyclic adamantyl system, however, no corresponding increase in angle is possible during either the decomposition of the peroxy ester or the thermolysis of the azoalkane. The second point that emerges is that a linear relationship is found between the thermolysis constants of both fragmentations of bridgehead compounds and the rate of solvolysis of the alkyl bromides, and even the slopes of the two lines in Figure 10 are very similar. Ionization and radical formation are evidently inhibited by the same strain effects [41b], but the formation of the carbonium ion reacts more strongly to these effects. The similarity of the slopes of the straight lines in Figure 10 suggests that the maximum deformation or additional straining of the bicyclic ring that is possible in radical formation is reached even in the transition state of the thermolysis of peroxy esters.

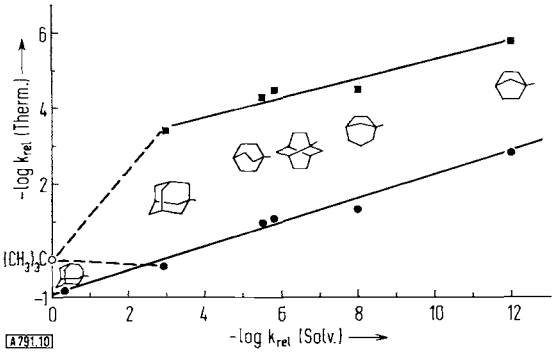
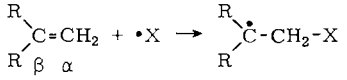


Fig. 10. Linear relation between free energies of thermolysis and of solvolysis of bridgehead compounds. Thermolysis of R—N=N—R at 300 °C in benzene (see Table 4); thermolysis of R—COO—$OC(CH_3)_3$ at 80 °C (see Table 3); solvolysis of RBr in 80% ethanol at 25 °C. ■: azo compounds; ●: peroxy esters.

With the aid of this interpretation of the bond energies, it also recently became possible to explain the influence of α-methyl groups on the rate of thermolysis of peroxy esters [41c].

This approach cannot be used directly to explain the anti-Markownikoff orientation in free-radical additions [8, 15g] and polymerizations [15c]. Since these are

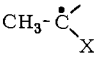


exothermic propagation steps, it is again to be expected from the Hammond principle [12] that the structure of the transition state is still similar to that of the olefin. The decrease in the angle that accompanies radical formation on the α-C atom is thus not very far advanced in the transition state. The strain energy curve in Figure 9 is now followed from right to left. The strain energy increases appreciably only with a large decrease in the angle at the α-C atom. The anti-Markownikoff orientation of these reactions is therefore presumably due simply to the stronger steric screening of the more highly alkylated β-C atom. This hypothesis was discussed by *Walling* as an adequate explanation [2a].

Competition constants for free-radical additions should be capable of providing verification of this. Only a few investigations of this type have been carried out so far [42,43]. Ethylene and isobutylene have comparable methyl affinities, which are 5 to 10 times as great as those of *cis*- and *trans*-2-butene [42]. This can be explained by the stronger screening of the secondary C atom in the butenes. The reactivity of olefins with cyclopropyl radicals actually decreases monotonically with alkylation; this has been explained by a transition state resembling a π-complex [43a]. The reactivity of the olefins is strongly increased only by substituents having π-bond systems [42,43]. This may also be partly due to polar effects [44]. The fact that only terminal olefins polymerize readily points in the same direction. These views also make the orientations in intramolecular free-radical additions seem less remarkable [44a].

5. Polar Effects in Free-Radical Reactions

The discussion has so far been confined to unsubstituted alkyl radicals. Besides the phenyl and vinyl groups mentioned earlier, however, there are also other substituents that can stabilize adjacent free-radical centers by resonance. On the other hand, the ESR spectra of such radicals show that this effect should not be overestimated. The β-CH_3 coupling constants of the radicals *(28)* are proportional to the spin



(28)

density on the β-C atom [4b]. The β-C—H coupling constants are therefore a good measure of the ability of substituents X to reduce the spin density on the α-C atom by resonance [45]. It can be seen from Table 7 [4b] that the maximum decrease in the spin density on the α-C atom with the substituents indicated is

[41c] *C. Rüchardt* and *I. Mayer-Ruthardt*, Chem. Ber., in press.

[42] *M. Szwarc* and *J. H. Binks*: Theoretical Organic Chemistry, Kekulé Symposium, 1958. Butterworths, London 1958, p. 262; see also ref. [2a], p. 498.

[43] See also ref. *W. A. Pryor* and *T. R. Fiske*, Trans. Faraday Soc. *65*, 1865 (1969); *S. C. Dickermann, D. J. De Souza, M. Fryd, I. S. Megna*, and *M. M. Skoultchi*, J. Org. Chem. *34*, 714 (1969); *M. Capka* and *V. Chvalovsky*, Collect. Czech. Chem. Commun. *33*, 2872 (1968).

[43a] *A. P. Stefani, L.-Y. Y. Chuang*, and *H. E. Todd*, J. Amer. Chem. Soc. *92*, 4168 (1970).

[44] *A. D. Jenkins*, Advan. Free-Radical Chem. *2*, 139 (1967).

[44a] *M. Julia*, Pure Appl. Chem. *15*, 167 (1967).

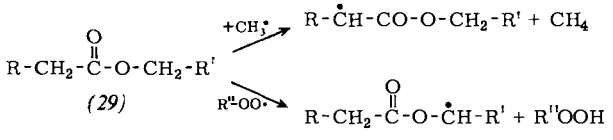
[45] See also *H. Fischer*, Z. Naturforsch. *19a*, 866 (1964); *20a*, 428 (1965).

Table 7. Decrease in the spin density on the α-C atom in *(28)* by substituents X [4b].

X	CH_3	CH_2OH	COOR	CN	COC_2H_5	OH	OC_2H_5
Rel. spin density (H = 100%)	91.9	92.1	92.8	85.2	83.8	84.0	82.2

only 17%, and that the alkoxycarbonyl group is comparable in this respect to *e.g.* a methyl group.

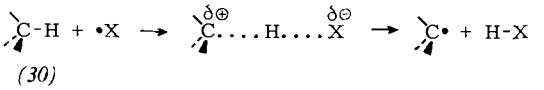
The decrease in the spin density is a qualitative indication of the radical-stabilizing effect of a substituent. It must therefore be expected that this relatively small effect accelerates the formation of radicals only when the transition state occurs late on the reaction coordinate, and so already has a strong radical character. No kinetic data have been reported in which this radical-stabilizing substituent effect could be observed in isolation. Substituent effects in free-radical chemistry have mostly been investigated in exothermic reactions in which the transition state still resembles the starting compound. How, then, can substituents affect the energy level of a transition state that is not yet very like the radical? It was found that the influence of one and the same substituent, *e.g.* on the rate of radical formation by hydrogen transfer, differs with the attacking radical. Thus



esters of carboxylic acids are preferentially attacked by methyl radicals on the α-methylene group of the acid, whereas in autoxidation by peroxy radicals, the attack occurs preferentially on the α-methylene group of the alcohol [46].

Similarly, the abstraction of hydrogen from α-benzylmalonates by methyl radicals occurs preferentially from the benzyl position, while methoxy radicals remove the tertiary hydrogen from the α-position with respect to the carbonyl group [47]. Ether functions activate α-hydrogen atoms much more strongly for the attack of a *tert*-butoxy or peroxy radical in autoxidations [48] than for the attack of a phenyl radical [49]. The free-radical chlorination of butyric acid occurs mainly in the β-position, whereas methyl radicals prefer the α-position [50]. The list of examples of this apparently contradictory reactivity behavior is almost endless [51].

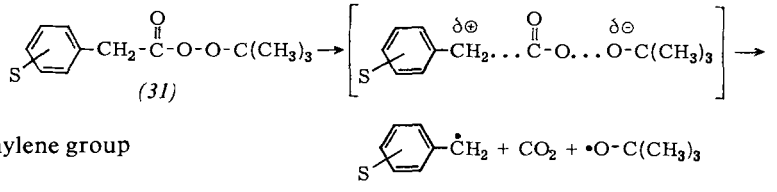
An explanation for the dependence of the reactivity on the attacking radical is provided by consideration of the charge separation in the transition state of free-radical reactions, which is referred to as "polar effects" in free-radical reactions [51, 52]. When a radical X with an electronegative central atom attacks a C–H bond *(30)*, the electrons are drawn more strongly to the attacking radical in the transition state. This leads to partial charges, the delocalization of which by adjacent substituents lowers the energy level of the transition state, and so increases the rate of radical formation.



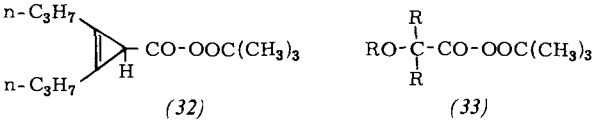
(30)

The mesomeric charge distribution in the transition state explains why the reactivities of substituted toluenes with halogen atoms or with trichloromethyl or peroxy radicals can be described by the substituent constants σ and σ^+ [52]. The greater the electronegativity of X, the greater are the charge separation and the substituent effect. Polar effects of this nature were first recognized in copolymerization, and have been studied particularly extensively in this connection [44]. α-Alkyl groups can also influence radical formation by a polar effect.

Polar effects also have a strong influence on the rate of fragmentation of peroxy esters [13, 41c]. Thus the rates of decomposition of substituted *tert*-butyl peroxyphenylacetates *(31)* follow a σ^+ relation [53]. The



low thermal stabilities of *tert*-butyl dipropylcyclopropenylpercarboxylate *(32)* and of the α-alkoxy and α-aryloxy peroxy esters *(33)* have been explained by



(32) *(33)*

[46] *D. J. Trecker* and *R. S. Foote*, J. Org. Chem. *33*, 3527 (1968).

[47] *H. C. McBay*, *O. Tucker*, and *A. Milligan*, J. Org. Chem. *19*, 1003 (1954).

[48] *C. Walling* and *M. J. Mintz*, J. Amer. Chem. Soc. *89*, 1515 (1967); see *e.g.*, *E. G. E. Hawkins*: Organic Peroxides. E. and F. F. Spon, London 1961, p. 385.

[49] *R. F. Bridger* and *G. A. Russell*, J. Amer. Chem. Soc. *85*, 3754 (1963).

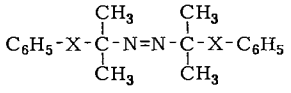
[50] *Bruylants et al.*, Bull. Soc. Chim. Belges *66*, 367 (1957); *M. S. Kharasch*, *H. C. McBay*, and *W. H. Urry*, J. Org. Chem. *10*, 394 (1945).

[51] For review, see *R. S. Davidson*, Quart. Rev. Chem. Soc. *1967*, 249.

[52] See, *e.g.*, *R. Breslow*: Organic Reaction Mechanisms. Benjamin, New York 1967, Vol. 7; *E. S. Huyser* and *K. L. Johnson*, J. Org. Chem. *33*, 3972 (1968); *E. S. Huyser*, J. Amer. Chem. Soc. *82*, 394 (1960); *H. Sakurai* and *A. Hosomi*, *ibid. 89*, 458 (1967); *T. Yamamoto* and *T. Otsu*, Chem. Ind. (London) *1967*, 787; *M. A. DaRooge* and *L. R. Mahoney*, J. Org. Chem. *32*, 1 (1967); *J. D. Bacha* and *J. K. Kochi*, *ibid. 30*, 3272 (1965); *J. A. Howard* and *K. U. Ingold*, Can. J. Chem. *41*, 1744 (1963), and literature cited therein.

[53] *P. D. Bartlett* and *C. Rüchardt*, J. Amer. Chem. Soc. *82*, 1756 (1960); *C. Rüchardt* and *H. Böck*, Chem. Ber. *100*, 654 (1967).

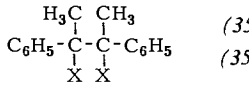
polar effects on the charge distributions in the transition state of the homolytic fragmentation [13, 54, 55]. However, alkoxy groups in the α-position, as in *(34b)*, do not decisively change the rate of decomposition of the azo compound *(34a)* [56]. As expected, therefore, polar effects are of no great importance in the



(34a), X = CH_2, $\Delta H^{\neq}$ = 35.6 kcal/mole, $\Delta S^{\neq}$ = +4.1 e.u.

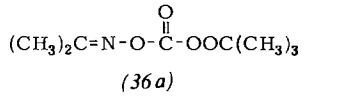
(34b), X = O, $\Delta H^{\neq}$ = 32.3 kcal/mole, $\Delta S^{\neq}$ = −2.5 e.u.

thermolysis of symmetrical azoalkanes. It also follows from this result that α-alkoxy groups cannot have any great radical-stabilizing influence. This is also shown by the fact that *(35a)* is thermally more stable than *(35b)* [57].



(35a), X = CH_3O
(35b), X = CH_3

The dominating influence of polar effects on radical formation reactions in which the transition state occurs early on the reaction coordinate, such as the fragmentation of peroxy esters, can also be seen from the high thermal stability of acetone *O-tert*-butylperoxycarbonyloxime *(36a)* [58]. Though a fragmentation could lead directly to the oxime radical *(36b)*,

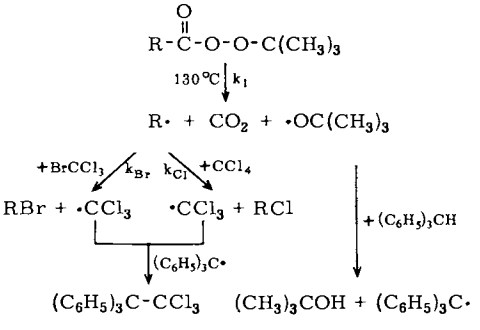


(36a) *(36b)*

the stability of which is known [59], *(36a)* decomposes as slowly as *tert*-butyl perbenzoate, and hence probably with simple cleavage of the peroxide bond in the slow step of the thermolysis [13]. No decomposition-promoting polar effect such as that found in *(31)* is to be expected in *(36a)*. The above-mentioned influence of the ring size on the rate of decomposition of cycloalkyl peroxy esters and its correlation with the ^{13}C coupling constants of the cycloalkanes also agree with the action of polar effects on the decomposition of peroxy esters. Since the chain-carrying radicals in free-radical substitutions and additions usually have a central hetero atom or strongly electronegative substituents, their reactivity is always influenced in a similar manner by polar effects. Until very recently, therefore, it was often assumed that the observed reactivity sequences were due to the stability of the radicals formed in the propagation steps. Since the relations found between structure and reactivity largely corresponded to those for the formation of carbonium ions (understandably, in view of the concept of polar effects), it was assumed that the stabilities of free radicals and of carbonium ions depend in the same manner on the structure. However, this conclusion is invalid, since the free radical character is not very well developed in the transition state of the exothermic propagation steps.

6. Selectivity of Free-Radicals

Another method of obtaining information about the stabilization of free radicals could be the determination of their selectivity in competing reactions. A relationship is often assumed to exist between the reactivity of an agent and its selectivity [59a]. The more reactive or the less stabilized a particle is, the lower its selectivity is expected to be. This selectivity principle was very successfully used by *H. C. Brown* in the investigation of electrophilic aromatic substitutions [60]. To determine the selectivity of aryl or alkyl radicals, the ratio of the rates of reaction of these radicals with CCl_4 and bromotrichloromethane were determined.



This competition system was tested in many respects. It was found that reliable competition constants $r = k_{Br}/k_{Cl}$ can be obtained on addition of triphenylmethane as an inhibitor. The analytical determination of the alkyl bromides and alkyl chlorides obtained is very simple. The competition constant r is calculated from these values with the aid of the following equations (the subscript e denotes the end of the reaction):

$$\frac{d[RBr]}{d[RCl]} = \frac{[RBr]_e}{[RCl]_e} = \frac{k_{Br}\,[BrCCl_3]}{k_{Cl}\,[CCl_4]}$$

$$r = \frac{k_{Br}}{k_{Cl}} = \frac{[RBr]_e\,[CCl_4]}{[RCl]_e\,[BrCCl_3]}$$

An important factor in the choice of this competition system was that the leaving group is the same, *i.e.* the CCl_3 radical, in both transfer reactions. Polar effects

[54] *C. Rüchardt* and *H. Schwarzer*, Chem. Ber. *99*, 1878 (1966).

[55] *C. Rüchardt*, *H. Böck*, and *I. Ruthardt*, Angew. Chem. *78*, 268 (1966); Angew. Chem. internat. Edit. *5*, 253 (1966); Chem. Ber., in press.

[56] *A. Ohno* and *Y. Ohnishi*, Tetrahedron Lett. *1969*, 4405.

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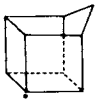
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should thus be approximately the same in both competing reactions. This is confirmed by the results in Table 8 [61].

Substituted phenyl radicals differ by only about 20% in their selectivity. Even steric effects due to *o*-substituents have no great influence. It is interesting to compare these competition constants with those of aliphatic radicals. The difference between the selectivities of primary and secondary alkyl radicals is very small; however, their selectivity is about five times as great as that of the phenyl radical. If the selectivity is assumed to be determined by the stability of the radical, it may be concluded that primary and secondary alkyl radicals have roughly equal stabilities, whereas aryl radicals are more reactive. However, the competition constant of the secondary radical is probably lowered slightly by a steric effect, so that the difference between primary and secondary radicals should be greater in value and opposite in direction. A steric effect of this type is found for the neooctyl radical. The competition constants of cyclic radicals are rather lower than those of open-chain radicals. The change in r with ring size is probably again due to increased steric screening of the radical center in rings of medium size.

Table 8. Competition constants $r = k_{Br}/k_{Cl}$ of the reaction of R· with $BrCCl_3$ and CCl_4 [61]. Yields: extreme values of 10—12 experiments.

R·	Yield (%) RBr + RCl	r (±5—10%)	T (°C)
4-CH_3O—C_6H_4·	59—73	129	130
4-CH_3—C_6H_4·	39—99	150	130
4-*t*-C_4H_9—C_6H_4·	26—59	150	130
C_6H_5·	58—85	144	130
C_6H_5·	24—50	184	104
C_6H_5· [a]	70—84	257	80
4-F—C_6H_4·	29—54	123	130
4-Cl—C_6H_4·	28—45	124	130
4-CN—C_6H_4·	19—68	128	130
2-Cl—C_6H_4·	29—87	128	130
2-CH_3—C_6H_4·	31—51	81	130
2,4,6$(CH_3)_3C_6H_2$·	41—81	86	130
1-$C_{10}H_{17}$·	40—63	103	130
2-$C_{10}H_7$·	39—65	107	130
1-*n*-C_8H_{17}·	45—56	678	130
2-*n*-C_8H_{17}·	63—70	580	130
1-neooctyl·	30—65	520	130
cyclo-C_3H_5·	23—43	278	110
cyclo-C_4H_7·	17—23	573	110
cyclo-C_5H_9·	43—52	662	110
cyclo-C_6H_{11}·	55—90	566	110
cyclo-C_7H_{13}·	44—75	407	110
cyclo-C_8H_{15}·	49—89	451	110
cyclo-C_9H_{17}·	47—73	442	110
cyclo-$C_{10}H_{19}$·	50—70	505	110
cyclo-$C_{11}H_{21}$·	50—62	568	110
cyclo-$C_{12}H_{23}$·	42—67	583	110
$C_6H_5CH_2$·	49—80	1700	80
9-triptycyl·	34—86	33	130
	30—60	73	130
	31—51	47	130
	40—66	59	80
	48—71	29	80
	31—47	170	130
	17—51	56	80
	37—76	100	80

[a] From phenylazotriphenylmethane.

The selectivity of the bridgehead radicals listed is interesting. One is inclined to draw the same conclusion from this as from the other experiments, *i.e.* that alkyl radicals prefer a planar arrangement, and any deviation from this is associated with an increase in energy and a decrease in selectivity. The small value for the adamantyl radical and the large value for the homocubyl radical are surprising. The screening of the radical center probably also plays some part here.

Why do radicals that differ so widely in their structures differ so little in their selectivities? We are again dealing with exothermic reactions, *i.e.* the R · · · Hal bond is only weakly developed in the transition state of the halogen transfer. The arrangement at the central C atom in R is still substantially unchanged or planar. A strain that varies strongly from radical to radical is to be expected only if the angle is considerably reduced in the transition state. We thus observe a process that is exactly the reverse of the radical formation discussed earlier.

The results presented show that many of the usual views on the relations between structure and reactivity in free-radical chemistry are in need of revision. In the absence of substituents, the strain in the ground state and the position of the transition state on the reaction coordinate are quantities that may explain the dependence of the reactivity on the structure. Polar effects and radical-stabilizing effects of unsaturated substituents such as vinyl and phenyl groups must be considered separately. The analysis carried out should be regarded merely as a starting point for the detailed explanation of reactivities in free-radical chemistry.

What is needed to enable a quantitative theory to grow from this starting point? Firstly, more kinetic data are required, particularly on the selectivity of free radicals. Secondly, more accurate information about the transition state of aliphatic free-radical propagation steps, *e.g.* in substitution, is necessary. A very promising line of investigation in this respect appears to be the molecular beam scattering experi-

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ments[62] which provides quantities such as the reaction cross section, and with which collision complexes can be studied. Finally, more detailed information on the energy relations in the ground state of the reaction, for example a quantitative theory of bond dissociation energies, is also necessary[11]. The quantum-chemical treatment of the σ bond may assume special importance here.

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The Ionization (Heterolysis) of Covalent Compounds as a Coordination-Chemical Phenomenon

By Viktor Gutmann[*]

The ionization of a covalent compound into a cation and an anion is a coordination-chemical phenomenon. The ions are formed with coordination either by nucleophilic attack of an electron pair donor or by electrophilic attack of an electron pair acceptor. The dielectrically controlled component of the ionization affects only the degree to which it occurs. It is shown that the ionization generally increases with increasing donor strength of the donor or with increasing acceptor strength of the acceptor. For a given M, the ease of ionization of the M–X bond increases in the order X = fluoride < chloride < bromide < iodide. These general aspects are discussed with the aid of examples.

1. Introduction[**]

The ionizing power of a substance, *e.g.* a solvent, is its ability to form cations and anions from molecules. However, the conditions required for ion formation by heterolysis of a covalent bond have remained largely uncertain over the decades since Arrhenius, particularly because of the frequent failure to distinguish between the concepts of ionization (ion formation) and ion dissociation (dissociation of ion associates).

An ionizing solvent is usually taken to be one that can form electrically conducting solutions. However, the electrical conductivity of a solution is due only to unassociated ions, whereas ion associates such as ion pairs make little or no contribution.

Since the dissociation of ion associates is largely dependent on the dielectric constant (ε) of the solution, it is not surprising that attempts have been made to use the dielectric constant of the solvent as a measure of its ionizing power. This necessarily led to innumerable contradictions, however, since the ionization of a covalent bond cannot be induced merely by a high dielectric constant. Perchloric acid is completely dissociated in water (ε = 81) but completely undissociated in anhydrous sulfuric acid (ε = 80), while triphenylcarbinol is not dissociated in water but is almost completely dissociated in anhydrous sulfuric acid.

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[**] The following abbreviations are used in this article: acac: 2,4-pentanedionate (acetylacetonate); en: ethylenediamine; Et: ethyl; Me: methyl; Ph: phenyl. The abbreviations for the solvents are given in Table 2.

2. The Electrostatic Model

When a substance consisting of ions, *i.e.* an ionic crystal, is dissolved, the energy required for the dissolution process is at least mostly supplied by solvation of the ions. The solvate bonds between the ion and the solvent molecule are often partly electrostatic in nature, so that the solvation depends in part on the polarity of the solvent molecules. Since the dielectric constant is also important to the solvation of ions if the interaction is purely electrostatic, the di-

electric constant and the dipole moment are regarded as criteria of the ionizing properties of a solvent [1–4].

These views do not, however, allow a satisfactory description of the formation of ions as a result of the heterolysis of a covalent bond.

3. General Description of Ionization by Coordination

Though *Meerwein* [5] pointed out the importance of complex formation "for increasing the ionizability of weak electrolytes", he had not recognized ionization as a coordination-chemical process. The coordination-chemical approach plays an important part in organic chemistry in the interpretation of the reaction event as a whole, including reactions that proceed by an ionic mechanism. In these reactions the ions are in equilibrium (if equilibrium is in fact reached), but they are usually present only in very low concentrations, and their formation as intermediates is usually shown only by the reaction mechanism.

Though the importance of coordination for ionization and hence for the establishment of ion equilibria in solution (including nonaqueous solvents) has been referred to in several reviews [6–14] during the past few years, this view is not widely enough known and evidently has not been presented in sufficient detail.

Numerous additions or modifications will still have to be made to the description of the ionization of a covalent compound as a coordination phenomenon, particularly in relation to quantitative treatment and reaction mechanisms. Nevertheless, its significance is so general that there appears to be justification for presenting it with the aid of some examples.

A molecule containing predominantly covalent bonds is not ionized by a substantially non-coordinating, though polar, solvent having a high dielectric constant, such as nitrobenzene, and forms nonconducting solutions in such solvents [9]. As will be shown later by numerous examples, ionization occurs only as a result of coordination [9–14], but the degree of ionization also depends on the dielectric constant of the medium. It is therefore convenient to deal separately with the coordination-dependent component of the ionization and the dielectric-dependent component.

3.1. The Coordination-Dependent Component

The case of heterolysis of a covalent bond between unlike atoms,

$$\overset{\delta+}{M}-\overset{\delta-}{X}$$

will increase with increasing attraction or repulsion of electrons from the more electropositive M to the more electronegative X. This is brought about

(a) by nucleophilic attack of an electron donor D at M:

$$D\rightarrow \overset{\delta+}{M}-\overset{\delta-}{X}$$

(b) by electrophilic attack of an electron acceptor A at X:

$$\overset{\delta+}{M}-\overset{\delta-}{X}\rightarrow A$$

Coordination with electron donors in accordance with (a) stabilizes the resulting cations, *e.g.*:

$$(CH_3)_3SnI + D \rightleftharpoons [(CH_3)_3SnD]^+ + I^-$$

Coordination with electron acceptors in accordance with (b), on the other hand, stabilizes the resulting anions: *e.g.*:

$$Ph_3CCl + A \rightleftharpoons [Ph_3C]^+ + [ACl]^-$$

Water owes its outstanding ionizing properties in part to the fact that it can coordinate both with electron pair acceptors (such as protons or many metal ions (*via* the oxygen)) and with electron pair donors, such as anions (with formation of hydrogen bonds) [9].

Whereas the ionization of inorganic compounds is frequently effected by nucleophilic attack by a donor, this is more difficult in organic compounds containing tetracoordinated carbon, and the ionization of organic substances usually results from electrophilic attack by an acceptor.

Finally, it will be shown in Section 7 that even pure covalent bonds, such as occur *e.g.* in the iodine molecule, are ionized by sufficiently strong coordination.

The ionization reactions can be described as substitution reactions. Case (a) is the substitution of X by D at M, and case (b) is the substitution of M by A at X.

The reactions can be precisely described by thermodynamic quantities. The equilibrium positions are determined by the changes in the free enthalpy. The

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enthalpy change $\Delta H_{D\cdot A}$ for the formation of the adduct D·A in the gas phase or in an "inert" medium is a measure of the strength of the donor-acceptor bond formed. The degree of ionization will increase with the strength of the resulting coordinate bonds in relation to that of the bonds that are broken.

Increased ionic character of the M–X bond, *i.e.* increased difference in the electronegativities of M and X, means higher bond strengths, with the result that the ionization becomes more difficult. Since the ionization results from a displacement of electrons in the region of the M–X bond, the polarizabilities are important; the greater the polarizabilities, the easier is the ionization. Iodides therefore generally ionize more readily than fluorides. For example, the ease of ionization of the hydrogen halides increases in the order HF $\ll$ HCl $<$ HBr $<$ HI.

In a medium having a low dielectric constant, coordination-induced ionization leads to ion associates, such as ion pairs:

$$\begin{aligned} D + M{-}X &\rightleftharpoons \{[DM]^+[X]^-\}^0 \\ \text{or } M{-}X + A &\rightleftharpoons \{[M]^+[AX]^-\}^0 \end{aligned} \quad (1);\ K_{ion}$$

which make no contribution to the electrical conductivity of the solution. The ionization constant K_{ion} is to be understood as the formation constant of the ion associates in accordance with eq. (1) in a medium having $\varepsilon = 1$.

Large differences in reaction entropy are to be expected between complex formation by neutral donors and by anionic donors, and particularly on transition from weakly solvating to strongly solvating solvents, as will be shown later.

3.2. The Dielectric-Dependent Component

The degree of dissociation [eq. (2)] of the ion associates formed by coordination [eq. (1)] into ions that can migrate independently of each other depends on the dielectric constant (ε) of the medium; the dissociation constant K_{diss} increases with increasing dielectric constant.

$$\begin{aligned} \{[DM]^+[X]^-\}^0 &\rightleftharpoons [DM]^+[X]^- \\ \text{or } \{[M]^+[AX]^-\}^0 &\rightleftharpoons [M]^+[AX]^- \end{aligned} \quad (2);\ K_{diss}$$

The dielectric properties of aprotic donor solvents can be qualitatively described by the dissociation constants K_{diss} found for quaternary ammonium salts in solution in these solvents.

Since the concentration of the ion associates formed in accordance with eq. (1) is decreased by increasing dissociation in accordance with eq. (2), the ionization equilibrium of eq. (1) is disturbed by the dissociation of eq. (2) [9].

The dielectric-dependent component of the ionization is of practically no importance in the comparison of two donor solvents having similar dielectric constant. It must, however, be taken into account in the comparison of solvents having different dielectric constants; its importance increases with decreasing donor strength of the solvents and with increasing difference between their dielectric constants [9].

However, the ionization is always brought about by the coordination-dependent component, while the degree to which it occurs is determined by the interplay of the coordination-dependent and the dielectric-dependent components, as is shown by the following example.

Let three aprotic donor solvents be available for the ionization of the compound M–X, *i.e.*

D_1 with $\varepsilon = 10$ and medium donor strength,

D_2 with $\varepsilon = 35$ and medium donor strength,

D_3 with $\varepsilon = 10$ and high donor strength.

Let us assume that in the two solvents of medium donor strength (D_1 and D_2), the ionization constants for the coordination-dependent ion pair formation in accordance with eq. (1) is $K_{ion} = 1$, and let the corresponding constant in the solvent of high donor strength (D_3) be $K_{ion} = 3$. On the basis of the assumed dielectric constants, the dissociation constants for the dissociation of the ion associates in accordance with eq. (2) are $K_{diss} \approx 10^{-4}$ for D_1 and D_3, and $K_{diss} \approx 10^{-2}$ for D_2. Calculation now shows that M–X can be ionized to a greater degree in a solvent having a low dielectric constant but a high donor strength (D_3) than in a solvent having a high dielectric constant but only a medium donor strength (D_2) (Table 1).

Table 1. Extent of ionization of M–X at $c = 10^{-2}$ mole/l under the arbitrarily assumed conditions.

Solvent	Assumed ε	K_{diss}	Donor strength	Assumed K_{ion}	% Ionization
D_1	10	10^{-4}	medium	1	53
D_2	35	10^{-2}	medium	1	75
D_3	10	10^{-4}	high	3	77

The dissociation constants of acids and bases may therefore be used for comparison of the acid strengths or base strengths in a given solvent, *i.e.* at a fixed dielectric constant, but the dissociation constants of a given acid or base in solvents with different dielectric constants cannot be compared. Though NH_3 is a stronger donor than water, hydrogen chloride has a much smaller acid constant in liquid ammonia than in water. The reason for this is that though the ionization in accordance with eq. (1) takes place to approximately the same extent in both solvents, the dissociation of the ion pairs in accordance with eq. (2) is more extensive in water, owing to the high dielectric constant of this solvent. On the other hand, the acid constant of acetic acid is about the same in both solvents, since acetic acid is much more strongly ionized in accordance with eq. (1) in liquid ammonia.

Thus the coordination in accordance with eq. (1) is always the initiating factor, and the dielectric constant of the solvent is the regulating factor, in the ionization of a covalent compound.

4. Ionization by Nucleophilic Attack by Donors

The degree of ionization of a given compound M–X by nucleophilic attack of a neutral donor increases with increasing stability of the resulting cation $[DM]^+$ in comparison with that of the unionized M–X [9–14a]. In many cases this is the same as saying that the coordinate bond D–M formed must be stronger than the M–X bond that must be broken.

The strength of a coordinate bond depends on:

1. the donor properties of the donor,
2. the acceptor properties of the acceptor,
3. steric effects, and
4. specific interactions such as hydrogen bonding.

4.1. Donor Properties of Donors

The donor strength of a molecule for the formation of charge-transfer complexes is considered to be given as an absolute property of the molecule by the ionization energy [15].

Since the ionization potential of a molecule is defined as the energy required to remove an electron completely from the gaseous molecule, whereas the electron remains in the molecule in the formation of a donor-acceptor bond, it is clear that no information about the electron pair donor properties can be obtained from the ionization potentials [14a]. For example, the ionization potentials of pyridine and xylene are very similar, as are those of methylamine and benzene; CS_2 has roughly the same ionization potential as NH_3 or $(CH_3)_2O$, and those of hexane and ethanol are also roughly equal.

It is therefore convenient to define the donor strength as a relative quantity with respect to a reference acceptor [16]. The experimental determination of the degree of interaction between a donor and the reference acceptor is also simple, since ΔH and ΔG values for donor-acceptor reactions in a substantially inert solvent are relatively easy to obtain.

Antimony(v) chloride was chosen as the reference acceptor, since it forms 1:1 adducts with many donors.

$$D + SbCl_5 \rightleftharpoons D{\cdot}SbCl_5; \quad -\Delta H_{D\cdot SbCl_5}$$

$$K_{D\cdot SbCl_5} = \frac{a_{D\cdot SbCl_5}}{a_D{}^a \times a_{SbCl_5}}$$

On investigation of this reaction with several neutral donors in highly dilute solution in a fairly inert medium, *i.e.* 1,2-dichloroethane, it was found that $\log K_{D\cdot SbCl_5}$ is proportional to $-\Delta H_{D\cdot SbCl_5}$ [10 to 12, 14, 16, 17] (Fig. 1); the entropy contributions are therefore constant in these reactions

$$a \log K_{D\cdot SbCl_5} + b = -\Delta H_{D\cdot SbCl_5} = DN_{SbCl_5} \equiv Dn$$

It is therefore justifiable to use the ΔH value as a measure of the donor properties with respect to $SbCl_5$. The negative $\Delta H_{D\cdot SbCl_5}$ value is known as the donor number DN_{SbCl_5}, donor intensity, or donicity Dn [10–12, 14, 16, 17]. It is also a measure of the nucleophilicity or the Lewis base strength.

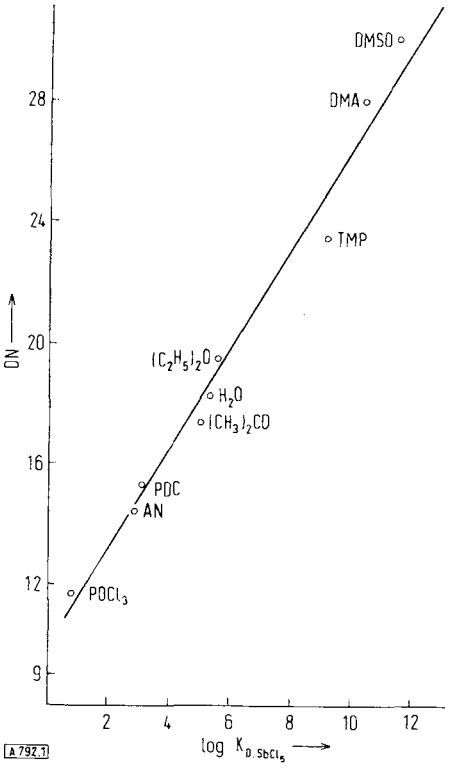


Fig. 1. Relation between Dn ($-\Delta H_{D\cdot SbCl_5}$) and log $K_{D\cdot SbCl_5}$ for several donors D.

The donicity expresses the total interaction of a donor with $SbCl_5$, including the electrostatic interactions. The reaction enthalpies of many donor-acceptor reactions using the same donor D are proportional to the acceptor strength of A, *e.g.* iodine, phenol, trimethyltin chloride, and many ions of d metals [10, 16]. The entropy components are again constant here.

The donicity of a donor solvent thus also approximately expresses the donor strength with respect to this acceptor. It would be an unrealistic, though very useful, approximation to regard the donicity as a molecular property; it cannot be determined strictly quantitatively, since the ability to form a coordinate bond also depends on the properties of the other

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reactant. Donicity is therefore a qualitative, at best semiquantitative value, like electronegativity, which is nevertheless extremely useful.

In this sense, the donicity has proved to be a valuable guide in the assessment of the ionizing power of a donor. The ionizing power of a donor solvent generally increases with its donicity and its dielectric constant (Table 2).

Table 2. *Dn* and ε of donor solvents.

Solvent	*Dn*	ε
1,2-Dichloroethane	—	10.1
Sulfuryl chloride	0.1	10.5
Tetrachloroethylene carbonate	0.2	9.2
Thionyl chloride	0.4	9.2
Acetyl chloride	0.7	15.8
Benzoyl chloride	2.3	23.0
Nitromethane (NM)	2.7	35.9
Dichloroethylene carbonate	3.2	31.8
Nitrobenzene (NB)	4.4	34.8
Acetic anhydride	10.5	20.7
Phosphorus oxide chloride	11.7	14.0
Benzonitrile	11.9	25.2
Selenium oxide chloride	12.2	46.0
Monochloroethylene carbonate	12.7	62.0
Acetonitrile (AN)	14.1	38.0
Sulfolane	14.8	42.0
Propylene carbonate (PDC)	15.1	69.0
Benzyl cyanide	15.1	18.4
Ethylene sulfite	15.3	41.0
Isobutyronitrile	15.4	20.4
Propionitrile	16.1	27.7
Ethylene carbonate	16.4	89.1
Phenylphosphorus oxide difluoride	16.4	27.9
Methyl acetate	16.5	6.7
n-Butyronitrile	16.6	20.3
Acetone	17.0	20.7
Ethyl acetate	17.1	6.0
Water	18.0	81.0
Phenylphosphorus oxide dichloride	18.5	26.0
Diethyl ether	19.2	4.3
Tetrahydrofuran (THF)	20.0	7.6
Diphenylphosphorus oxide chloride	22.4	—
Trimethyl phosphate (TMP)	23.7	6.8
Tributyl phosphate (TBP)	23.7	6.8
Dimethylformamide (DMF)	26.6	36.1
N,N-Dimethylacetamide (DMA)	27.8	28.9
Dimethyl sulfoxide (DMSO)	29.8	45.0
N,N-Diethylformamide	30.9	—
N,N-Diethylacetamide	32.2	—
Pyridine (py)	33.1	12.3
Hexamethylphosphoramide (HMPA)	(38.8) [a]	30.0

[a] Under the conditions of the calorimetric measurement, partial ionization of the adduct $SbCl_5$ · HMPA is found to take place.

Conductivity measurements on the donor-acceptor system in a substantially inert solvent having a sufficiently high dielectric constant, such as nitrobenzene (*Dn* = 4.4; ε = 34.8 at 25 °C) [9], may be used for the determination of the coordination-dependent contribution.

Figures 2 and 3 show the changes in the equivalent conductivities of $(CH_3)_3SnI$ solutions in nitrobenzene ($c \approx 7 \times 10^{-2}$ mole/l) on addition of donors. A comparison of the conductivities at given molar ratios of donor to acceptor show that they increase with increasing donicity of the donor (exception: pyridine). The conductivity in nitrobenzene is a measure only of the content of free ions, and not of the content of associated ions. The content of associated ions is proportional to the content of free ions if the association constants of the associated ion pairs are approximately the same [9]. This is in fact so in this case, as is shown by conductivity measurements on $(CH_3)_3SnI$ in the strong donor solvents HMPA, DMSO, DMF, and pyridine and their evaluation by the method of *Fuoss* and *Kraus*, according to which $(CH_3)_3SnI$ is completely ionized as a 1,1 electrolyte in HMPA, DMSO, or DMF [9].

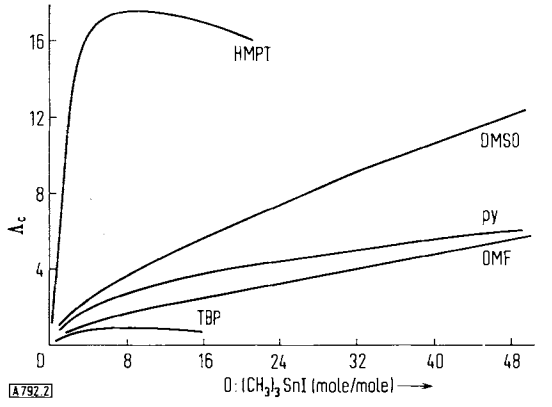


Fig. 2. Equivalent conductivity of 7×10^{-2} M $(CH_3)_3SnI$ solutions in nitrobenzene in the presence of aprotic donor solvents, upper region (HMPT = HMPA).

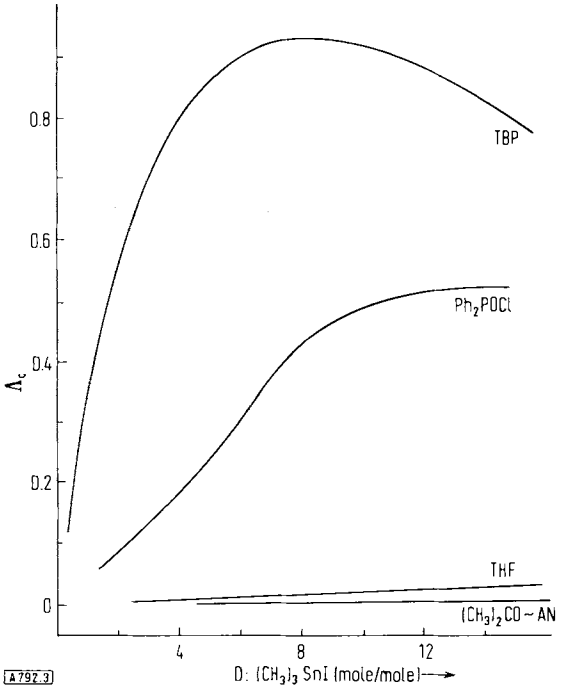


Fig. 3. Equivalent conductivity of 7×10^{-2} M $(CH_3)_3SnI$ solutions in nitrobenzene in the presence of aprotic donor solvents, lower region.

It follows that comparison of the equivalent conductivities at a constant molar ratio in nitrobenzene gives a direct measure of the relative ionizing power of donor solvents, which increases in the order nitrobenzene < acetonitrile < acetone < THF < Ph_2POCl < tributyl phosphate < DMF (?) < pyridine < DMSO < HMPA.

The proportionality between the donicity and the ionizing power of a donor solvent for $(CH_3)_3SnI$ can be demonstrated directly only if the donor strengths of the donors toward $(CH_3)_3SnI$ are known. These

thermodynamic data are not obtainable, but quantitative data on the $\Delta H_{D\cdot A}$ values have been reported for the adduct formation between $(CH_3)_3SnCl$ and the donors investigated. Since the corresponding enthalpies of adduct formation for the acceptor molecules $(CH_3)_3SnCl$ and $(CH_3)_3SnI$ will be proportional, the relation between the donicity and the ionizing power appears to be obvious.

Another example of the increasing ionization of a metal compound with increasing donicity of the donor solvent is found in the behavior of cobalt(II) iodide[10,13,14]. In nitromethane (NM; *Dn* = 2.7, ε = 35.9), this compound forms a tetrahedral adduct $CoI_2(NM)_2$, which is molecularly dissolved[18]. Partial ionization with self-complexing (see Section 6) occurs in propylene carbonate (*Dn* = 15.1, ε = 69), while complete ionization occurs in a solvent having a high donicity (DMSO; *Dn* = 29.8)[19], *e.g.*

$$CoI_2 + 6\,DMSO \rightleftharpoons [Co(DMSO)_6]^{2+} + 2\,I^-$$

Even when a large supply of iodide ions is present, iodide ions do not enter the coordination sphere of the hexasolvated metal ion, since the donor properties of the solvent molecule are incomparably better than those of the iodide ion[14,19]. Since the donor properties of the chloride ion are much better and the strength of the Co–Cl bond is similar to that of the Co–DMSO bond, $CoCl_2$ is not completely ionized in DMSO[10,19,20].

4.2. The Solvation of Anions in Donor Solvents

Ionization by nucleophilic attack can naturally be effected not only by neutral donors but also by ions. Thus the halide and pseudohalide ions are donors. In a donor solvent, the anions must compete with the solvent molecules, and may therefore be regarded, in relation to these molecules, as competing ligands. Ionization by anions is therefore possible in a non-coordinating or weakly coordinating solvent.

$$M{-}X + n\,X^- \rightleftharpoons [MX_{(n+1)}]^{n-} \qquad (3)$$

As was mentioned earlier, both $(CH_3)_3SnI$ and CoI_2 form nonconducting solutions in the practically non-coordinating solvent nitromethane (*Dn* = 2.7, ε = 35.9). If iodide ions are added, the stoichiometric quantity is sufficient for the formation of the iodo complex.

In a donor solvent whose donor properties are not very different from those of the iodide ions, on the other hand, an excess of iodide ions must be used to achieve complete formation of the iodo complex. Finally, with a neutral donor whose donor properties are much better than those of the competing ligand, ionization by nucleophilic attack of D takes place instead of formation of the halogenometalate, even when X^- is present in a large excess[19] (Table 3).

Table 3. Molar ratio X^- : Co^{2+} required for quantitative formation of $[CoX_4]^{2-}$ from Co^{2+} and X^- in solvents having different donicities.

Donor	*Dn*	N_3^-	Cl^-	Br^-	I^-
NM	2.7	4	4	4	5
PDC	15.1	4	4.5	4.3	7.8
AN	14.1	8	16	40	[a]
DMA	27.8	4	16	[a]	[a]
DMSO	29.8	20	200	[a]	[a]
HMPA	38.8	27	460	[a]	[a]

[a] No formation of $[CoX_4]^{2-}$ even at molar ratios greater than 200.

Any attempt to fix the donicity for competing ligands X^-, *e.g.* halide and pseudohalide ions, meets with fundamental difficulties, since the assumption that has been tacitly made so far, *i.e.* that the strength of the metal-ligand bond depends mainly on the nature of the ligand and not on the nature of the acceptor, is invalid.

Measurements on the equilibria between bis(2,4-pentanedionato)oxovanadium $[VO(acac)_2]$ and X^- show[21] that the order of the donor strengths of halide and pseudohalide ions toward $VO(acac)_2$ is: $I^- < Br^- < Cl^- < (F^-) \approx NCS^- < N_3^- \approx (CN^-)$. Their donor properties are roughly compared in Figure 4 with those of a number of solvent molecules

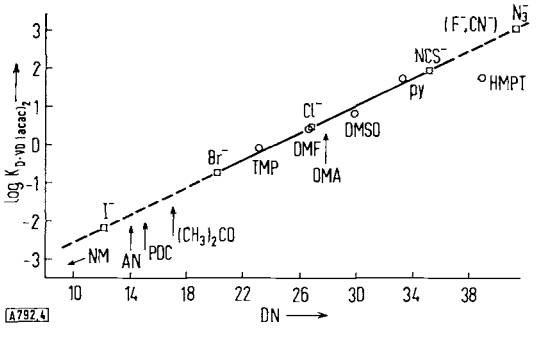


Fig. 4. log $K_{D\cdot VO(acac)_2}$ values for halide and pseudohalide ions and aprotic donor solvents, and their relation to *Dn* (HMPT = HMPA).

Table 4. ΔG^0 values for the reactions of halide and pseudohalide ions and neutral donors with $VO(acac)_2$ in acetonitrile, and donicities of the donors.

Donor	$G^0_{D\cdot VO(acac)_2}$	*Dn*
N_3^-	−4.2	(42)
CN^-	−4.2	(42)
NCS^-	−2.7	(35)
F^-	−2.7	(35)
HMPA	−2.5	38.8
py	−2.47	33.1
Ph_3PO	−2.11	32.5
DMSO	−1.14	29.8
Cl^-	−0.83	(27)
DMF	−0.63	26.6
TMP	−0.24	23.0
Br^-	+0.65	(20)
Acetone	+1.30	17.0
PDC	+1.75	15.1
I^-	2.0	(14)

[18] *V. Gutmann* and *K. H. Wegleitner*, Monatsh. Chem. *99*, 368 (1968).

[19] *V. Gutmann* and *O. Bohunovsky*, Monatsh. Chem. *99*, 740 (1968).

[20] *V. Gutmann* and *L. Hübner*, Monatsh. Chem. *93*, 1261 (1962).

[21] *V. Gutmann* and *U. Mayer*, Monatsh. Chem. *99*, 1382 (1968).

(neutral donors), but it should be emphasized that the "donicities" for X^- ions are not identical with the reaction enthalpies $-\Delta H_{X^-\cdot SnCl_5}$, and are therefore given in parentheses in Table 4.

Table 5 shows that the entropies of solvation of halide ions are much higher in DMSO than in water, since water has a more pronounced liquid structure than DMSO. In general, the donor strength of X^- decreases with increasing solvation [14a].

Table 5. ΔG^0, ΔH^0, and ΔS^0 for the solvation of halide ions in DMSO and H_2O.

	Solvent	Cl^-	Br^-	I^-
ΔG^0	DMSO	−56.4	−52.6	−47.5
(kcal · mole^{-1})	H_2O	−67.4	−60.4	−51.3
ΔH^0	DMSO	−67.9	−63.4	−56.8
(kcal · mole^{-1})	H_2O	−72.8	−64.7	−54.3
ΔS^0	DMSO	−38.4	−36.1	−31.4
(cal · mole^{-1} deg^{-1})	H_2O	−18.2	−14.4	−10.1

According to Table 6, the free enthalpies of solvation of the halide ions are lower in HMPA than in the other donor solvents, *i.e.* HMPA is only weakly solvating. The difference between the ΔG^0 values for the Cl^- ion in DMSO and in HMPA is 4.5 kcal · mole^{-1}. The donor strength of the Cl^- ion is accordingly higher in HMPA than in DMSO. The formation of the $[CoCl_4]^{2-}$ complex in HMPA (with a large excess of Cl^-), which is unexpected on the basis of the donicity, is explained by the relative increase in the donor strength of the chloride ion due to the extremely low solvation [14a].

Table 6. Free enthalpies of solvation ΔG^0 (kcal · mole^{-1}) of halide ions in donor solvents.

Donor	Cl^-	Br^-	I^-
AN	−55.4	−51.8	−46.0
Sulfolane	−56.0	—	−46.0
H_2O	−67.4	−60.4	−51.4
DMF	−55.1	−50.8	−45.7
DMA	−53.3	−49.4	−45.1
DMSO	−56.4	−52.6	−47.5
HMPA	−51.9	−47.8	—

However, the formation of the $[CoCl_4]^{2-}$ ion in DMSO is also unexpected, since the chloride ion in acetonitrile is a weaker donor than DMSO. Thus the decrease in the donor strength of an X^- ion on transition from the gas phase into a solvating medium also depends on the ratio of the free enthalpy of solvation to the free enthalpy of reaction of the complex formation process as a whole. The greater the latter value, the weaker is the influence of solvation [14a]. Since this thermodynamic effect and the solvation effect (the Cl^- ion is more strongly solvated in DMSO than in acetonitrile) partly balance each other, $[CoCl_4]^{2-}$ is formed in DMSO only in the presence of a large supply of chloride ions. In dimethylacetamide (DMA), on the other hand, these two effects reinforce each other, so that the complex is formed much more readily in DMA, despite the similarity of the donicities of DMSO and DMA [14a].

The tendency to solvate anions decreases in the series: $H_2O > ROH \gg DMSO \approx ES > AN \approx NM > DMF > DMA > HMPA$.

4.3. Acceptor Properties of MX

The $\Delta H_{D\cdot A}$ values are roughly proportional to the donicity of the donor for A = iodine, phenol, trimethyltin chloride, and antimony(III) chloride, and the entropy contributions are constant in these cases (Fig. 5) so that for the interaction of the donors with these acceptors, the donicity of the donor is an approximate measure of the ionization of the acceptor.

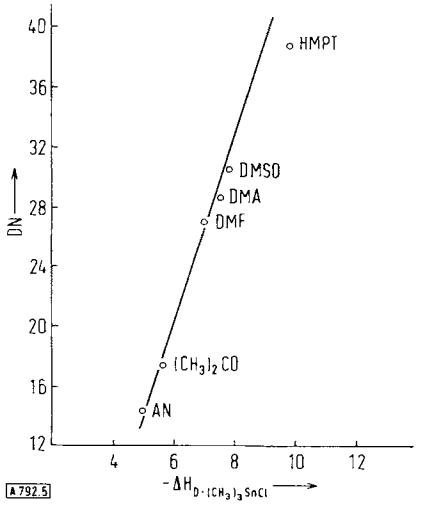


Fig. 5. Relation between *Dn* and $-\Delta H_{D\cdot(CH_3)_3SnCl}$ (HMPT = HMPA).

Polarographic studies, which will not be described in detail here [22], have shown that numerous metal ions, *e.g.* Mn^{2+}, Zn^{2+}, Cr^{2+}, Co^{2+}, Ni^{2+}, and Cu^{2+}, also approximately satisfy the conditions mentioned. As will be shown later, however, the situation may be more complicated because of the higher coordination numbers toward the donor molecules.

The deviations from the donicity-ionizing power relation become pronounced in the case of very "hard" or very "soft" metal ions [23].

Hard ions, such as the alkali metal ions, may be ignored in the present discussion in view of their low tendency to form covalent bonds, but the situation presented by very soft metal ions may be discussed.

The readily polarizable, soft metal ions include in particular the ions of noble metals in low oxidation states [23], *e.g.* Pd^{2+}, Pt^{2+}, Ag^+, and Hg_2^{2+}. These ions react preferentially with readily polarizable donor atoms, *i.e.* I > Br > Cl ≫ F; Te ≈ Se ≈ S ≫ O; Sb ≈ As ≈ P ≫ N. Their iodides are thus more difficult to ionize than their chlorides. The ionizability of silver halides in water increases in the order AgI < AgBr < AgCl ≪ AgF, and is generally increased by interaction with the strong donor ammonia.

[22] *V. Gutmann* and *R. Schmid*, Monatsh. Chem. *100*, 2113 (1969).

[23] *R. G. Pearson*, J. Amer. Chem. Soc. *85*, 3533 (1963).

Moreover, the concept of the donicity can no longer be used, since the neutral donors with S or P donor atoms, *e.g.* triphenylphosphine, can stabilize the cations better than the O and N donors discussed so far.

Whereas tin(IV) iodide, as expected, is extensively ionized in DMSO (high donicity of DMSO and low donicity of the iodide ion), the same solvent causes practically no ionization of mercury(II) iodide, the metal ion of which is soft [24]. This is partly because $mercury^{II}$ binds iodide ions much more strongly than tin^{IV}, and partly because DMSO is preferentially coordinated *via* the sulfur to the mercury(II) ion, but *via* the oxygen to tin(IV) iodide. Since the Hg^{II}-S bond is weaker than the Sn^{IV}-O bond and the Hg^{II}-I bond is stronger than the Sn^{IV}-I bond, ionization of HgI_2 in DMSO is practically impossible, and iodo complexes can in fact be formed in this medium [24]:

$$\begin{array}{rcl} SnI_4 + 4\,DMSO & \rightleftharpoons & [SnI_2(DMSO)_4]^{2+} + 2I^- \\ HgI_2 + 2\,I^- & \rightleftharpoons & [HgI_4]^{2-} \\ \hline SnI_4 + 4\,DMSO + HgI_2 & \rightleftharpoons & [SnI_2(DMSO)_4]^{2+}[HgI_4]^{2-} \end{array}$$

The assumption made in the early sections that the donor-acceptor interaction is almost independent of the properties of the acceptor is thus valid only for a certain group of acceptors, *i.e.* those that are neither very hard nor very soft, and for these acceptors the concept of donicity can be used.

4.4. Steric Effects

Steric effects will become apparent above all when the acceptor ions or molecules are small and have a high coordination number with respect to the donors, and/or when the donor molecules are very bulky.

Whereas the cobalt(II) ion is octahedrally coordinated by nearly all the solvent molecules listed in Table 1 [10,19], tetrahedral coordination occurs in hexamethylphosphoric triamide (HMPA) [25], evidently because of the great bulk of the donor molecules. The enthalpy of solvation of the $[Co(HMPA)_4]^{2+}$ ion is much lower than one would expect from the donicity of HMPA, whereas the enthalpy of solvation of $CoI_2(HMPA)_2$ is roughly as expected [26]. It has already been mentioned that iodide ions cannot enter the coordination sphere of the cobalt(II) ion solvated with DMSO. Though HMPA has a higher donicity than DMSO, it is easy to replace an HMPA molecule by iodide on cobalt [26]:

$$[Co(HMPA)_4]^{2+} + I^- \rightleftharpoons [Co(HMPA)_3I]^+ + HMPA$$

It is clear from these two phenomena that the solvating bonds are significantly weaker in $[Co(HMPA)_4]^{2+}$ than in $CoX_2(HMPA)_2$.

Investigation of the solvent complexes with the aid of broad-line NMR spectroscopy have also shown that the coordination center in $[Co(HMPA)_4]^{2+}$ moves in relation to the ligand shell at room temperature [26]. The cobalt(II) ion "rattles", so to speak, in the relatively rigid ligand framework formed by four HMPA molecules. This "rattling effect" does not occur in $CoX_2(HMPA)_2$, since the HMPA molecules no longer hinder each other and can move close enough to the coordination center to form relatively rigid solvating bonds. Accordingly, it is practically impossible to substitute the last two HMPA molecules, whereas the first HMPA molecule in $[Co(HMPA)_4]^{2+}$ can be displaced even by a weak donor such as the iodide ion [26]. The ease of substitution increases with the donicity of the competing ligand ($I^- < Br^- < Cl^-$). All four possible complexes are formed in the chloro system, only the first two, *i.e.* $[Co(HMPA)_3Br]^+$ and $[Co(HMPA)_2Br_2]$, in the bromo system, and essentially only $[Co(HMPA)_3I]^+$ in the iodo system, since CoI_2 is largely ionized in HMPA [27].

$$[Co(HMPA)_2I_2] + HMPA \rightleftharpoons [Co(HMPA)_3I]^+ + I^-$$

4.5. Specific Donor-Acceptor Interactions

"Specific donor-acceptor interactions" refers collectively to all the factors that have not yet been discussed and that influence the degree of the coordination-dependent ionization, except kinetic effects. These factors are mostly concerned with the nature of the donor-acceptor bond. It is known, for example, that the free enthalpies of hydration of some metal ions, *e.g.* Mn^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, and Cd^{2+}, are greater than one would expect from the donicity [11]. This effect has been attributed to the additional bonding of the water molecules coordinated to the metal ion by hydrogen bonds, and the hydration shell reinforced in this way has been referred to as the "Royal Core of Water Molecules" [28–31]. It has recently been shown that this effect occurs particularly with softer metal ions, but not with the alkali or alkaline earth metal ions [11].

It can be seen from the behavior of $(CH_3)_3SnI$ described above that pyridine and dimethylformamide have approximately equal ionizing properties for $(CH_3)_3SnI$ in nitrobenzene, whereas DMF should have a weaker action than pyridine according to the donicities. Evaluation of the results of conductivity measurements on solution of $(CH_3)_3SnI$ in pure DMF shows that the ion association here is higher than expected. This ion association is chemical in nature; the acidity of the formyl protons is probably

[24] *F. Gaizer* and *M. T. Beck*, J. Inorg. Nucl. Chem. *29*, 21 (1927).

[25] *J. T. Donoghue* and *R. S. Drago*, Inorg. Chem. *1*, 866 (1962).

[26] *V. Gutmann*, *A. Weisz*, and *W. Kerber*, Monatsh. Chem. *100*, 2096 (1969).

[27] *V. Gutmann* and *A. Weisz*, Monatsh. Chem. *100*, 2104 (1969).

[28] *L. I. Katzin* and *E. Gevert*, J. Amer. Chem. Soc. *72*, 5457 (1950).

[29] *C. K. Jørgensen*: Inorganic Complexes. Academic Press, New York 1963, p. 21 ff.

[30] *L. I. Katzin*, J. Chem. Phys. *23*, 2055 (1955).

[31] *L. I. Katzin*, J. Chem. Phys. *36*, 3034 (1962).

increased to such an extent by coordination of DMF to Sn that hydrogen bonds are formed to the iodide ions. This interpretation agrees with the results of ^{1}H-NMR studies. Only in infinitely dilute solution do the coordinated DMF molecules lose their ability to coordinate with the iodide ions, and they can then coordinate only with the solvent molecules. The coordinated $[Sn(CH_3)_3]^+$ cation carries with it a "second" solvent layer, and is therefore rather less mobile [9].

This interpretation does not conflict with the fact that alkali metal halides are practically completely dissociated in DMF. On the contrary, it is possible to see the analogy with the acidities of aqueous solutions of alkali metal ions, which do not exercise any acidic function, since the partly electrostatic hydration leaves the bonding in the water molecules of the hydrate almost unchanged from that in the free water molecules [11]. On the other hand, coordination of water with formation of more strongly covalent bonds, *i.e.* with soft metal ions, leads to increased acidity and to an increased tendency toward hydrogen bond formation [11] (see Table 7).

Table 7. Enthalpies of hydration and pK_a of pairs of hydrated ions of the same charge and of similar ionic radius.

Aquo ions	Property	r_0 (ion) (Å)	$-\Delta H$ (kcal/mole)	pK_a in water at 25 °C
Na^+	hard	0.96	93	14
Cu^+	soft	0.95	115	11
K^+	hard	1.33	73	14
Ag^+	soft	1.26	112	10
Mg^{2+}	hard	0.65	437	12.2
Cu^{2+}	soft	0.69	499	7.3
Ca^{2+}	hard	0.99	362	12.6
Cd^{2+}	soft	0.97	428	9.0
Sr^{2+}	hard	1.13	327	13.1
Hg^{2+}	very soft	1.10	443	3.6

The specific interactions also include π-donor interactions of some donors with certain acceptors. The donicity of benzene is very low, since it has practically no n-donor properties and exhibits no π-donor properties toward $SbCl_5$. It can, however, act as a π-donor *e.g.* toward iodine or aluminum halides. $AlBr_3$ and benzene exhibit considerable electrical conductivity, particularly in the presence of hydrogen halide [32, 33].

5. Ionization by Electrophilic Attack of Acceptors

Triphenylchloromethane is molecularly dissolved in most donor solvents, for example acetonitrile, and is ionized only on addition of acceptors. The acceptor strength, which is a direct measure of the electron affinity, is important to the degree of ionization. In addition to the coordination-dependent component of the ionization, the dielectric-dependent component must also be considered. This component can be eliminated to allow the study of the coordination-dependent component by carrying out the investigations in an inert solvent having a suitable dielectric constant, *e.g.* acetonitrile. The behavior of triphenylchloromethane in acetonitrile on addition of various acceptors is determined by the acceptor strengths of acetonitrile and of the additives. Trihalides and pentahalides are found to be strong acceptors for chloride ions, while dihalides and tetrahalides are much weaker. The $[Ph_3C]^+$ ion is always formed in the same unsolvated state, irrespective of the acceptor and the solvent [34]. Dichlorides, trichlorides, and pentachlorides coordinate with one chloride ion to form mononuclear complexes, while tetrachlorides coordinate either with one chloride ion to form dinuclear complexes or with two chloride ions per acceptor molecule to form mononuclear anionic complexes. However, the ion pair does not dissociate to the expected degree.

The formation constants of the chloro complexes depend both on the nature of the acceptor and on the solvent. As is shown by Table 8, the formation constants are greater in acetonitrile (Dn = 14.1) than in phenylphosphorus oxide dichloride (Dn = 18.5) [35], as expected.

Table 8. log K values of the $[Ph_3C]^+[MCl_{(n+1)}]^-$ complexes in acetonitrile (AN) and $PhPOCl_2$.

Acceptor chloride	Chloro complex	log K in AN	log K in $PhPOCl_2$
$ZnCl_2$	$[ZnCl_3]^-$	1.84	0.72
$HgCl_2$	$[HgCl_3]^-$	1.64	−0.7
BCl_3	$[BCl_4]^-$	1.32	1.03
$AlCl_3$	$[AlCl_4]^-$	1.75	−0.72
$SbCl_3$	$[SbCl_4]^-$	0.70	−1.60
$SnCl_4$	$[SnCl_5]^-$	4.30	1.19
$TiCl_4$	$[TiCl_5]^-$	1.89	0.72
PCl_5	$[PCl_6]^-$	0.5	−2.50
$SbCl_5$	$[SbCl_6]^-$	5.1	1.56

For metals of the same period, chlorides with even numbers of ligands (dichlorides and tetrachlorides) are weaker chloride ion acceptors than those with odd numbers of ligands (trichlorides and pentachlorides). Lone pairs of electrons act as pseudoligands; for example, $SbCl_3$ acts as a pseudotetrachloride and $TeCl_4$ as a pseudopentachloride. However, the lone pairs of electrons basically reduce the affinity for chloride ions, so that $SbCl_3$ is a weaker chloride ion acceptor than $SnCl_4$, and $TeCl_4$ is weaker than $SbCl_5$. The chlorometalate ions also follow this rule. Moreover, the formation constants also depend on the size of the acceptor; for chlorides of a given group they increase from the first period to the fifth, but decrease slightly in the sixth [35]: $BCl_3 < AlCl_3 < GaCl_3 < InCl_3 < TiCl_3$; $SiCl_4 < GeCl_4 < SnCl_4 < PbCl_4$.

[32] *E. Wertyporoch*, Ber. dtsch. chem. Ges. *64*, 1369 (1931).

[33] *A. Wohl* and *E. Wertyporoch*, Ber. dtsch. chem. Ges. *64*, 1357 (1931).

[34] *M. Baaz*, *V. Gutmann*, and *O. Kunze*, Monatsh. Chem. *93*, 1142 (1962).

[35] *M. Baaz*, *V. Gutmann*, and *O. Kunze*, Monatsh. Chem. *93*, 1162 (1962).

In the absence of an "inert" medium, triphenylchloromethane ionizes in acceptor solvents, *e.g.*

$$Ph_3CCl + HCl \rightleftharpoons [Ph_3C]^+[HCl_2]^-$$
$$Ph_3CCl + AsCl_3 \rightleftharpoons [Ph_3C]^+[AsCl_4]^-$$

the degree of ionization increasing with the acceptor strength of the solvent and with its dielectric constant. Ph_3CCl is practically 100% ionized and dissociated in anhydrous sulfuric acid.

Further examples of ionization by electrophilic attack of an acceptor are the formation of nitrosyl compounds from nitrosyl halide and acceptor halide [36–39]:

$$NOCl + FeCl_3 \rightleftharpoons [NO]^+ + [FeCl_4]^-$$
$$NOF + BrF_3 \rightleftharpoons [NO]^+ + [BrF_4]^-$$

the ionization of $SbCl_5$ in excess Ph_2POCl [40]:

$$Ph_2POCl + SbCl_5 \rightleftharpoons [Ph_2PO]^+ + [SbCl_6]^-$$

and the ionization of acceptors in weak acceptor solvents, *e.g.* in liquid bromine(III) fluoride [41]:

$$(BrF_3)_{(n+1)} + NbF_5 \rightleftharpoons [(BrF_3)_nBrF_2]^+ + [NbF_6]^-$$

or in liquid sulfur dioxide [42]:

$$SbCl_5 \cdot CH_3COCl \overset{SO_2}{\rightleftharpoons} [CH_3CO]^+ + [SbCl_6]^-$$

6. Autocomplexing (Ligand Disproportionation)

It has already been said that the degree of ionization in a donor solvent increases with decreasing donor strength of the competing ligand X^-, and that there is a relatively high tendency toward the formation of anionic complexes in a solvent having a very low donicity [10, 14]:

$$MX + n\,X^- \rightleftharpoons [MX_{n+1}]^{n-} \qquad (3)$$

If the bond energies of M–D and M–X are not too different, both processes, *i.e.* ionization and complex formation with competing ligands, can occur together. The competing ligands X^- liberated by ionization of M–X bonds in accordance with reaction (1) can compete with the neutral donors in a nucleophilic attack on unionized M–X units in accordance with reaction (3) to form anionic complexes. The result is known as autocomplexing or ligand disproportionation [eq. (4)]:

$$2\,MX + n\,D \rightleftharpoons [MD_n]^+[MX_2]^- \qquad (4)$$

The dielectric constant naturally also plays a part in autocomplexing. If two solvents having equal donicities but different dielectric constants are available, stronger autocomplexing is to be expected in the solvent with the higher dielectric constant.

Tin(IV) iodide forms a yellow, non-conducting solution in nitrobenzene [43]. On addition of a donor, the solution becomes electrically conducting. At $D:SnI_4 = 4:1$, the conductivity increases with the *Dn* of the donor: THF < TBP < DMF < DMSO < HMPA (Fig. 6). At $D:SnI_4 = 2:1$, autocomplexing predominates, with formation of the red ion $[SnI_6]^{2-}$.

$$3\,SnI_4D_2 \rightleftharpoons 2\,[SnI_3D_3]^+ + [SnI_6]^{2-}$$

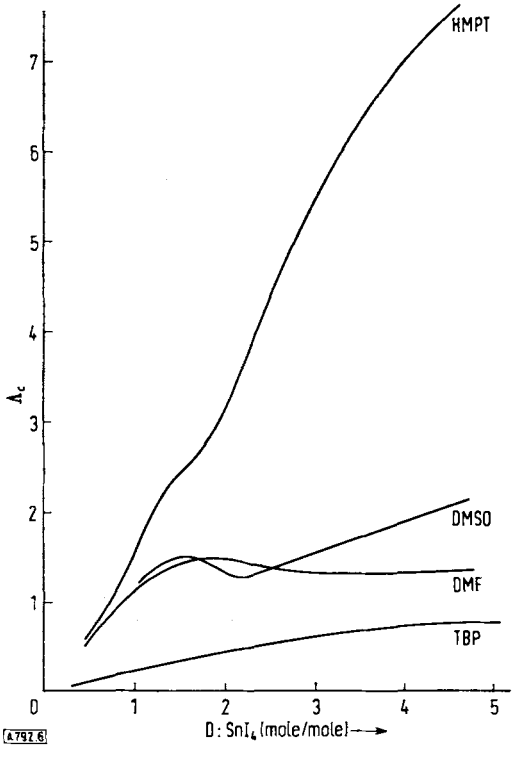


Fig. 6. Equivalent conductivity of $\approx 10^{-2}$ M SnI_4 solutions in nitrobenzene in the presence of aprotic donor solvents (HMPT = HMPA).

Breakdown of the hexaiodostannate ion begins at higher donor concentrations:

$$[SnI_6]^{2-} + 2\,D \rightleftharpoons [SnI_4D_2] + 2\,I^-$$

The iodide ions liberated react with the cation, again with reformation of the adduct [43]

$$[SnI_3D_3]^+ + I^- \rightleftharpoons [SnI_4D_2] + D$$

This is the reason for the change in the course of the curve in the region of $D:SnI_4 = 2:1$, as well as for the decrease in the intensity of the spectrum of the

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[38] *A. A. Woolf* and *H. J. Emeléus*, J. Chem. Soc. *1950*, 1050.
[39] *A. G. Sharpe* and *A. A. Woolf*, J. Chem. Soc. *1951*, 798.
[40] *V. Gutmann* and *J. Imhof*, Monatsh. Chem. *101*, 1 (1970).
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[43] *U. Mayer* and *V. Gutmann*, Monatsh. Chem. *101*, 997 (1970).

hexaiodostannate ion. The increase in conductivity on further addition of donor, which is observed particularly in HMPA, is due to the ionization of the adduct [43]:

$$[SnI_4D_2] + n\,D \rightleftharpoons [SnI_{(4-n)}\ D_{(n+2)}]^{n+} + n\,I^-$$

SnI_4 gives yellow solutions in nitrobenzene (molecularly dissolved SnI_4), slightly orange-yellow in THF (weak autocomplexing), deep red in tributyl phosphate (extensive autocomplexing), pale red in DMF (autocomplexing and ionization to form free iodide ions), and colorless in DMSO (no autocomplexing, but ionization) [43]. According to *Gaizer* and *Beck* [24], the ionization in very dilute DMSO solution may proceed as far as the formation of the solvated Sn^{4+} ion [24].

Cobalt(II) iodide is molecularly dissolved in nitromethane (NM; $Dn = 2.7$) [13]. Partial autocomplexing occurs in acetonitrile (AN; $Dn = 14.1$), and autocomplexing is practically complete in propylene carbonate (PDC; $Dn = 15.1$, $\varepsilon = 69$) [14,18]:

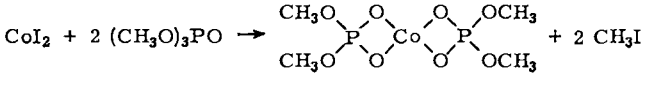
$$CoI_2 + 2\,NM \rightleftharpoons [CoI_2(NM)_2]$$

$$2\,CoI_2 + 6\,PDC \rightleftharpoons [Co(PDC)_6]^{2+} + [CoI_4]^{2-}$$

In DMSO ($Dn = 29.8$), the cationic solvate $[Co(DMSO)_6]^{2+}$ is so much more stable than Co units with iodide as ligands that complete ionization occurs instead of autocomplexing [19].

$$CoI_2 + 6\,DMSO \rightleftharpoons [Co(DMSO)_6]^{2+} + 2\,I^-$$

The situation in trimethyl phosphate is special, in that chelation can occur [44], *e.g.*



The self-ionization of water may also be regarded as coordination-induced autocomplexing, since the ionization of the covalent H–O bonds is a consequence of the coordination of water molecules by water molecules (with formation of hydrogen bonds). The self-ionization of the solvent therefore increases with increasing energy of the hydrogen bonds in the order $NH_3 < ROH < H_2O < HF$. Accordingly, weakly coordinating solvents such as liquid sulfur dioxide exhibit practically no self-ionization.

7. Some Further Examples of Coordination-Induced Ionization

Though numerous observations in nonaqueous solutions have been reported, it is difficult in most cases to coordinate the results, owing to the difference in the conditions under which they were obtained. Though a complete and above all critical discussion would be beyond the scope of this article, some arbitrarily chosen examples will be presented to illustrate what has been said in previous sections.

7.1. Boron(III) Halides

The ionization of boron(III) halides increases with increasing donicity of the solvent ($POCl_3 <$ $PhPOF_2 <$ $PhPOFCl <$ $PhPOCl_2 <$ $Ph_2POF <$ $Ph_2POCl <$ TBP < TMP < Ph_3PO < py < HMPA) and with decreasing strength of the B–X bond (*i.e.* $BF_3 <$ $BCl_3 <$ BI_3). The trihalides form adducts in nitrobenzene that do not make the solution conducting.

BF_3 and phosphoryl donors give adducts $R_3PO(BF_3)_2$ as well as those having the composition $R_3PO{\cdot}BF_3$. The equilibrium constants $K_{D\cdot BF_3}$ for the reactions

$$PhPOCl_2 \cdot BF_3 + D \rightleftharpoons PhPOCl_2 + D \cdot BF_3;\quad K_{D\cdot BF_3}$$

increase with the *Dn* of the donor [45]. The conductivity of the solutions in nitrobenzene at the composition $D \cdot BF_3$ is due to the presence of the ions formed by weak autocomplexing [45]:

$$2\,D \cdot BF_3 \rightleftharpoons [D_2BF_2]^+ + [BF_4]^-$$

The molar conductivities of the corresponding systems with boron(III) chloride are higher than those with BF_3, and at a molar ratio $D:BCl_3 = 1:1$ they increase with the *Dn* of the donor [40] ($POCl_3 <$ $PhPOF_2 <$ $PhPOFCl <$ $PhPOCl_2 <$ $Ph_2POCl <$ HMPA). The conductivity curves (Fig. 7) have a change of slope at a molar ratio $D:BCl_3 = 1:1$, which is due to the ionization by autocomplexing that has occurred up to this point:

$$2\,D \cdot BCl_3 \rightleftharpoons [D_2BCl_2]^+ + [BCl_4]^-$$

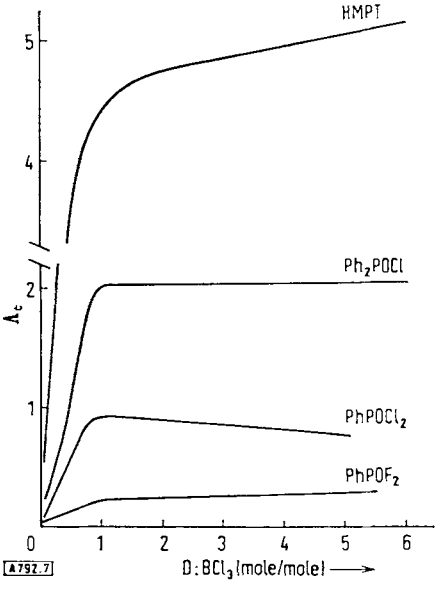


Fig. 7. Equivalent conductivity of $\approx 10^{-2}$ M BCl_3 solutions in nitrobenzene in the presence of aprotic donor solvents (HMPT = HMPA).

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This interpretation agrees with cryoscopic and NMR investigations [40], according to which further reactions take place in the BCl_3 systems with trimethyl and tributyl phosphates and with Ph_2POF. The two phosphates react with BCl_3 to give chelate formation and elimination of alkyl chloride, as with chlorides of various transition metals [44,46,47], and so give conductivity values that vary with time until the reaction is complete.

Autocomplexing also occurs with pyridine [40]:

$$2\,py + 2\,BCl_3 \rightleftharpoons [py_2BCl_2]^+ + [BCl_4]^-$$

Finally, the behavior [48] of the boron(III) iodide-pyridine complex, which has been described as "anomalous", is perfectly normal. Since the B–I bonds are significantly weaker than the boron-pyridine bonds, the $[BI_4]^-$ ion is unstable in the presence of pyridine, and ionization now occurs instead of autocomplexing. The adduct has the composition $BI_3(py)_2$, and is formulated as $[(py)_2BI_2]^+I^-$ [48]. These ions are also present in acetonitrile, where the iodide ions react further with iodine to form triiodide ions.

7.2. Organic Compounds

Many reactions in organic chemistry proceed *via* ions, but these are often present only in very small concentrations at equilibrium, and in many cases their formation as intermediates can only be deduced from the kinetic findings. OH^- ions often act as donors, and H^+ ions as acceptors.

A successful attack on the tetracoordinated C atom by a donor molecule with formation of a complex cation is difficult. An example of this is the formation of tetraalkylammonium salts from an amine and an alkyl halide:

$$RBr + NR_3 \rightarrow [NR_4]^+Br^-$$

The formation of the pentachlorocarbonate ion [49] in accordance with

$$CCl_4 + Cl^- \rightarrow [CCl_5]^-$$

has recently been described, and the possibility $[Cl_3-C-Cl-Cl]^-$ has been discussed for its structure. The reactions of CX_4 with strong donors, *e.g.* HMPA, could begin with an attack by this donor on a coordinated X ligand, and could lead in this way to ionization, *e.g.*

$$CCl_4 + HMPA \rightleftharpoons Cl_3CCl(HMPA) \rightleftharpoons [Cl_3C(HMPA)]^+Cl^-$$

The attack by the azide group could also follow this path, *e.g.* in the reaction [50]

$$CCl_4 + 3\,Cl_4SbN_3 \rightleftharpoons [C(N_3)_3]^+[SbCl_6]^- + 2\,SbCl_5$$

If the C atom is the more electronegative of the bonded atoms, *e.g.* in

$$\overset{\delta-}{F_3C}-\overset{\delta+}{I}$$

ionization by nucleophilic attack on the iodine by strong donors may be expected:

$$F_3C-I + 2\,D \rightleftharpoons [D_2I]^+[CF_3]^-$$

The ionization of compounds containing tetracoordinated carbon is possible by attack of an acceptor molecule, *e.g.*

$$(C_6H_5)_3CCl + HCl \rightleftharpoons [(C_6H_5)_3C]^+ + [HCl_2]^-$$
$$t\text{-}C_4H_9F + AsF_5 \rightleftharpoons [t\text{-}C_4H_9]^+ + [AsF_6]^-$$

Intermediate ionized complexes play a special part in many Friedel-Crafts reactions [51].

The ionization of a compound containing tricoordinated carbon results mainly from attack by a donor, as is shown by the ionic reactions of fluoroolefins, in the course of which very reactive anions are formed [52]. The ionization reactions are represented as follows [52–54]:

$$[RO]^- + F_2C{=}CF_2 \rightarrow [RO{-}CF_2{-}CF_2]^-$$
$$[C_6H_5NH]^- + F_2C{=}CF_2 \rightarrow [C_6H_5NH{-}CF_2{-}CF_2]^-$$
$$F^- + F_2C{=}CF{-}CF_3 \rightarrow [CF_3{-}CF{-}CF_3]^-$$

7.3. Organometallic Compounds

An example of the ionization of an organometallic compound by nucleophilic attack of a donor is provided by the reaction of benzylmagnesium chloride with HMPA, which gives the red color of the benzyl anion [55],

$$C_6H_5CH_2MgCl + HMPA \rightleftharpoons [(HMPA)MgCl]^+[C_6H_5CH_2]^-$$

a reaction that no longer occurs in DMSO, the coordinating power of which is only slightly weaker. On the other hand, trimethyltritylstannane cannot be ionized by coordination of HMPA with the tin to form a triphenylcarbanion, since the Sn–C bond is too stable [56].

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Carbonylmetal compounds can be ionized by donors with stabilization of the cations [57–61]. This usually leads to a hexacoordinated cation and a polynuclear carbonylmetalate ion, which is decomposed by heat. The ionizations proceed with simultaneous redox disproportionations [58, 59]:

$$4\ Fe(CO)_5 + 6\ py \rightleftharpoons [Fe(py)_6]^{2+}[Fe_3(CO)_{11}]^{2-} + 9\ CO$$

$$4\ Fe_3(CO)_{12} + 9\ en \rightleftharpoons 3\ [Fe(en)_3]^{2+}[Fe_3(CO)_{11}]^{2-} + 15\ CO$$

The conductivity of the pyridine compound in pyridine roughly corresponds to that of potassium picrate in the same solvent [60]. DMSO, alcohols, and ammonia give similar reactions [58,62]:

$$3\ Co_4(CO)_{12} + 24\ D \rightleftharpoons 4\ [CoD_6][Co(CO)_4]_2 + 4\ CO$$

$$Co_6(CO)_{16} + 12\ D \rightleftharpoons 2\ [CoD_6][Co(CO)_4]_2$$

Octacarbonyldicobalt is also ionized by coordination with triphenylphosphine, with stabilization of the cation [63]:

$$Co_2(CO)_8 + 3\ PPh_3 \rightleftharpoons [Co(CO)_3(PPh_3)_3]^+[Co(CO)_4]^- + CO$$

Another example of ionization by soft donors is provided by the behavior of $PdCl(\pi\text{-}C_4H_7)_2$, which gives the cationic complex with excess P-donors such as triphenylphosphine [64]:

$$PdCl(\pi\text{-}C_4H_7)_2 + 2\ PPh_3 \rightleftharpoons [(PPh_3)_2Pd(\pi\text{-}C_4H_7)_2]^+ + Cl^-$$

The conductivities in acetonitrile increase in the order $PPh_3 < PMe_2Ph < PEt_2Ph < PEt_3$ and increase until a molar ratio of 1:2 is reached; the increase in conductivity in the order $I < Br < Cl$ corresponds to the donor strengths of the halide ions toward soft acceptors.

Ionization by electrophilic attack of the acceptor $AlCl_3$ is probably responsible for the substitution of the Mn–Cl bond by CO in the presence of aluminum chloride [65]:

$$(CO)_3Mn(en)Cl + CO + AlCl_3 \rightleftharpoons [(CO)_4Mn(en)]^+[AlCl_4]^-$$

in the same way as carbonyl halides are ionized by acceptors:

$$Mn(CO)_5Cl + AlCl_3 \rightleftharpoons [Mn(CO)_5]^+[AlCl_4]^-$$

On the other hand, the interaction of halide ions with hexacarbonylmetal compounds leads to substitution of a carbonyl group with formation of complex anions [66–68]

$$M(CO)_6 + X^- \rightleftharpoons [M(CO)_5X]^- + CO$$

M = Cr, Mo, W; X = Cl, Br, I

7.4. Silicon Halides

Both the Si–F and the Si–Cl bonds are generally too strong to be ionized by coordination, even with strong donors. SiF_4 reacts with donors to form adducts having the composition SiF_4D_2, which are molecularly dissolved even in media having high dielectric constants. The dissociation deduced from cryoscopic measurements on $SiCl_4(py)_2$ in nitrobenzene [69] has not been verified, nor has the reported [70] conductivity of alkylchlorosilanes with 2,2′-bipyridyl in acetonitrile [71].

On the other hand, silyl cations can be formed by reaction of bromides and particularly of iodides with strong donors. *Wannagat* [72, 73] suggested an ionic structure for the compound $SiI_4(py)_4$, which was also formulated by *Schnell* [74] as $[Si(py)_4]^{4+} + 4I^-$. According to IR spectroscopic data, the cation contains hexacoordinated silicon [75, 76]:

$$[(py)_4SiI_2]^{2+} + 2\ I^-$$

On the basis of the spectra, the complexes of silyl bromides and silyl iodides with strong bases must be assumed to have an ionic structure with pentacoordinated silicon [77], *e.g.*:

$$[SiH_3(py)_2]^+Br^- \text{ and } [SiH_3(py)_2]^+I^-$$

They give highly conducting solutions in acetonitrile, unlike the compounds of the corresponding chlorides or fluorides [77].

Similarly, triphenylsilyl iodide is ionized in methylene chloride in the presence of 2,2′-bipyridyl (bipy) [78] (Fig. 8), as is shown by the IR spectra.

$$Ph_3SiI + bipy \rightleftharpoons [Ph_3Si(bipy)]^+I^-$$

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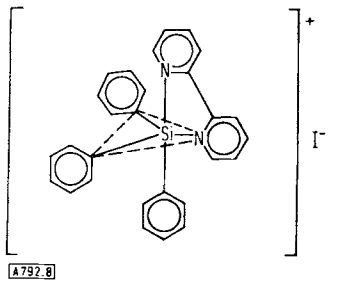


Fig. 8. Probable structure of $[Ph_3Si(bipy)]^+I^-$.

The conductivity of the compound in acetonitrile is roughly the same as that of $[H(bipy)]^+I^-$.

Silyl cations are formed by ionization of silyltetracarbonylcobalt $H_3SiCo(CO)_4$ or silylpentacarbonylmanganese $H_3SiMn(CO)_5$ under the influence of trimethylamine or pyridine. According to their IR spectra, the complexes are ionic [79]

$$H_3SiMn(CO)_5 + 2\ py \rightleftharpoons [H_3Si(py)_2]^+[Mn(CO)_5]^-$$

and are decomposed by hydrogen chloride:

$$[H_3Si(py)_2]^+[Mn(CO)_5] + 3\ HCl \xrightarrow{-100\,^\circ C} H_3SiCl + HMn(CO)_5 + 2\ pyHCl$$

7.5. Phosphoranes, Arsoranes, Stiboranes

R_3PI_2 is ionized in nitromethane,

$$R_3PI_2 \rightleftharpoons [R_3PI]^+ + I^-$$

whereas R_3PBr_2 and R_3PCl_2 are not. However, all three undergo ionization by complex formation with strong acceptors [80].

$$R_3PCl_2 + SbCl_5 \rightleftharpoons [R_3PCl]^+ + [SbCl_6]^-$$
$$R_3PI_2 + HgI_2 \rightleftharpoons [R_3PI]^+ + [HgI_3]^-$$

The ionization is also favored in a stronger donor solvent. The conductivities of phosphoranes, arsoranes, and stiboranes in acetonitrile [81] are given in Table 9; they decrease in the orders P > As > Sb and I > Br > Cl.

Table 9. Molar conductivities of phosphoranes, arsoranes, and stiboranes at $c = 10^{-2}$ mole/l in acetonitrile at 25 °C.

Compound	Λ (Ω^{-1} cm^2 mole^{-1})	Compound	Λ (Ω^{-1} cm^2 mole^{-1})
Ph_3PCl_2	78.1	Ph_3PBr_2	73.2
Ph_3AsCl_2	4.0	Ph_3AsBr_2	25.3
Ph_3SbCl_2	1.0	Ph_3SbBr_2	1.0

The following ionic equilibria have been postulated on the basis of electrolysis studies [82]:

$$2\ Ph_3PCl_2 \rightleftharpoons [Ph_3PCl]^+ + [Ph_3PCl_3]^-$$
$$Ph_3PBr_2 \rightleftharpoons [Ph_3PBr]^+ + Br^-$$

The particularly high conductivities of the iodides are due not only to greater ease of ionization of the El–I bonds but also to the partial decomposition of these compounds with formation of iodine, which acts as an acceptor and so stabilizes the anion:

$$Ph_3PI_2 \nearrow [PH_3PI]^+ + I^-$$
$$Ph_3PI_2 \searrow \tfrac{1}{2}\ Ph_3P + \tfrac{1}{2}\ [Ph_3PI]^+ + \tfrac{1}{2}\ I_3^-$$

7.6. Arsenic(III) Halides

Arsenic(III) chloride does not form adducts with ether, but does so with stronger donors such as tributyl phosphate (TBP), whose solutions are assumed from the Raman spectra to contain 1:2 adducts [83]. In these adducts, the donor molecules are situated at the apices of a distorted octahedron, and the lone pair of electrons occupies an equatorial position [84]. The ΔH values increase in the orders $AsCl_3 < AsBr_3 < AsI_3$ and TBP < DMA < HMPA [85]. The conductivities in HMPT also increase in the orders $AsCl_3 < AsBr_3 < AsI_3$ and TBP < DMA < HMPA, corresponding to the decrease in the donicities of the halide ions and the increase in the donicities of the donor molecules. The ionization of the adducts is attributed to the ligand exchange halide → donor on the arsenic^{III}:

$$AsX_3D + n\ D \rightleftharpoons [AsX_{(3-m)}D_{(n+1)}]^{m+} + m\ X^- \text{ with } m \leqslant 3$$

The ease of ionization increases with increasing *Dn* of the donor solvent and decreasing *Dn* of the competing ligand X^-.

Ionization also occurs with bidentate strong donors. The adducts AsX_3(2,2′-bipyridyl) give highly conducting solutions in nitrobenzene [86],

$$AsX_3 + bipy \rightleftharpoons [AsX_3(bipy)] \rightleftharpoons [AsX_2(bipy)]^+ + X^-$$

like the adduct formed from arsenic(III) iodide and *o*-phenylenebis(dimethylamine) [87].

7.7. Antimony(III) Halides

The ΔH values of the interaction SbX_3–HMPA in dichloroethane increase with increasing donicity of the solvent and with decreasing *Dn* of the halide ligands [85].

The conductivities of SbX_3–HMPA systems in nitrobenzene also increase in the same way. The con-

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[87] *G. J. Sutton*, Australian J. Chem. *11*, 420 (1958).

ductivity curves suggest that several equilibria are superimposed:

$$SbX_3D + n\,D \rightleftharpoons [SbX_{(3-m)}D_{(n+1)}]^{m+} + m\,X^- \text{ with } m \leqslant 3$$

7.8. Antimony(V) Halides

Antimony(v) chloride is a stronger acceptor than boron(III) chloride. It forms unionized solutions in nitrobenzene and in acetonitrile [88]. Addition of $POCl_3$, $PhPOF_2$, PhPOFCl, or $PhPOCl_2$ leads to the formation of adducts that are molecularly disperse, and not ionized, in nitrobenzene. On addition of stronger donors, *i.e.* Ph_2POF, Ph_2POCl, TMP, TBP, or Ph_3PO, there is practically no increase in conductivity up to a molar ratio of 1:1, since the nonconducting adducts are formed. The adducts are ionized only in the presence of an excess of donor (Fig. 9), presumably with autocomplexing [40].

$$2\,D \cdot SbCl_5 \rightleftharpoons [D_2SbCl_4]^+ + [SbCl_6]^-$$

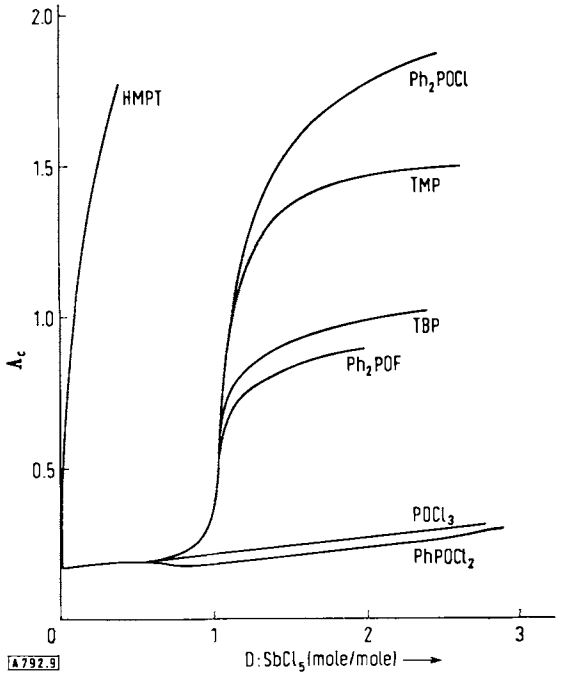


Fig. 9. Equivalent conductivity of $\approx 10^{-2}$ M $SbCl_5$ solutions in nitrobenzene in the presence of aprotic donor solvents (HMPT = HMPA).

With a very strong donor such as HMPA, the conductivity increases rapidly up to a molar ratio D:$SbCl_5$ = 1:1, since an ionized product is formed. The results of cryoscopic measurements agree with the postulated autocomplexing [40]:

$$2\,HMPA + 2\,SbCl_5 \rightleftharpoons [(HMPA)_2SbCl_4]^+ + [SbCl_6]^-$$

In the system $SbCl_5$–Ph_2POCl, the molecular weight found cryoscopically in the presence of an excess of donor is lower than it should be for the adduct $Ph_2POCl \cdot SbCl_5$, whereas autocomplexing should not affect the number of particles. The conductivity diagram shows that the ionization occurs only when the donor is present in excess, and corresponds to

$$Ph_2POCl + SbCl_5 \rightleftharpoons [Ph_2PO]^+ + [SbCl_6]^-$$

as has been found in principle, though to a much smaller extent, in solutions of $POCl_3$ or $PhPOCl_2$ [89]. The large excesses of donor required agree with the very weak chloride ion donor properties of the phosphorus oxide chlorides.

The ionizing properties of the donor solvents increase in the same order toward antimony(v) chloride as toward boron(III) chloride, but $SbCl_5$ is much less readily ionized with a given donor. This is partly due to the relatively high strength of the Sb–Cl bond, and partly to the higher coordinating power of boron(III) chloride toward oxygen donors. This also agrees with the fact that the observed affinity of antimony(v) chloride for chloride ions in $POCl_3$ and $PhPOCl_2$ is higher than that of boron(III) chloride [87].

The strong acceptor SbF_5 forms only one adduct with pyridine [90].

7.9. Iodine, Iodine Monochloride, and Iodine Bromide

Whereas we have so far been concerned with the ionization of covalent bonds having polar character, the ionization of a pure covalent bond will now be discussed with the iodine molecule as an example. Charge-transfer complexes of iodine are known, and the ΔH values for the interaction with donors generally increase with increasing donicity of the donor [10] (Table 10).

Table 10. Reaction enthalpies for adduct formation between iodine and donors having different donicities.

Donor	*Dn*	$-\Delta H_{D\cdot I_2}$
AN	14.1	1.9
Methyl acetate	16.5	2.5
Acetone	17.0	2.5
TBP	23.7	3.8
DMF	26.6	3.7
DMA	27.8	4.0
DMSO	29.8	4.4
py	33.1	7.8

The conductivities of the donor-iodine systems in nitrobenzene in the presence of light are relatively low, but again increase with the donicity of the donor [91].

The solutions of pyridine and iodine contain I_3^- anions and $[(py)_2I]^+$ cations, the existence of which

[88] *I. R. Beattie, P. J. Jones,* and *M. Webster,* J. Chem. Soc. *A 1969,* 218.

[89] *V. Gutmann* in *V. Gutmann*: Halogen Chemistry. Academic Press, New York 1968, Vol. 2, p. 399.

[90] *E. L. Muetterties,* Adv. Chem. Coord. Comp. *1961,* 513.

[91] *V. Gutmann* and *W. Frantsits,* Monatsh. Chem., in press.

appears to have been verified by the isolation of $[py_2I]\,[ClO_4]$ [92].

$$py + I_2 \rightleftharpoons py \cdot I_2$$
$$2\,pyI_2 \rightleftharpoons [(py)_2I]^+ + I_3^-$$

2,2'-Bipyridyl also exhibits double coordination to the iodine cation, with formation of a polymeric cation [93].

$$n\ bipy\ (ICl)_2 \rightleftharpoons [(bipy\ I)_n]^{n+} + n\ [ICl_2]^-$$

The ionization with a given donor increase with the polarity of the bond, *i.e.* in the order $I_2 < IBr < ICl$. For a given molar ratio the conductivities of the donor-acceptor systems in nitrobenzene increase from iodine to iodine monochloride, as well as with increasing donicity of the donor (*i.e.* TBP < DMA < DMSO < py < HMPA). The conductivity curves exhibit an irregular course at certain molar ratios [91], *e.g.* at D:A = 1:1 in the system D–ICl in nitrobenzene (Fig. 10). The autocomplexing observed up to this point

$$2\,D + 2\,ICl \rightleftharpoons [D_2I]^+ + [ICl_2]^-$$

is partly replaced at a molar ratio of 1:1 by the reformation of the charge transfer complex by decomposition of the $[ICl_2]^-$ ion, and the resulting chloride ions partly decompose the $[D_2I]^+$ ions:

$$[ICl_2]^- + D \rightleftharpoons ICl \cdot D + Cl^-$$
$$[D_2I]^+ + Cl^- \rightleftharpoons ICl \cdot D + D$$

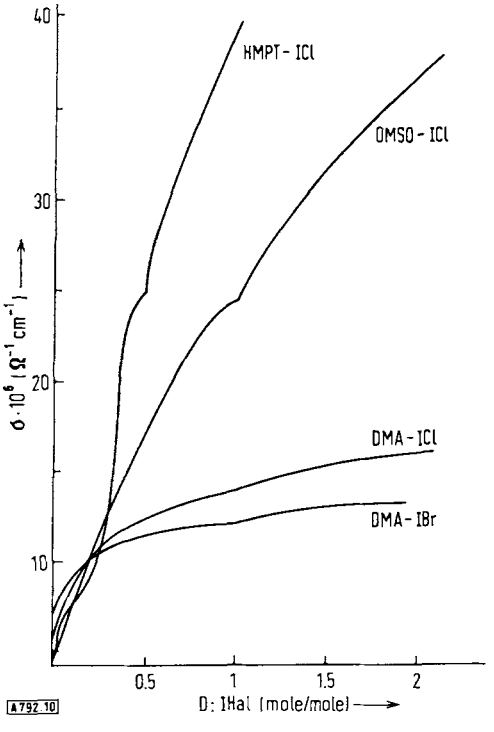


Fig. 10. Specific conductivity of 5×10^{-3} M iodine halide solutions in nitrobenzene in the presence of aprotic donor solvents (HMPT = HMPA).

[92] *H. Carlson*: Über eine neue Klasse von Verbindungen des positiv einwertigen Jods. S. Hirzel, Leipzig 1932.

[93] *A. I. Popov* and *R. T. Pflaum*, J. Amer. Chem. Soc. *79*, 570 (1957).

On further addition of donor, the conductivity again increases, and the extinction of the $[ICl_2]^-$ ion decreases, since ionization now predominates:

$$D + ICl \cdot D \rightleftharpoons [D_2I]^+ + Cl^-$$

The ionization of IBr and ICl is also possible only by electrophilic attack by a strong acceptor. The compounds $AlCl_3 \cdot 2ICl$ and $AlBr_3 \cdot 2IBr$ are good conductors of electricity in the fused state, and the results of transport measurements agree with the existence of the equilibria [94,95]:

$$AlCl_3 \cdot 2\,ICl \rightleftharpoons [I_2Cl]^+ + [AlCl_4]^-$$
$$AlBr_3 \cdot 2\,IBr \rightleftharpoons [I_2Br]^+ + [AlBr_4]^-$$

$SnCl_4$, $SbCl_5$, VCl_4, and $NbCl_5$ react similarly with iodine monochloride [95a], whereas $[ICl_2]^-$ ions are formed with PCl_5 [95a,95b]:

$$PCl_5 + ICl \rightleftharpoons [PCl_4]^+ + [ICl_2]^-$$

7.10. Titanium Halides

Titanium(III) chloride and titanium(III) bromide give acetonitrile (AN) adducts having the composition $TiX_3(AN)_3$ [96]. Their ionization *e.g.* in acetonitrile increases with increasing donor strength of the donor and from the chloride to the bromide. The molar conductivity of $(TiBr_3)_2(bipy)_3$ in acetonitrile is twice as high as that of $(TiCl_3)_2\,(bipy)_3$ [97]. According to spectral observations, the ionization can be formulated as follows:

$$(TiX_3)_2(bipy)_3 \rightleftharpoons \cdot[TiX_2(bipy)_2]^+ + [TiX_4(bipy)]^-$$

Anionic complexes are formed from titanium(III) halides both in acetonitrile and in propylene carbonate by addition of halide ions [98]:

$$TiX_3D_3 + X^- \rightleftharpoons [TiX_4D_2]^- + D$$
$$[TiX_4D_2]^- + 2\,X^- \rightleftharpoons [TiX_6]^{3-} + 2\,D$$

Complex cations are formed on addition of strong acceptors, *e.g.* $SbCl_5$ [98], as in the cases of VX_3 and CrX_3, in acetonitrile [99].

[94] *Ya. A. Fialkov* and *O. I. Shor*, Zh. Obshch. Khim. *23*, 369, 365 (1953).

[95] *Ya. A. Fialkov* and *O. I. Shor*, Zh. Obshch. Khim. *19*, 235 (1949).

[95a] *V. Gutmann*, Research *3*, 337 (1950); Z. Anorg. Allg. Chem. *264*, 151 (1951).

[95b] *J. A. Fialkow* and *A. A. Kuzmenko*, Zh. Obshch. Khim. *19*, 812, 1645 (1949).

[96] *R. J. H. Clark*, *J. Lewis*, *D. J. Machin*, and *R. S. Nyholm*, J. Chem. Soc. *1963*, 379.

[97] *G. W. A. Fowles* and *T. E. Lester*, J. Chem. Soc. *A 1968*, 1180.

[98] *V. Gutmann*, *A. Scherhaufer*, and *H. Czuba*, Monatsh. Chem. *98*, 619 (1967).

[99] *V. Gutmann*, *G. Hampel*, and *W. Lux*, Monatsh. Chem. *96*, 533 (1965).

Titanium(IV) chloride forms adducts with many donors [100]. In $[Cl_3PO]_2TiCl_4$, the electron repulsion of the donor molecules, even when they are present in large excess, *e.g.* as the solvent, is not sufficient to ionize a Ti–Cl bond [89]. The ionization is brought about only by the additional attraction of electrons by a strong acceptor [101, 102]:

$$D \rightarrow \overset{\frown}{Ti-X} \rightarrow A$$

$$POCl_3 + (Cl_3PO)_2TiCl_4 + SbCl_5 \rightleftharpoons [(Cl_3PO)_3TiCl_3]^+[SbCl_6]^-$$

On the other hand, hexachlorotitanate is formed on addition of chloride ions [103]. Dimeric anions [35] are obtained from triphenylchloromethane and $TiCl_4$ in $POCl_3$ [104], $PhPOCl_2$ [105], and PhCOCl [106].

$$2\ Ph_3CCl + 2\ TiCl_4 \rightleftharpoons 2\ [Ph_3C]^+ + [Ti_2Cl_{10}]^{2-}$$

Table 11. Stability constant K of the complex $[Ph_3C]_2[Ti_2Cl_{10}]$ in solvents having different donicities.

Solvent	*Dn*	$K_{[Ph_3C]_2[Ti_2Cl_{10}]}$
$PhPOCl_2$	18.5	5.3
$POCl_3$	11.7	16
PhCOCl	2.3	58

The stability constant of the complex decreases, as expected, with increasing donicity of the solvent [107] (Table 11).

7.11. Rhenium(III) Halides

The metal cluster structures in rhenium(III) halides are retained in donor solvents [107–110], and rhenium has a coordination number of seven in the resulting adducts $Re_3X_9L_3$. In solvents of medium *Dn*, such as acetonitrile and tetrahydrofuran, Re_3Cl_9 is ionized only in the presence of strong donors, *e.g.* bipyridyl [108].

The ionization in DMSO has been formulated as follows [107]:

$$Re_3Cl_9(DMSO)_3 + 3\ DMSO \rightleftharpoons [Re_3Cl_6(DMSO)_6]^{3+} + 3Cl^-$$

It may be assumed that Re_3Br_9 is ionized to a greater degree under similar conditions. In the bisarsenate complex $Re_3Br_3(AsO_4)_2(DMSO)_3$, six of the nine bromide ligands of Re_3Br_9 are substituted [111].

7.12. Thorium and Uranium Halides

The measured conductivities of the donor complexes of thorium halides and uranium(IV) halides in nitromethane are not strictly comparable, since the compositions of the complexes are different. The influence is seen clearly *e.g.* on comparison of $ThBr_4(HMPA)_2$ and $ThBr_4(HMPA)_3$. The conductivities increase from the chloride *via* the bromide to the iodide for a given donor, as well as with increasing donicity of the donor (Table 12).

Table 12. Molar conductivities of thorium(IV) halide and uranium(IV) halide complexes in nitromethane at $c \approx 10^{-3}$ mole/l.

Complex	Λ (Ω^{-1} cm^2 mole^{-1})	Ref.	Complex	Λ (Ω^{-1} cm^2 mole^{-1})	Ref.
$ThCl_4(HMPA)_2$	9.8	[112]	$UCl_4(HMPA)_2$	10.1	[112]
$ThBr_4(HMPA)_2$	48.5	[112]	$UBr_4(HMPA)_2$	11.3	[112]
$ThBr_4(HMPA)_3$	87.0	[112]			
$ThCl_4(DMSO)_5$	19.5	[112]	$UCl_4(DMSO)_3$	22.7	[112]
$ThBr_4(DMSO)_6$	99.0	[112]			
$ThCl_4(DMA)_4$	17.7	[113]	$UCl_4(DMA)_5$	36.6	[115]
$ThI_4(DMA)_6$	162.0	[114]	$UI_4(DMA)_4$	275.0	[114]
$Th(NCS)_4(DMA)_4$	13.0	[113]	$U(NCS)_4(DMA)_4$	22.6	[116]

8. Conclusion

The electrostatic model of dissociation allows an extensive description of the behavior of ionic compounds in solution. The enthalpy of solvation is used for the dissolution process, and the degree of dissociation in solution is largely dependent on the dielectric constant of the medium. The description of the ionization of covalent compounds, on the other hand,

[100] *I. Lindqvist*: Inorganic Adduct Molecules of Oxo-Compounds. Springer, Berlin 1963.

[101] *G. A. R. Bryntse* and *I. Lindqvist*, Acat Chem. Scand. *14*, 949 (1960).

[102] *M. Baaz*, *V. Gutmann*, and *M. Y. A. Talaat*, Monatsh. Chem. *91*, 548 (1960).

[103] *V. Gutmann* and *F. Mairinger*, Monatsh. Chem. *92*, 720 (1961).

[104] *M. Baaz*, *V. Gutmann*, and *J. R. Masaguer*, Monatsh. Chem. *92*, 590 (1961).

[105] *M. Baaz*, *V. Gutmann*, and *J. R. Masaguer*, Monatsh. Chem. *92*, 582 (1961).

[106] *V. Gutmann* and *G. Hampel*, Monatsh. Chem. *92*, 1048 (1961).

[107] *V. Gutmann* and *G. Paulsen*, Monatsh. Chem. *100*, 358 (1969).

[108] *F. A. Cotton* and *R. A. Walton*, Inorg. Chem. *5*, 1802 (1966).

[109] *B. H. Robinson* and *J. E. Fergusson*, J. Chem. Soc. *1964*, 5683.

[110] *J. E. Fergusson*, Coord. Chem. Rev. *1*, 459 (1966).

[111] *F. A. Cotton* and *S. J. Lippard*, J. Amer. Chem. Soc. *88*, 1882 (1966).

[112] *K. W. Bagnall*, *D. Brown*, *P. J. Jones*, and *J. G. H. du Preez*, J. Chem. Soc. *1966*, 737.

[113] *K. W. Bagnall*, *D. Brown*, *P. J. Jones*, and *P. S. Robinson*, J. Chem. Soc. *1964*, 2531.

[114] *K. W. Bagnall*, *D. Brown*, *P. J. Jones*, and *J. G. H. du Preez*, J. Chem. Soc. *1965*, 3594.

[115] *K. W. Bagnall*, *A. M. Deane*, *T. C. Markin*, *P. S. Robinson*, and *M. A. A. Stewart*, J. Chem. Soc. *1961*, 1611.

[116] *K. W. Bagnall*, *D. Brown*, and *R. Cotton*, J. Chem. Soc. *1964*, 2527.

requires a coordination-chemical interaction between the solute and the solvent or an added complexing agent, the complexing agent acting either as a donor or as an acceptor. The degree of ionization is essentially determined by the coordination-induced ionization and by the dissociation of the ion associates, which depends on the dielectric constant of the medium.

The few arbitrarily chosen examples show the significance of the coordination-induced ionization of covalent compounds to numerous important reaction types in every field of chemistry and electrochemistry, in aqueous and in nonaqueous solutions. The donicity is a more than qualitative, possibly even semiquantitative characteristic for electron pair donors, and facilitates the choice of a suitable solvent for ionization or for certain reactions.

The relations presented allow the removal of a number of contradictions or uncertainties in the literature and the logical classification of many individual facts in general categories. Incentives are also provided to further systematic and particularly quantitative studies, *e.g.* of a kinetic, thermochemical, or structural nature. Finally, it is to be hoped that the present article will promote the use of strong donors or acceptors both as solvents and as reactants, and hence also chemistry in nonaqueous media.

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Degenerate Carbonium Ions[***]

By Ronald E. Leone and Paul von R. Schleyer[*]

Carbonium ions are called "degenerate" when they rearrange through finite energy barriers to give products whose gross structures are identical with those of the starting ions. In such degenerate rearrangements ("automerizations"), individual atoms and groups become mixed but the overall structure is conserved. Automerizations can be observed by noting the dispersal of isotopic labels, the loss of optical activity, or the temperature dependence of NMR spectra. In certain cases, a combination of well-known rearrangement processes results in complete mixing of all atoms, C or H. The 2-norbornyl and 9-barbaralyl cations are examples of fully degenerate systems; conditions can be found where both give but single-line NMR spectra.

1. Introduction

Chemists have always been especially interested in rearrangements because they violate the principle of minimum structural change [1]. Originally rearrangements leading to changes in molecular or structural formula were examined. Clearly there must also be a class of degenerate rearrangements in which individual atoms and bonds become interchanged, but which only lead to products of the same gross structure (*i.e.*, identical except for the special features which enable detection of the rearrangement) as that of the starting material. These transformations can only be followed by special techniques such as the loss of optical activity, the dispersal of an isotopic label, the observation of equivalence by NMR, *etc.* The most striking of these degenerate rearrangements are those capable of mixing all atoms of a given kind completely. Bullvalene is the best known organic molecule of this type; every Cope rearrangement returns to bullvalene and at only a little above room temperature all hydrogen and carbon atoms become equivalent on the NMR time scale [2].

Carbonium ions are particularly prone to rearrangement [3], and it would be expected that many examples of degeneracy could be found within this class of reaction intermediates. In recent years considerable effort has been directed toward the study of carbonium ions, either as stable cations or as solvolysis intermediates, capable of undergoing degenerate rearrangements. It is this group of carbonium ions which will be reviewed here, with major emphasis placed on ions capable of multiple degeneracy. *Balaban* has recently developed a mathematical treatment of multiple 1,2-shifts in carbonium ions on the basis of the theory of graphs [4].

A degenerate carbonium ion shall be defined as a carbonium ion which can rearrange through a finite energy barrier in such a fashion as to regenerate the same gross structure (as defined above) as that of the starting ion. The degen-

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[***] The following abbreviations have been used: Ac = acetyl; Bs = brosyl (*p*-bromobenzenesulfonyl); *t*-Bu = *tert*-butyl; DNB = 3,5-dinitrobenzoyl; Et = ethyl; Me = methyl; Ph = phenyl; PNB = *p*-nitrobenzoyl; SOH = solvent; Ts = tosyl (*p*-toluenesulfonyl).

[1] *G. W. Wheland*: Advanced Organic Chemistry. Wiley, New York 1960, 3rd Edit., pp. 48ff.

[2] *W. von E. Doering* and *W. Roth*, Tetrahedron *19*, 715 (1963); *J. F. M. Oth, R. Merényi, G. Engel*, and *G. Schröder*, Tetrahedron Lett. *1966*, 3377; *G. Schröder, J. F. M. Oth*, and *R. Merényi*, Angew. Chem. *77*, 774 (1965); Angew. Chem. internat. Edit. *4*, 752 (1965).

[3] For examples, see *Y. Pocker* in *P. D. Mayo*: Molecular Rearrangements. McGraw-Hill, New York 1963, Vol. 1, p. 1; *J. A. Berson, ibid.* p. 111; *R. Breslow, ibid.* p. 233.

[4] *A. T. Balaban, D. Färcasiu*, and *R. Bănică*, Rev. Roum. Chim. *11*, 1205 (1966).

erate rearrangement of such an ion is an automerization [5], *i.e.*, a reaction process in which both the molecular formula and structural formula of the starting material are conserved (see Table 1). The preservation of enantiomeric purity shall not be a necessary requirement. Thus enantiomeric cations and their racemic mixtures, but not diastereomeric cations, will be assumed to have the same gross structure.

We will consider rearrangements whereby an optically active cation is racemized by an automerization or an isotopic label dispersed by an automerization to be examples of degeneracy. In fact, automerizations can often be detected by the techniques of using optically active or isotopically tagged precursors.

Table 1. Definition of rearrangement, isomerization, and automerization (based on ref. [5])[a].

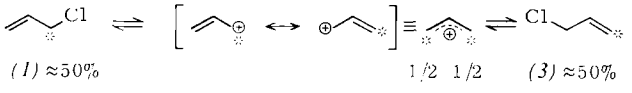
Molecular formula	Structural formula [b]	Name
not conserved	not conserved	rearrangement
conserved	not conserved	isomerization
conserved	conserved	automerization

[a] Because of historical precedent, we believe it is better to regard these categories as being *inclusive* rather than *exclusive*. Thus, an isomerization is a special kind of rearrangement and an automerization is a special kind of isomerization (or rearrangement).

[b] For convenience, enantiomers and isotopically labeled compounds, but not diastereomers, will be considered here to have the same structural formula.

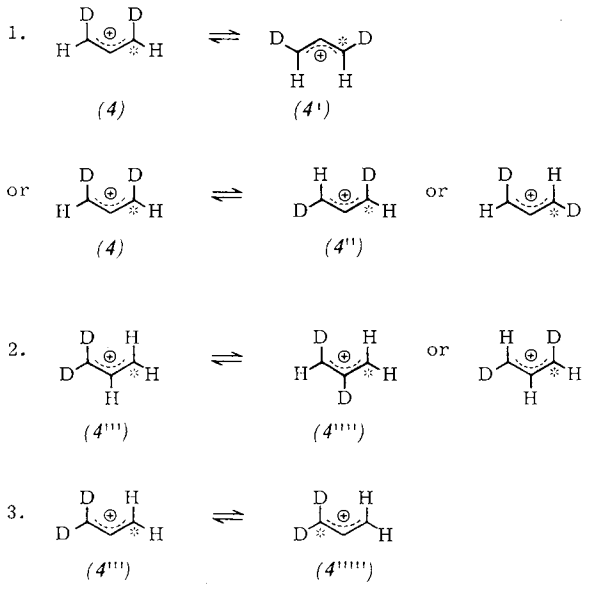
A number of carbonium ions, through resonance, possess equivalent ("homotopic") [6] atoms or groups. Examples are the termini of the allyl cation and all the carbon-hydrogen units in the tropylium ion. Such systems do not involve degenerate rearrangements in the sense of the above definition, but for the purposes of this review it is nevertheless convenient to discuss some of these cases since resonance (*e.g.*, allyl resonance) is also important in helping to achieve degeneracy in some cations. In these instances, resonance contributes to the overall rearrangement mechanism whereby the original ion structure is regenerated.

The problem of distinguishing between a degenerate cation rearrangement and equivalence through resonance can be illustrated by the allyl cation. The labeled allyl chloride *(1)* shown below generates on solvolysis an allyl cation *(2)* which contains two positions made equivalent by reso-



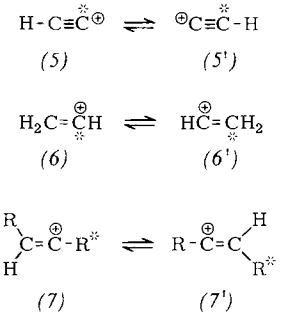
nance [7]. The chloride product contains a label at the two positions shown in *(1)* and *(3)*. The interconversion of the chlorides, *(1)* into *(3)*, is degenerate, but cation *(2)* does not undergo a degenerate rearrangement (in the sense of our definition) since the equivalence of positions in *(2)*, a *single* species, arises through resonance. However, automerizations are in principle possible for the allyl cation. Three types of potentially degenerate processes serve as examples, of which only the first has actually been observed: 1) *cis-trans* isomerization [8]; 2) interchange of hydrogens; and 3) interchange of carbon atoms.

These last three processes differ from the one described above in that they require interchange of atoms and passage



over an energy barrier to render positions equivalent (degenerate rearrangement) while the above case involves no interchange of atoms and no energy barrier (equivalence through resonance).

Based on the definition of a degenerate carbonium ion presented above, it appears that the simplest degenerate rearrangements possible in cations are *(5)* ⇌ *(5')*, *(6)* ⇌



(6'), and *(7)* ⇌ *(7')*. In these cases simple hydrogen interchanges produce degeneracy of the carbonium ions.

Experimentally, investigations have not yet been carried out to detect these possible degeneracies. However, the possibility of a degenerate 1,2-hydride shift in the ethyl cation *(8)* has been investigated [9]. To achieve full degeneracy in *(8)* all five hydrogens must be exchanged, but this has not yet been realized.

$$\underset{(8)}{CD_3-CH_2^{\oplus}} \rightleftharpoons \underset{(8')}{{}^{\oplus}CD_2-CH_2D} \rightleftharpoons \textit{etc.}$$

[5] *A. T. Balaban* and *D. Fărcasiu*, J. Amer. Chem. Soc. *89*, 1958 (1967).

[6] *K. Mislow*, personal communication.

[7] *P. B. D. de la Mare* in [3], p. 27.

[8] *P. von R. Schleyer, T. M. Su, M. Saunders*, and *J. C. Rosenfeld*, J. Amer. Chem. Soc. *91*, 5174 (1969); *J. M. Bollinger, J. M. Brinich*, and *G. A. Olah, ibid. 92*, 4025 (1970); *N. C. Deno, R. C. Haddon*, and *E. N. Nowak, ibid. 92*, 6691 (1970).

[9] *C. C. Lee* and *M. K. Frost*, Can. J. Chem. *43*, 526 (1965); *J. D. Roberts* and *J. A. Yancey*, J. Amer. Chem. Soc. *74*, 5943 (1952); *P. C. Myhre* and *E. Evans, ibid. 91*, 5641 (1969).

The potential degenerate rearrangements of the allyl cation discussed above represent a higher level of complexity. These allyl and ethyl cation examples illustrate the definition of a degenerate carbonium ion. More complicated degenerate cations will be reviewed as outlined below. We will discuss two main categories of degenerate ions: 1) those of the formula $(CH)_n^+$ where n is odd (see Section 3) and 2) those of the type not having the $(CH)_n^+$ empirical formula (see Section 4).

A classification of degenerate carbonium ions may also be made on the basis of the atoms or groups undergoing interchange. In priciple there are three kinds of ions: 1) those exhibiting carbon atom degeneracy; 2) those exhibiting hydrogen atom degeneracy; and 3) those exhibiting combined carbon and hydrogen atom degeneracy. In practice all three types of degenerate carbonium ions have been observed.

Carbon atom degeneracy involves the interchange of carbon atoms with or without their respective attached hydrogen. Complete carbon degeneracy means that all carbon atoms are capable of interchanging and becoming equivalent. Partial carbon degeneracy implies that only some of the carbons in the ion become equivalent. In theory carbon degeneracy can be detected by ^{13}C scrambling within the ion. However, experimentally this form of degeneracy is usually determined by proton label scrambling. Carbon degeneracy should give rise to a single NMR signal for the protons attached to the interchangeable carbon atoms and scrambling of a hydrogen istope label at the interchangeable positions. Recent developments in ^{13}C-NMR spectroscopy have opened up the way to direct observation of carbon degeneracies.

Hydrogen atom degeneracy involves interchange of hydrogens while the carbon skeleton of the ion remains fixed. Complete hydrogen degeneracy means the interchange and equivalence of all hydrogen atoms on the carbon surface of the molecule. Such a process will result in a single peak for the ^1H-NMR spectrum of the ion. Partial hydrogen degeneracy refers to the interchange of only some hydrogen atoms in the ion without altering the basic carbon framework.

Combination of both carbon and hydrogen atom degeneracies is possible and this can also result in the equivalence of all carbons and hydrogens of the carbonium ion. Specific examples of the forms of degeneracy mentioned above will be discussed in detail later in this paper. It has been observed experimentally that degenerate ions of the $(CH)_n^+$ series show degenerate properties only through carbon degeneracy and are often capable of complete mixing of all carbon atoms. Degenerate ions outside the $(CH)_n^+$ series can exhibit all types of degeneracy, but often these ions are not capable of complete degeneracy.

The interest in studying degenerate carbonium ions revolves around the following three questions:

1) Can degeneracy be achieved, and if so, to what extent?

2) What is the mechanism whereby the degeneracy is achieved?

3) Are there any special properties resulting from degeneracy? For example, are the carbonium ions especially stable or especially unstable?

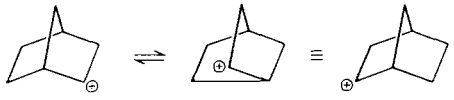
The degenerate carbonium ions already studied will be discussed in terms of these three considerations.

2. Reaction Processes Leading to Degeneracy

2.1. Wagner-Meerwein Rearrangement (1,2-Carbon Shift)

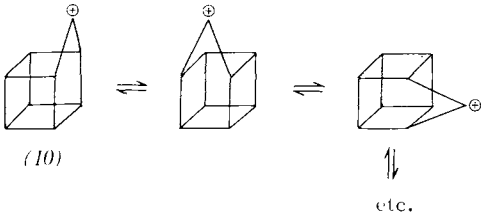
Probably the most important rearrangement process for degenerate carbonium ions is the Wagner-Meerwein rearrangement or 1,2-carbon shift [10,11]. This process allows interchange of carbon atoms and consequently is the basis for many observed carbon automerizations. The ions listed are examples of degenerate ions arising from 1,2-carbon shifts:

2-norbornyl cation *(9)* (see Section 4.6)



(9)

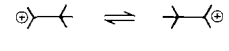
9-homocubyl cation *(10)* (see Section 3.4.1)



(10)

etc.

dimethyl-*tert*-butylcarbonium ion *(11)* (see Section 4.2).

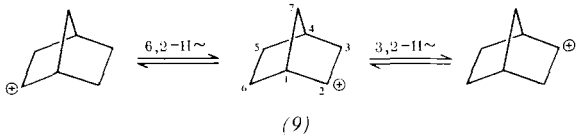


(11)

2.2. 1,2-Hydride and 1,3-Hydride Shifts

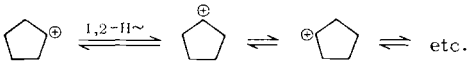
Migration of a hydrogen from one adjacent carbon atom to another [12] is responsible for the hydrogen degeneracy observed in some ions. A hydride shift can only contribute to degeneracy when the two carbon atoms involved bear a symmetrical relationship to each other. Consider the examples shown below. Note that hydride shifts are not energetically favorable in the $(CH)_n^+$ ions since in all cases such shifts would result in bridgehead or vinyl carbonium ions:

2-norbornyl cation *(9)* (see Section 4.6)



(9)

cyclopentyl cation *(12)* (see Section 4.1)



(12)

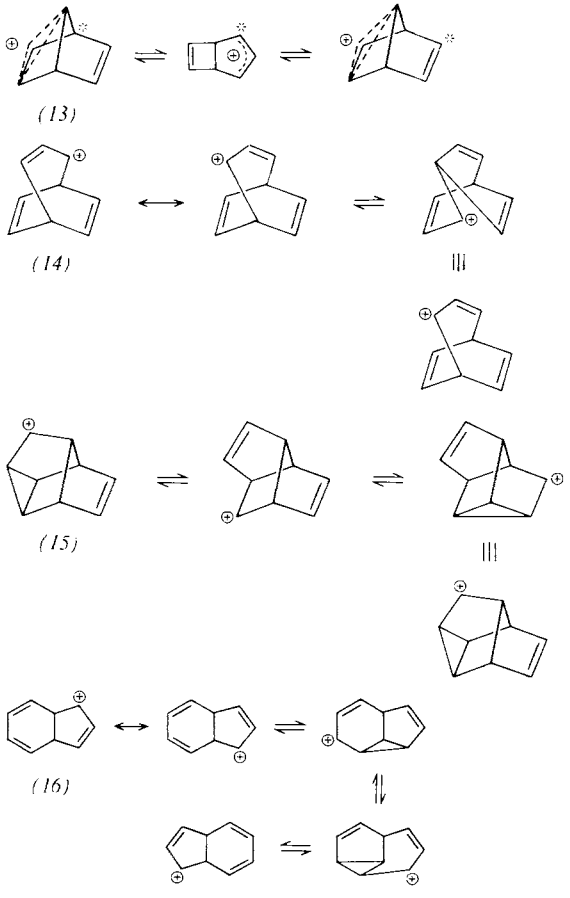
[10] *G. Wagner* and *W. Brickner*, Ber. dtsch. chem. Ges. *32*, 2302 (1899).

[11] *H. Meerwein*, Liebigs Ann. Chem. *396*, 200 (1913); *405*, 129 (1914); *417*, 255 (1918).

[12] For a review, see *J. L. Fry* and *G. J. Karabatsos* in *G. A. Olah* and *P. von R. Schleyer*: Carbonium Ions. Interscience, New York 1970, Vol. 2, Chapter 14.

2.3. Double Bond Participation: 1,2-Vinyl Shift and Homoallylic Rearrangement

Double bond participation refers to the electronic participation of a carbon-carbon double bond in stabilizing a positive charge at a site two carbon atoms removed from the double bond [13,14]. In some cases this participation may result in a 1,2-vinyl shift or a homoallylic rearrangement. Both of these processes can contribute to carbon degeneracy. A 1,2-vinyl shift was observed in the degenerate norbornadienyl cation *(13)* (see Section 3.3.2) and may be potentially involved in the degeneracy of other ions *e.g. (14)* (see Section 3.4.4). Homoallylic rearrangement is presumably also involved in other ion degeneracies such as as *(15)* and *(16)* (see Sections 3.4.3 and 3.4.5 respectively).



(13)

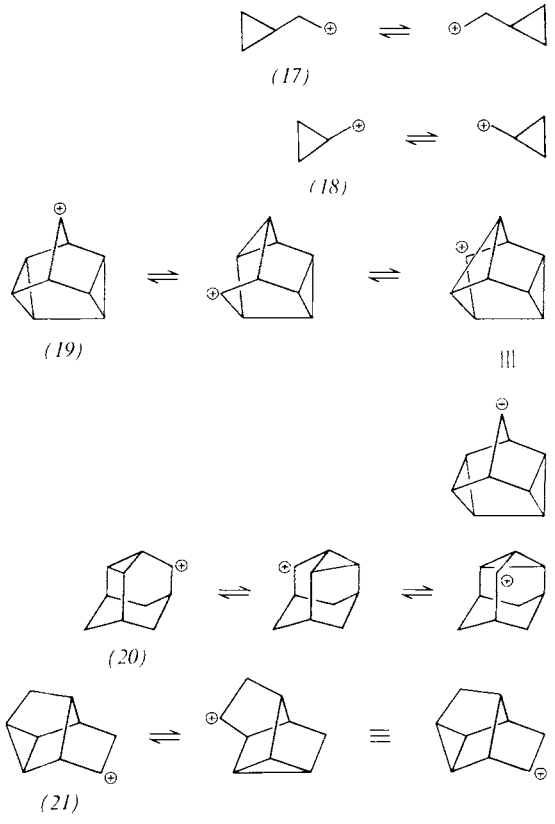
(14)

(15)

(16)

2.4. Participation of a Cyclopropane Ring

The bonds of a cyclopropane ring are capable of participating in charge delocalization [15,16]. Such delocalization can give rise to either a degenerate homocyclopropylcarbinyl rearrangement [17] (cation *(17)* is the parent system) or a degenerate cyclopropylcarbinyl-cyclopropylcarbinyl rearrangement [18] (cation *(18)* is the parent system).



(17)

(18)

(19)

(20)

(21)

The 9-pentacyclo[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]nonyl cation *(19)* (see Section 3.4.2) and the 8-tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonyl cation *(21)* (see Section 4.11) are examples of the first type, and the 8,9-cyclo-2-adamantyl cation *(20)* (see Section 4.9) is an example of the second type.

2.5. Allyl Resonance

Allyl resonance [7], as applied to degenerate carbonium ions, refers to the simultaneous delocalization of positive charge over two allylic carbon atoms which are symmetrically disposed in the ion. The resonance can render two positions on an ion equivalent and can contribute to carbon degeneracy when coupled with one of the other rearrangement processes mentioned above. Cations *(14)* and *(16)* shown in Section 2.3 serve as examples.

3. $(CH)_n^+$ Series of Degenerate Carbonium Ions

Degenerate carbonium ions having the empirical formula $(CH)_n^+$ where n is odd are directly related to hydrocarbons of the form $(CH)_m$ where m is even. Recently *Balaban* published a mathematical treatment for the derivation of all possible valence isomers of $(CH)_m$ hydrocarbons [19]. Potentially degenerate carbonium ions can in theory be derived either by replacement of a carbon-carbon double bond in such a hydrocarbon by a $\rangle C^+-H$ unit or by insertion of a $\rangle C^+-H$ unit into any carbon-carbon single bond. The

[13] *C. W. Shoppee*, J. Chem. Soc. *1946*, 1147; *M. Simonetta* and *S. Winstein*, J. Amer. Chem. Soc. *76*, 18 (1954).

[14] *S. Winstein, H. M. Walborsky*, and *K. Schrieber*, J. Amer. Chem. Soc. *72*, 5795 (1950); *S. Winstein, M. Shatavsky, C. Norton*, and *R. B. Woodward, ibid. 77*, 4183 (1955).

[15] *P. von R. Schleyer* and *G. W. Van Dine*, J. Amer. Chem. Soc. *88*, 2321 (1966); *P. von R. Schleyer* and *V. Buss, ibid. 91*, 5880 (1969), and further literature cited there; see also *J. C. Martin* and *B. R. Ree, ibid. 91*, 5882 (1969); *B. R. Ree* and *J. C. Martin, ibid. 92*, 1660 (1970).

[16] a) *H. Tanida, T. Tsuji*, and *T. Irie*, J. Amer. Chem. Soc. *89*, 1953 (1967); b) *M. A. Battiste, C. L. Deyrup, R. E. Pincock*, and *J. Haywood-Farmer, ibid. 89*, 1954 (1967).

[17] *R. R. Sauers* and *R. W. Ubersax*, J. Org. Chem. *31*, 495 (1966).

[18] a) *K. B. Wiberg* and *G. Szeimies*, J. Amer. Chem. Soc. *90*, 4195 (1968); *92*, 571 (1970); b) *G. A. Olah, D. P. Kelly, C. L. Jeuell*, and *R. D. Porter, ibid. 92*, 2544 (1970); c) *Z. Majerski* and *P. von R. Schleyer, ibid. 92* (1970), in press.

[19] *A. T. Balaban*, Rev. Roum. Chim. *11*, 1097 (1966).

hydrocarbon isomers under consideration have four, six, eight, or ten carbon atoms and the corresponding carbonium ions contain three, five, seven, or nine carbon atoms. Table 2 shows the relationship between the carbonium ions and the hydrocarbons from which they can be derived. All of the ions shown in the Table have the potential for either complete or partial carbon degeneracy, although in fact this may not be observed. It should also be noted that certain ions, such as the cyclopropenyl cation *(22)* and the tropylium ion *(26)*, are not truly degenerate in the sense of our definition since in these ions all the carbon atoms are equivalent through resonance.

All the $(CH)_n^+$ carbonium ions are similar in that they are potentially capable of mixing carbon atoms only by carbon-carbon bond breaking and formation. In these cases the hydrogens also remain attached to the carbon atoms, thus making the interchanging carbon-hydrogen units equivalent. This degeneracy is of the same form as that observed in bullvalene *(51)*. Just as some of the $(CH)_m$ hydrocarbons represent interconvertible valence isomers, some of the $(CH)_n^+$ ions are also interconvertible.

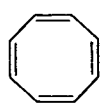
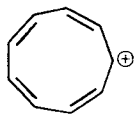
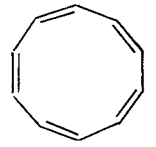
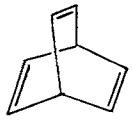
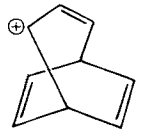
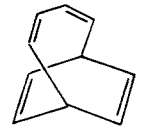
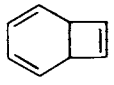
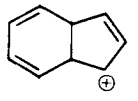
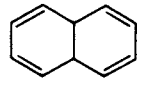
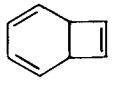
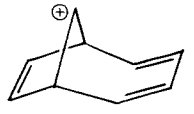
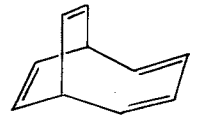
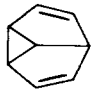
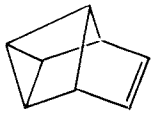
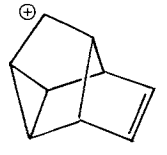
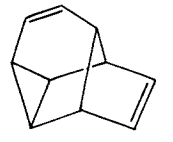
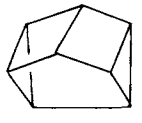
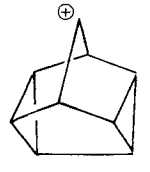
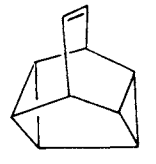
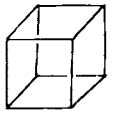
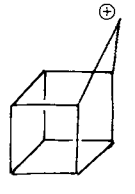
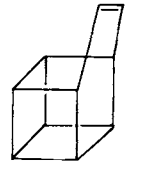
As an alternative to the derivation of $(CH)_n^+$ ions from $(CH)_m$ hydrocarbons, potentially degenerate $(CH)_n^+$ ions can also be constructed by noting that the ion must contain a $\rangle C^+-H$ unit, plus an appropriate number of single bonds, double bonds, and rings to maintain the $(CH)_n^+$ empirical formula. All carbon atoms in the ion must bear a hydrogen atom; but vinyl and acetylenic cations will be excluded. Consequently, $C_3H_3^+$, $C_5H_5^+$, $C_7H_7^+$, and $C_9H_9^+$ ions can have only certain structures.

In the $C_3H_3^+$ group there is only one possibility, the cyclopropenyl cation *(22)*, in which there is one ring and one double bond. For the $C_5H_5^+$ group there are three possible structures: the cyclopentadienyl cation *(23)*, monocyclic and containing two double bonds; the bicyclo[2.1.0]-pentenyl cation *(24)*, bicyclic and containing one double bond; the homotetrahedryl cation *(25)*, tricyclic and con-

Table 2. $(CH)_m$ hydrocarbons, m = 4,6,8,10, and $(CH)_n^+$ ions, n = 3,5,7,9.

$(CH)_m$ Hydrocarbons	$(CH)_n^+$ Ions	$(CH)_m$ Hydrocarbons
	$C_3H_3^+$ *(22)*	C_4H_4 *(33)*
C_4H_4 *(33)*	$C_5H_5^+$ *(23)*	C_6H_6 *(35)*
	(24)	*(36)*
(34)	*(25)*	*(45)*
C_6H_6 *(35)*	$C_7H_7^+$ *(26)*	C_8H_8 *(38)*
(36)	*(13)*	*(39)*
(36)	*(27)*	*(40)*
(37)	*(28)*	*(46)*
(37)	*(29)*	*(47)*

Table 2. (continued).

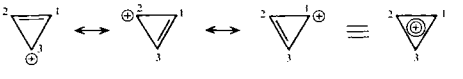
$(CH)_m$ Hydrocarbons	$(CH)_n^+$ Ions	$(CH)_m$ Hydrocarbons
C_8H_8  (38)	$C_9H_9^{\oplus}$  (30)	$C_{10}H_{10}$  (48)
 (39)	 (14)	 (49)
 (40)	 (16)	 (50)
 (40)	 (31)	 (49)
 (41)	 (32)	 (51)
 (42)	 (15)	 (52)
 (43)	 (19)	 (53)
 (44)	 (10)	 (54)

taining no double bonds. For the $C_7H_7^+$ group there are many possible structures of which only the more important ones will be considered here. The tropylium ion *(26)* is monocyclic and can be thought of as having three double bonds. The norbornadienyl cation *(13)* contains two rings and two double bonds; similarly, the bicyclo[3.2.0]heptadienyl cation *(27)* is bicyclic and contains two double bonds. The quadricyclyl cation *(28)* has four rings and no double bonds, and the homoprismyl cation *(29)* is tetracyclic with no double bonds.

Extension of this construction format to the $C_9H_9^+$ ions should be apparent and the multiplicity of possible structures increases with the larger number of carbon atoms. In this paper only those $C_9H_9^+$ ions which have been studied to some degree will be discussed (see Section 3.4). Their structures are shown in Table 2.

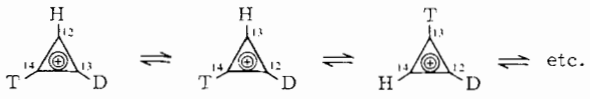
3.1. $C_3H_3^+$ Ions

The simplest example of a $(CH)_n^+$ potentially degenerate carbonium ion is the $C_3H_3^+$ cyclopropenyl cation *(22)*; all three carbon atoms can become equivalent by allyl resonance. This system is not degenerate by the definition



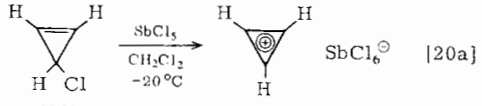
(22)

advanced in Section 1. However, in principle cation *(22)* could exhibit true degenerate rearrangements if the carbon atoms or the hydrogen atoms were to interchange positions. Such a possibility could be detected by studying ion *(55)* in which there are two sets of labels. Such an investigation, admittedly difficult to undertake, has not yet been carried

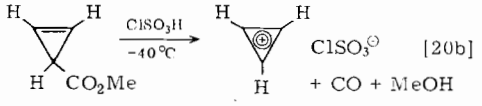


(55) *(55')* *(55'')*

out. Recently cation *(22)* was obtained by two independent routes [20], and the carbonium ion salt *(22')* showed a single peak at τ −0.87 in fluorosulfonic acid [20a]. These results indicate both the aromatic character of the ion and that all carbons and hydrogens are equivalent.



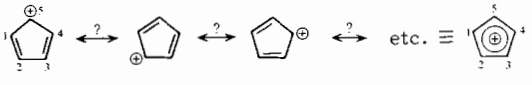
(56) *(22')* [20a]



(57) *(22'')* [20b]

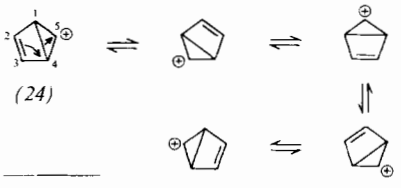
3.2. $C_5H_5^+$ Ions

In the $C_5H_5^+$ family of cations there are three potentially degenerate carbonium ions. The first of these is the cyclopentadienyl cation *(23)*. Presumably all carbon atoms in this ion could become equivalent by resonance. However, as in the case of the cyclopropenyl cation, this is not an example of true carbon degeneracy. The cyclopentadienyl cation is thought not to be an aromatic system and is expected to be destabilized. The pentaphenyl [21a,22] and pentachloro [21b,22] derivatives have been prepared. The former has a singlet and the latter a triplet ground state [22].



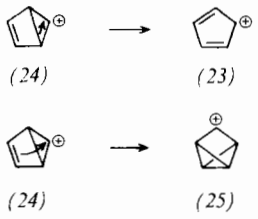
(23)

A second degenerate ion possibility in the $C_5H_5^+$ group is the bicyclo[2.1.0]pentenyl cation *(24)*. This ion is capable of rearranging to regenerate its own structure, but the carbon atoms do not interchange with each other. Cation *(24)* may also rearrange into the cyclopentadienyl cation *(23)* or the homotetrahedryl cation *(25)*.



(24)

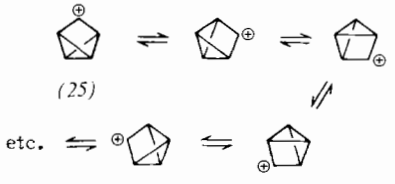
These rearrangement possibilities indicate to some degree the interconvertibility of the $C_5H_5^+$ ions. However, all the cations, *(23)*, *(24)*, and *(25)*, are destabilized by either



(24) *(23)* *(24)* *(25)*

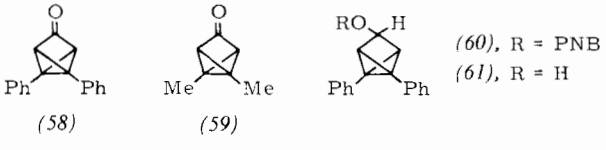
ring strain or nonaromatic character. It is difficult to predict at present whether cation *(24)* would be stable enough to exist or undergo any of the rearrangements shown above.

The first example of a truly degenerate carbonium ion in the $(CH)_n^+$ series is the homotetrahedryl or tricyclo[2.1.0.0^{2,5}]pentyl cation *(25)*. In this ion there is the possibility of complete carbon degeneracy resulting in the positional exchange of all C−H units through 1,2-carbon shifts. If each C−H unit were somehow uniquely identified, it has been calculated ([no. of C atoms]! divided by the molecular symmetry number = 5!/2 = 60) there would be 60 possible arrangements for *(25)* [23].



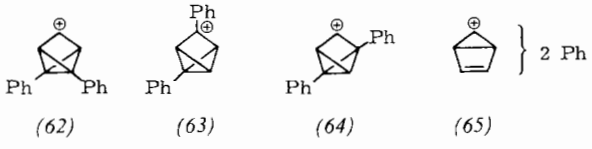
(25)

The parent tricyclo[2.1.0.0^{2,5}]pentane system has not yet been synthesized, but 1,5-diphenyltricyclo[2.1.0.0^{2,5}]pentan-3-one *(58)* [24] and 1,5-dimethyltricyclo[2.1.0.0^{2,5}]-pentan-3-one *(59)* [25] have been prepared. Solvolysis of



(58) *(59)* *(60)*, R = PNB *(61)*, R = H

the *p*-nitrobenzoate *(60)* has been carried out [26], but no structure was assigned with certainty to the solvolysis products. Solvolysis of *(60)* in 70% acetone indicated definitely only that ionization was accelerated and that the product was not 1,5-diphenyltricyclo[2.1.0.0^{2,5}]pentan-3-ol. *(61)*. The absence of *(61)* from the reaction products indicates that ion *(62)* cannot be the immediate precursor of the products.



(62) *(63)* *(64)* *(65)* 2 Ph

Possibly the products arise from ions like *(63)*, *(64)*, or *(65)*, although further study is needed.

[20] a) *R. Breslow, J. T. Groves*, and *G. Ryan*, J. Amer. Chem. Soc. *89*, 5048 (1967); b) *D. G. Farnum, G. Mehta*, and *R. G. Silberman*, *ibid. 89*, 5048 (1967); c) *R. Breslow* and *J. T. Groves*, *ibid. 92*, 984 (1970).

[21] a) *R. Breslow, H. W. Chang*, and *W. A. Yager*, J. Amer. Chem. Soc. *85*, 2033 (1963); b) *R. Breslow, R. Hill*, and *E. Wasserman*, *ibid. 86*, 5349 (1964).

[22] *R. Breslow, H. W. Chang, R. Hill*, and *E. Wasserman*, J. Amer. Chem. Soc. *89*, 112 (1967).

[23] *P. von R. Schleyer, J. J. Harper, G. L. Dunn, V. J. Di Pasquo*, and *J. R. E. Hoover*, J. Amer. Chem. Soc. *89*, 698 (1967).

[24] *S. Masamune*, J. Amer. Chem. Soc. *86*, 735 (1964).

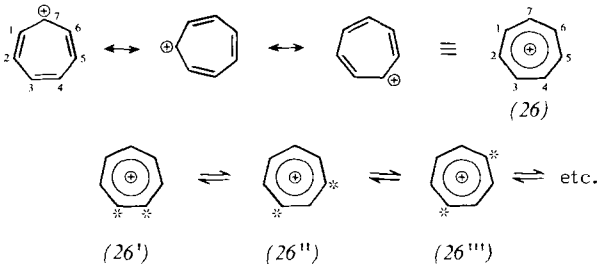
[25] *W. von E. Doering* and *M. Pomerantz*, Tetrahedron Lett. *1964*, 961.

[26] *S. Masamune, K. Fukumoto, Y. Yasunari*, and *D. Darwish*, Tetrahedron Lett. *1966*, 193.

3.3. $C_7H_7^+$ Ions

3.3.1. Tropylium Cation

Within the $C_7H_7^+$ group of potentially degenerate carbonium ions, the monocyclic tropylium cation *(26)* represents the simplest example. This ion has been shown to possess aromatic character and a planar D_{7h} structure [27a]. All the carbon and hydrogen atoms are equivalent and the NMR spectrum of the tropylium ion consists of a single line. This system is not truly degenerate by our definition since the equivalence of all carbons and hydrogens arises through resonance and the atoms do not interchange positions. Cation *(26)* could in theory exhibit degenerate rearrangements if the carbons were to interchange as shown in *(26')*,



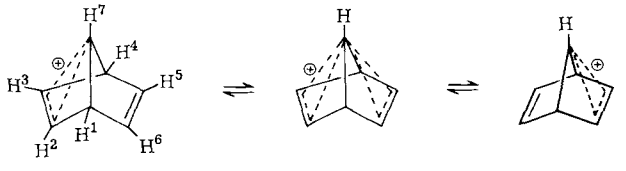
(26)

(26') *(26'')* *(26''')*

(26''), and *(26''')*. Such a labeling study has not yet been carried out [27b].

3.3.2. 7-Norbornadienyl Cation and Bicyclo[3.2.0]heptadienyl Cation

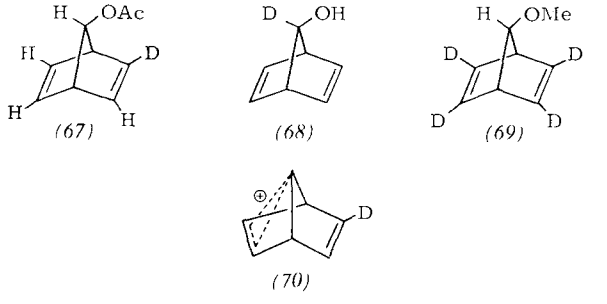
The 7-norbornadienyl cation *(13)* undergoes a degenerate rearrangement which leads to the equivalence of five carbon atoms in the ion [28]. In a search for "bridge flipping" (the



(13) *(66)* *(13')*

NMR spectrum of *(13)*: H-1 and H-4: τ = 4.88; H-5 and H-6: τ = 3.90; H-7: τ = 6.73; H-2 and H-3: τ = 2.54.

interconversion of *(13)* to *(13')* through *(66)*) in this species, it was observed that the NMR spectrum at −77 °C in FSO_3H showed a broadening of the signals for protons bound to carbons C-7, C-1 and C-4, C-5 and C-6, but not for those bound to C-3 or C-2. The nature of the rearrangement was determined by studying the NMR spectra of the ions derived from the labeled precursors *(67)*, *(68)*, and *(69)*.

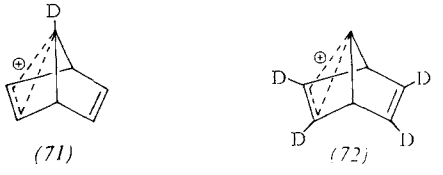


(67) *(68)* *(69)* *(70)*

[27] a) *D. Lloyd*: Carbocyclic Non-Benzenoid Aromatic Compounds. Elsevier, Amsterdam 1966, p. 98; b) cf. *A. S. Siegel*, J. Amer. Chem. Soc. *92*, 5277 (1970).

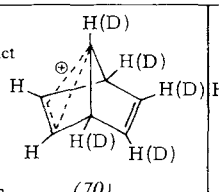
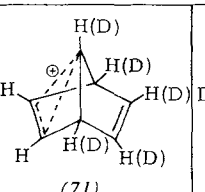
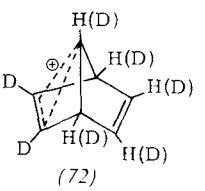
[28] *R. K. Lustgarten, M. Brookhart*, and *S. Winstein*, J. Amer. Chem. Soc. *89*, 6350 (1967).

In FSO_3H at −73 °C *(67)* exhibited the same four-signal spectrum as that of *(13)* with the intensity of the signal for H-5 and H-6 (unbound vinyl) one half that of the signal for H-2 and H-3 (bound vinyl). When the cation *(70)* solution was warmed to −47 °C, the deuterium label scrambled over positions 1, 7, 4, 5, and 6 with a rate constant of 3×10^{-4} s^{-1} but not over positions 2 and 3. This was evidenced in the NMR spectrum by the peak intensities approaching a ratio of 2:1.6:1.6:0.8 for the bound vinyl, unbound vinyl, bridgehead, and bridge protons, respectively. It was found that the deuterium label is incorporated sequentially at the different positions. The label appeared first at the bridgehead positions, 1 and 4, and then at the bridge position, 7. Similar rearrangements at similar rates were also observed for ions *(71)* and *(72)* derived from precursors *(68)* and *(69)* (see Table 3). These rearrangements indicate the existence of partial carbon degeneracy in the 7-norbornadienyl cation.

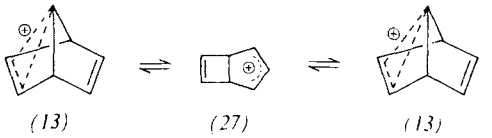


(71) *(72)*

Table 3. Rates and free energies of activation of degenerate rearrangements of the 7-norbornadienyl cation (from ref. [28]).

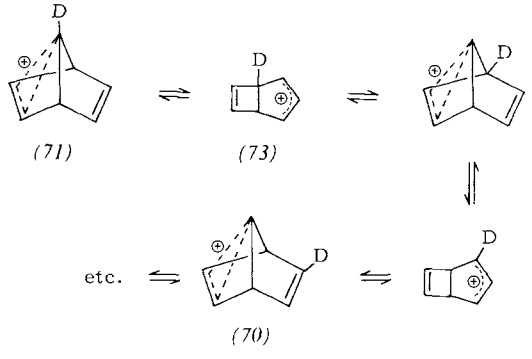
Product			
Cation	*(70)*	*(71)*	*(72)*
	1/5 D	1/5 D	2/5 D
	at each C atom		at each of 5 C atoms
Temperature (°C)	−47	−55	−50
$10^4 k$ (s^{-1})	3	1.7	2
ΔG^+ (kcal/mole)	16.7	16.4	16.7

The mechanism proposed for the 5-carbon degenerate rearrangement is ring contraction to the bicyclo[3.2.0]hepta-



(13) *(27)* *(13)*

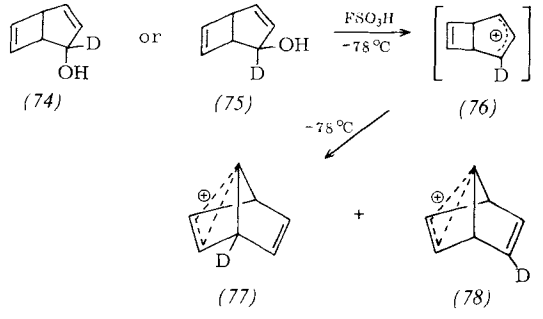
dienyl cation *(27)* followed by ring expansion back to the 7-norbornadienyl cation *(13)*. For labeled ion *(71)* this would give rise to a sequence in which the bound vinyl group moves stepwise around the five-membered ring of *(73)*.



(71) *(73)* *(70)*

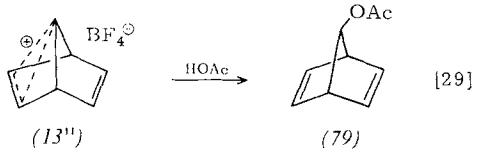
Evidence to support this mechanism comes from the NMR spectra of ions derived from the deuterated *cis*- and *trans*-bicyclo[3.2.0]heptadienols *(74)* and *(75)*.

When either alcohol was extracted into FSO_3H at $-78\,^{\circ}C$, and the carbonium ion solution was observed within 120 s, the NMR spectrum was that of ion *(77)* plus ion *(78)* with no trace of signal for cation *(76)*.



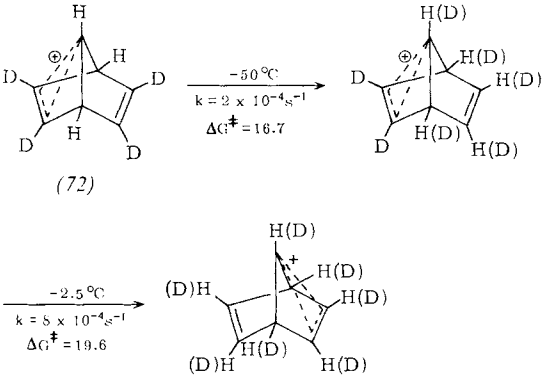
(74) *(75)* *(76)* *(77)* *(78)*

This result agrees with a mechanism in which the first formed [3.2.0] cation ring-expands to the [2.2.1] ion with either carbon of the cyclobutene vinyl function undergoing a 1,2-shift as the migrating vinyl group becomes the bound vinyl in *(77)* and *(78)*. The authors noted that neither ring contraction nor ring expansion of these systems occurs in solvolyzing solvents where carbonium ion lifetimes are very short compared to those in FSO_3H.



(13'') *(79)* *(80)* *(81)*

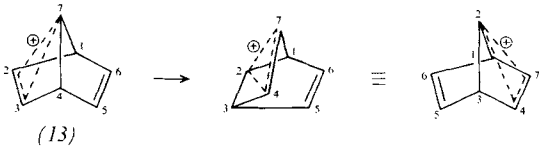
The 7-norbornadienyl cation *(13)* also undergoes a slower rearrangement which results in C-2 and C-3 becoming equivalent with C-5 and C-6 [31]. This equilibration of bound and unbound vinyl groups in *(13)* was studied by observing the NMR spectrum of cation *(72)* at higher temperatures. Cation *(72)* at $-50\,^{\circ}C$ has a deuterium atom at each bound vinyl position but only 2/5 of a deuterium atom at each unbound vinyl position as a result of degenerate five-carbon scrambling. At about $0\,^{\circ}C$ proton incorporation into the bound vinyl positions is observed, and the bound and unbound vinyl signals approach equal intensity.



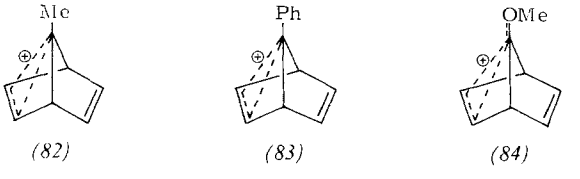
(72)

The second rearrangement process requires 3 kcal/mole more activation energy than that for the five-carbon scrambling. Coupled with the more rapid degenerate five-carbon rearrangement, all seven carbon atoms of the 7-norbornadienyl cation *(13)* could become scrambled (complete carbon degeneracy). A possible mechanism for the second rearrangement process is bridge flipping and the value of $\Delta G^{\ddagger}$ for the rearrangement (19.6 kcal/mole) represents a lower limit on the energy barrier for this process.

Other mechanisms besides bridge flipping are possible for the equilibration of the two vinyl groups in *(13)* (for example, a 1,2-shift of an unbound vinyl carbon as shown below); some 7-substituted norbornadienyl cations were studied to further test this hypothesis. The 7-methylnorbornadienyl cation *(82)* was investigated [31]; the NMR spectrum of *(82)* in FSO_3H gave evidence for an unsymmetrical species at $-45\,^{\circ}C$.

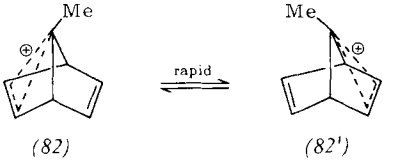


(13)



(82) *(83)* *(84)*

As the temperature was raised, the vinyl signals began to broaden and eventually coalesced at $-14\,^{\circ}C$. The methyl peak remained sharp at all times and the bridgehead signal sharpened to a pentuplet. These results indicated averaging of only the vinyl proton environments, which must have occurred by bridge flipping. The rate constant



(82) *(82')*

for this process at $-14\,^{\circ}C$ was 189 s^{-1} and $\Delta G^{\ddagger}$ was 12.4 kcal/mole. The 7-phenylnorbornadienyl *(83)* and 7-methoxynorbornadienyl *(84)* cations were also studied under the assumption that substituents better able to accommodate a positive charge would stabilize a symmetrical cation more than an unsymmetrical cation [32]. Both these cations at $-100\,^{\circ}C$ showed equivalence of all four vinyl protons. By examining the chemical shifts of the phenyl hydrogens in *(83)*, it was concluded that the phenyl group

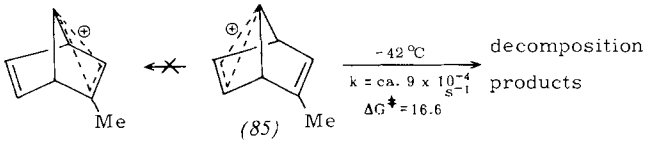
[29] *P. R. Story* and *M. Saunders*, J. Amer. Chem. Soc. *84*, 4876 (1962).

[30] *P. R. Story* and *B. J. A. Cooke*, Chem. Commun. *1968*, 1080.

[31] *M. Brookhart, R. K. Lustgarten*, and *S. Winstein*, J. Amer. Chem. Soc. *89*, 6352 (1967).

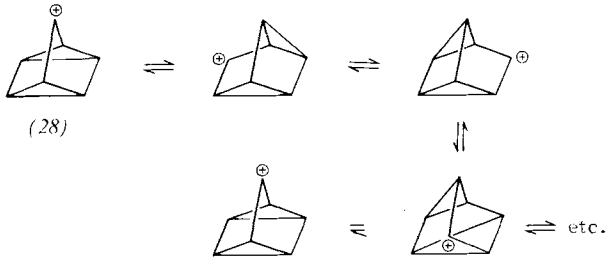
[32] *M. Brookhart, R. K. Lustgarten*, and *S. Winstein*, J. Amer. Chem. Soc. *89*, 6354 (1967).

was not sustaining considerable positive charge. Hence, it was concluded that *(83)* is best represented as unsymmetrical, yet undergoing rapid bridge-flipping with a barrier of < 7.6 kcal/mole. Recent work on the 2-methyl-7-norbornadienyl cation *(85)* indicates bridge flipping is not a favorable process when a substituent is located in one of the vinyl groups [33]. It was observed that *(85)* decomposed rather than undergoing bridge flipping.

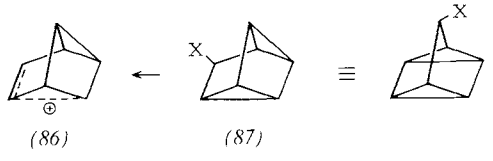


3.3.3. Quadricyclyl or 3-Tetracyclo[3.2.0.0^{2,7}.0^{4,6}]-heptyl Cation

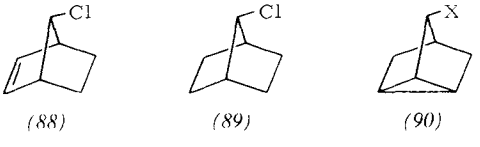
The quadricyclyl cation *(28)* has the potential for complete carbon degeneracy if continuous cyclopropylcarbinyl-cyclopropylcarbinyl rearrangements occur. The positive charge can be distributed to all carbons by such a mech-



anism involving both cyclopropyl rings. However, present evidence supports structure *(86)* as best representing the carbonium ion intermediate derived from the solvolysis of quadricyclane derivatives *(87)*. This charge delocalized cation would not necessarily exhibit the degenerate re-



arrangements as shown above. Cation *(86)* was first proposed to account for the remarkable reactivity of quadricyclane derivatives [34, 35]. It was found that 7-quadricyclyl chloride *(87)*, X = Cl, was less reactive than *anti*-7-norbornenyl chloride *(88)* by a factor of only 100 and more reactive than 7-norbornyl chloride *(89)* by approximately 10^9. Quadricyclane derivatives were found to be only about 30 – 40 times more reactive than the corresponding nortricyclane compounds *(90)* which contain only one cyclopropane ring [34]. The net effect of the second cyclopropane



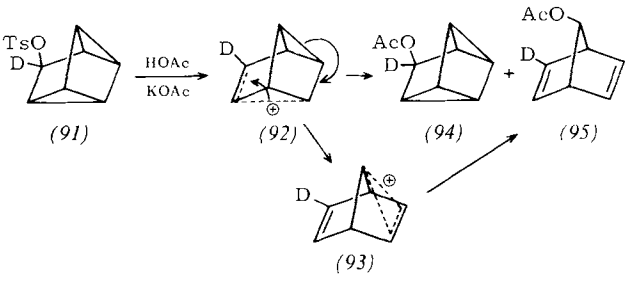
[33] *R. K. Lustgarten, M. Brookhart,* and *S. Winstein,* J. Amer. Chem. Soc. *90*, 7364 (1968).

[34] *H. G. Richey, Jr.* and *N. C. Buckley,* J. Amer. Chem. Soc. *85*, 3057 (1963).

[35] *P. R. Story* and *S. R. Fahrenholtz,* J. Amer. Chem. Soc. *86*, 527 (1964).

ring appears to be negligible. This is similar to the participation of only one carbon-carbon double bond in the 7-norbornadienyl cation [31].

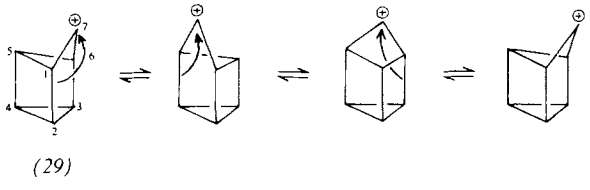
The solvolysis of 7-deuterioquadricyclyl tosylate *(91)* at 25 °C for 2 – 3 days in acetic acid containing an excess of



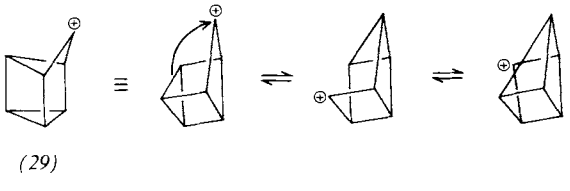
potassium acetate gave a 75% yield of a product mixture consisting of an approximately 50:50 ratio of *(94)* and *(95)* [36]. Both the quadricyclyl acetate *(94)* and the 7-norbornadienyl acetate *(95)* contained one deuterium by analysis of their NMR and mass spectra. This experiment indicates that the hydrogens of the quadricyclyl cation are not scrambled by rearrangement, thus ruling out a structure in which the positive charge is delocalized over two or more equivalent carbons. Hence, the quadricyclyl cation represents an example of a nondegenerate ion. The results above indicate the interconvertibility of the quadricyclyl and norbornadienyl cations *(92)* and *(93)*. The rearrangement of *(92)* to *(93)*, and subsequently to *(95)*, appears to be highly stereospecific.

3.3.4. Homoprismyl or 7-Tetracyclo[3.2.0.0^{2,4}.0^{3,6}]-heptyl Cation

The homoprismyl cation *(29)* represents another potentially degenerate $C_7H_7^+$ carbonium ion. This ion has not yet been studied, but is unique in that it may undergo several rearrangement possibilities. It could exhibit degenerate properties through Wagner-Meerwein rearrangements as shown below. This kind of process would result in fourfold partial carbon degeneracy; the four carbons of the cyclo-

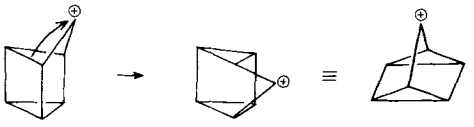


butane ring bearing the positive charge would become equivalent. A second kind of process, participation of the three-membered ring in a homocyclopropylcarbinyl rearrangement, could serve to delocalize the positive charge over three carbons.



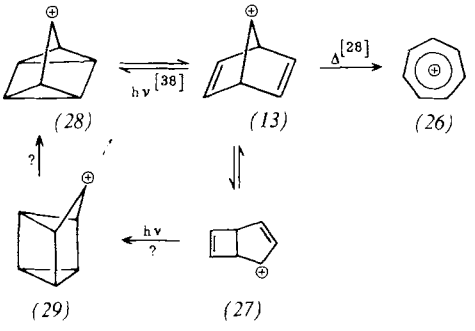
[36] *P. R. Story* and *S. R. Fahrenholtz,* J. Amer. Chem. Soc. *88*, 374 (1966).

(charge delocalization over all seven carbon atoms). However, a third rearrangement process exists for *(29)*, that of cyclobutane ring participation. This process would serve to destroy the homoprismyl ring system and generate the quadricyclyl cation *(28)*.



(29) *(28)*

The last rearrangement mentioned above points out the relationship between the homoprismyl cation and other $C_7H_7^+$ ions. It is further interesting to note that *(29)* hypothetically could be formed by a photochemical cycloaddition within the bicyclo[3.2.0]heptadienyl cation [37].

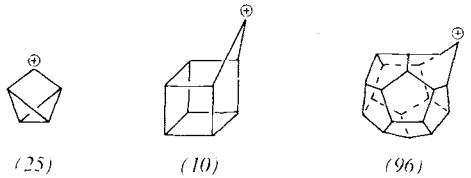


(28) *(13)* *(26)* *(29)* *(27)*

3.4. $C_9H_9^+$ Ions

3.4.1. 9-Homocubyl or 9-Pentacyclo-[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]nonyl Cation

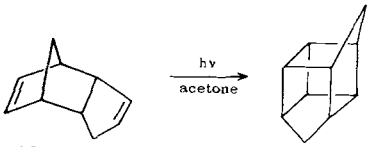
The 9-homocubyl cation *(10)* represents one of the most interesting potentially degenerate carbonium ions within the $C_9H_9^+$ group. This cation, like the homotetrahedryl cation *(25)* (see Section 3.2) and the homododecahedryl cation *(96)*, belongs to a series of homologous ions based on regular polyhedra [23]. These three ions are similar in



(25) *(10)* *(96)*

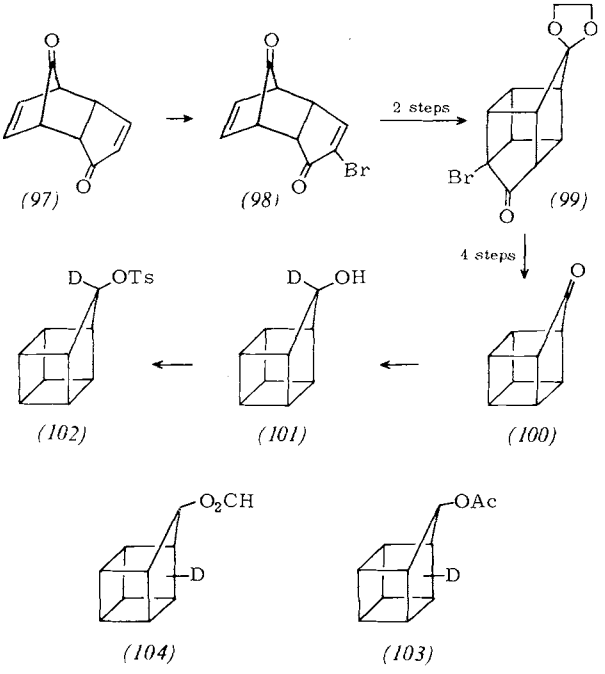
that they are all capable of complete carbon degeneracy by employing only 1,2-carbon shifts. All C-H units can exchange positions, thus making all carbon atoms and hydrogen atoms equivalent. The homododecahedryl cation *(96)* has not yet been investigated and the parent hydrocarbon, dodecahedron, has not been synthesized.

[37] An analogous reaction is the photosensitized intramolecular cyclization of cyclopentadiene dimer to pentacyclo[5.3.0.0^{2,5}.0^{3,9}.0^{4,8}]decane; see *G. O. Schenck* and *R. Steinmetz*, Chem. Ber. *96*, 520 (1963).



[38] The photochemical conversion of norbornadiene to quadricyclene has been carried out; see *W. G. Dauben* and *R. L. Cargill*, Tetrahedron *15*, 197 (1961); *G. S. Hammond, N. J. Turro*, and *A. Fischer*, J. Amer. Chem. Soc. *83*, 4674 (1961).

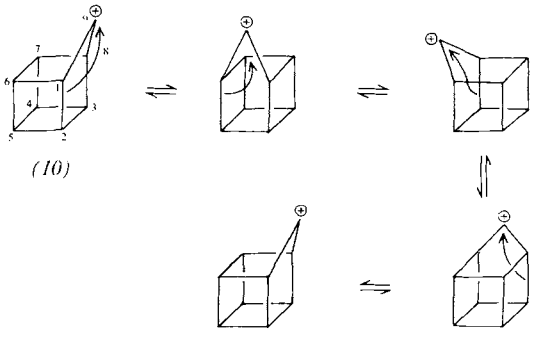
Investigations by workers at Smith, Kline and French Laboratories and Princeton University were first to indicate that the predicted degeneracy of the 9-homocubyl cation *(10)* could be achieved under solvolytic conditions [23]. The degeneracy of *(10)* was demonstrated by studying the deuterium labeling pattern obtained in the solvolysis products of the deuterated tosylate *(102)*. The synthesis of *(102)* involves photochemical cycloaddition of *(98)* to *(99)* and lithium tetradeuterioaluminate reduction of homocubanone *(100)* to form *(101)* as key steps. The NMR spectrum of *(102)* indicated essentially com-



(97) *(98)* *(99)* *(100)* *(101)* *(102)* *(103)* *(104)*

plete absence of the absorption peak for the proton at C-9. The course of the rearrangements was followed by the appearance and integration of this signal in the spectra of the solvolysis products. Solvolysis of deuterated 9-homocubyl tosylate *(102)* exhibited good first order kinetics in both acetic and formic acid, and in both cases the sole products isolated were 9-homocubyl acetate *(103)* and formate *(104)* with the deuterium label scrambled. The acetolysis rate constant at 25 °C was approximately 400 times faster than that expected from the carbonyl frequency of *(100)*. This enhanced rate suggests that the 9-homocubyl cation *(10)* may have a bridged structure.

There are two mechanistic possibilities for deuterium scrambling in *(10)*. One possibility is a stereospecific process involving bridged or rapidly equilibrating ions which This process combined with the Wagner-Meerwein rearrangement would result in complete carbon degeneracy



(10)

would make five carbon atoms and their attached hydrogens equivalent, provided no stereochemical leakage occurred. This mechanism, which is shown below, would scramble the deuterium label around only one five-membered ring.

A second possibility, a non-stereospecific reaction path, would allow distribution of the positive charge and the deuterium label to all nine carbons. This would also permit the interchange of all C–H units in the manner exhibited by bullvalene [2].

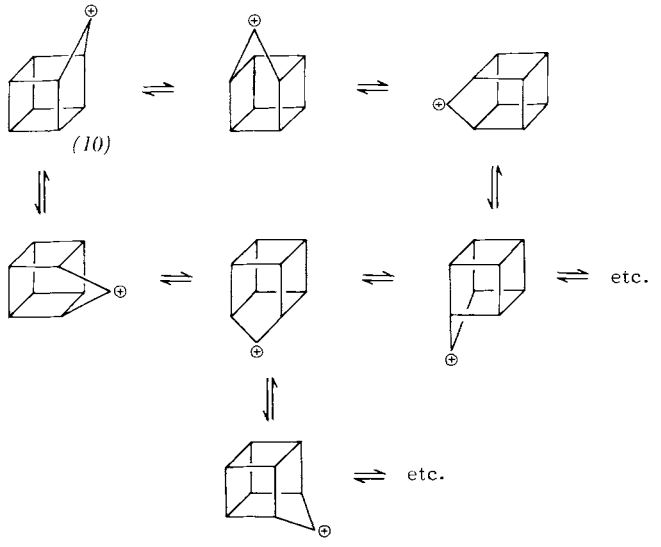


Table 4 shows the labeling pattern calculated for each process at each rearrangement stage.

Table 4. Percentage of D remaining at C-9 in the 9-homocubyl system as a function of the number of 1,2-C,C rearrangements (from ref. [23]).

	No. of rearrangements								
	1	2	3	4	5	6	7	8	∞
%D at C-9, stereospecific process	50	37.5	31.3	27.3	24.8	23.1	22.1	21.4	20.0
%D at C-9, nonstereospecific process	50	37.5	31.3	27.0	23.7	21.2	19.3	17.7	11.1

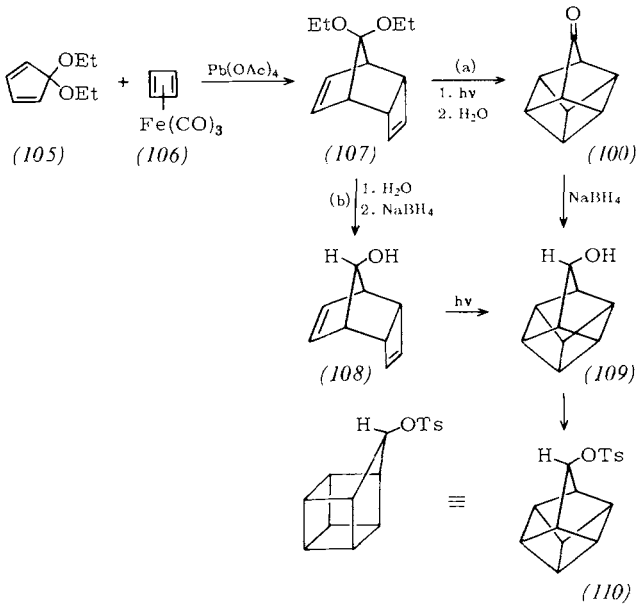
The experimental results were the following: In buffered acetic acid at 125 °C for more than 10 half-lives, 36% D remained at C-9 after solvolysis. In unbuffered acetic acid at the same temperature and time, 22.5% D remained at C-9, indicating more than five rearrangements had occurred. In refluxing unbuffered formic acid only 10% D remained at C-9 with the other 90% D distributed throughout the molecule. This preliminary experiment in formolysis indicated that the full degeneracy of *(10)* could be achieved, but attempts to repeat this result have not succeeded [39].

Work by *Pettit* and *Barborak* on the homocubyl cation *(10)* further verified the findings described above [40]. These investigators employed both a different synthesis and a different deuterium labeling pattern to show that *(10)* when generated in acetic acid undergoes several stereospecific degenerate rearrangements before forming the acetate.

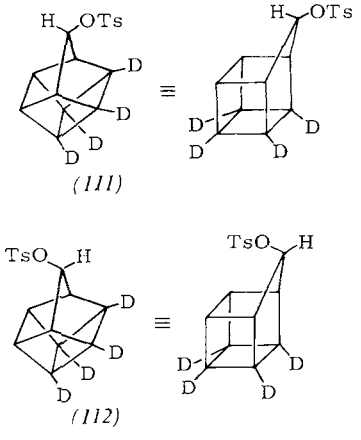
[39] *W. G. Dauben*, personal communication.

[40] *J. C. Barborak* and *R. Pettit*, J. Amer. Chem. Soc. *89*, 3080 (1967).

Two synthetic pathways (a) and (b) were used to prepare 9-homocubyl tosylate *(110)*. Substitution of perdeuteriocyclobutadienetricarbonyliron for *(106)* gave a tetra-



deuterio derivative of *(110)*. Path (a) afforded an equal mixture of the two tosylates *(111)* and *(112)*, while path (b) gave only isomer *(111)*.



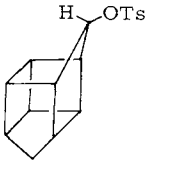
A sample of *(111)* and another consisting of an equal mixture of *(111)* and *(112)* was solvolyzed in acetic acid at 120 °C for 30 hours, and the acetates and unreacted tosylates were recovered. The percentage of deuterium at C-9 was measured to determine the extent of rearrangement. The amount of deuterium appearing at this position also depends on the stereospecificity of the rearrangement process. In a stereospecific process involving repeated migration of the carbon atom *trans* to the leaving group, *(111)* should show twice as much deuterium at C-9 as that of a mixture of *(111)* and *(112)* since *(112)* cannot generate deuterium at C-9 in such a process. In a nonstereospecific rearrangement process both samples should give the same amount of deuterium at C-9. The acetate formed from *(111)* showed 26.1% deuterium at C-9, while that from *(111)* and *(112)* showed 12.3%. The rearrangement appears to be stereospecific under these conditions. These results indicate that almost four Wagner-Meerwein shifts had occurred during solvolysis (see Table 5).

Table 5. Percentage of D at C-9 accompanying 1,2-shifts of *(111)* (from ref. [40]).

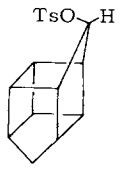
No. of 1,2-shifts	0	1	2	3	4	5	6	∞
% D at C-9	0	0	12.5	21.9	28.1	32.2	35.0	40.0

The above results compare favorably with those of the workers at Smith, Kline and French Laboratories and Princeton University. However, the recovered tosylates from *(111)* and *(112)* were also examined and these contained deuterium a C-9 to a larger degree than that observed for the acetates. Approximately twice as much deuterium appeared at C-9 in the reaction of *(111)* as with the mixture of *(111)* and *(112)*. This result indicates stereospecific rearrangement through internal return of the tosylate ion pair and contrasts with the result of the first group of workers which indicated that stereochemical leakage could at least occur in formolysis.

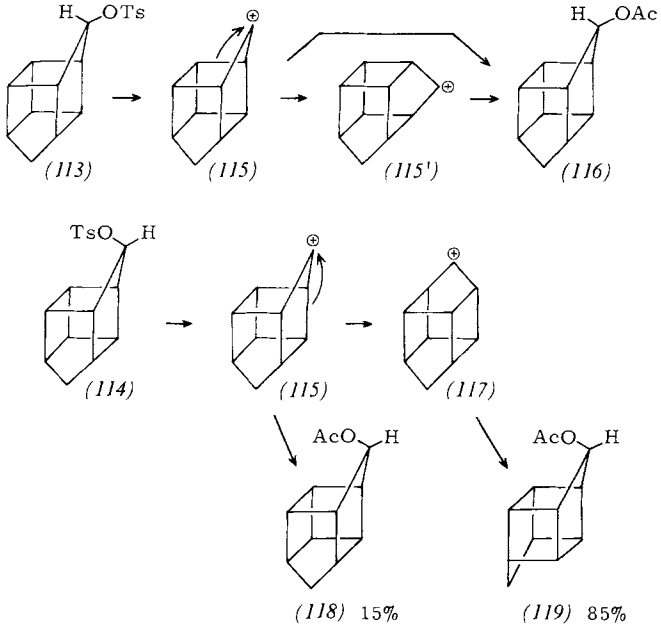
Studies have also been carried out on the bishomocubyl systems *(113)* and *(114)* [41]. The solvolysis of these tosylates is of interest since the cations generated from *(113)* and *(114)* undergo rearrangements similar to the homocubyl cation *(10)*. In these cases the migration of the second methano carbon bridge serves as a means of detecting the rearrangements. The acetolysis (unbuffered) of tosylates *(113)* and *(114)* gave the acetates *(116)* and *(119)* as major products, which can be rationalized as



(113)

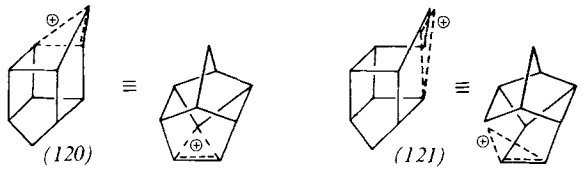


(114)



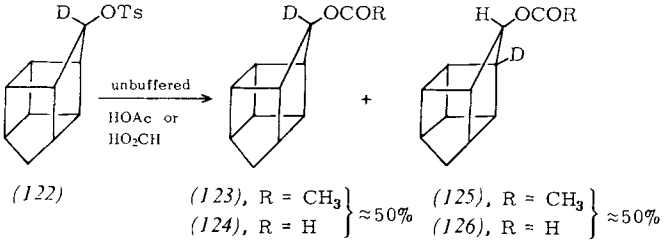
(118) 15% *(119)* 85%

arising *via* 1,2-alkyl shifts through cations *(115)*, *(115')*, and *(117)* followed by substitution with retention of configuration. Alternatively, the results can be explained by assuming that the bridged carbonium ions *(120)* and *(121)* are intermediates in the solvolyses of *(113)* and *(114)*,



(120) *(121)*

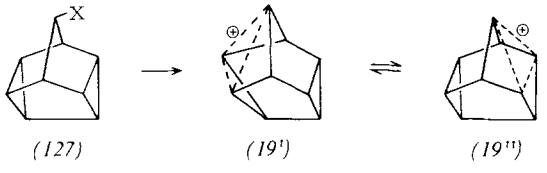
respectively. Recent work on the deuterated tosylate *(122)* supports the intermediacy of the bridged ion *(12)* or its equivalent of two rapidly equilibrating classical ion pairs in the solvolysis of *(113)* [42]. The results of the solvolyses of the bishomocubyl systems are in direct analogy with those for the homocubyl compounds.



(122) *(123)*, R = CH_3 *(124)*, R = H ≈50% *(125)*, R = CH_3 *(126)*, R = H ≈50%

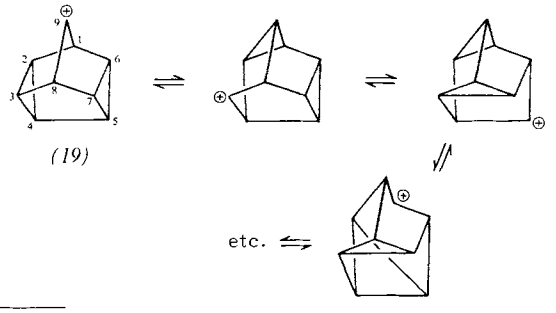
3.4.2. 9-Pentacyclo[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]nonyl Cation

The 9-pentacyclo[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]nonyl cation *(19)* is another ion of the $C_9H_9^+$ group which possesses the unique structural and symmetry properties that could result in multiple carbon degeneracy. Cation *(19')*, derived from the solvolysis of *(127)*, is an analog of the *cis*-3-bicyclo-[3.1.0]hexyl cation [43] (see Section 4.7) and should be capable of threefold degeneracy by means of a homocyclopropylcarbinyl rearrangement *(127)* → *(19')*. There is also the possibility of a bridge-flip rearrangement which can again regenerate a cation identical with the original. The combination of both processes at the same time would make all positions interchangeable and all nine carbon



(127) *(19')* *(19'')*

atoms would become equivalent. An alternative way of representing this possibility of complete degeneracy in *(19)* is by successive, discrete carbon-carbon bond shifts from the two participating cyclopropyl rings (all ions formed are identical).



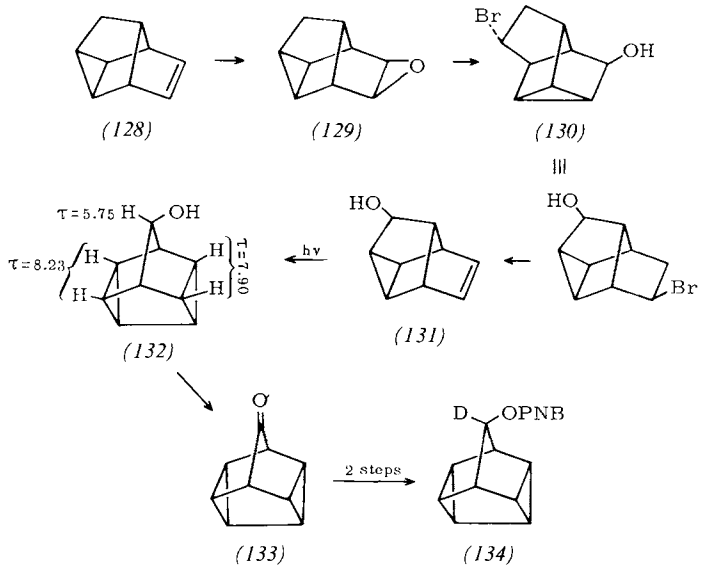
(19)

[41] *W. L. Dilling* and *C. E. Reineke*, Tetrahedron Lett. *1967*, 2547.

[42] *W. L. Dilling*, *R. A. Plepys*, and *R. D. Kroening*, J. Amer. Chem. Soc. *91*, 3404 (1969).

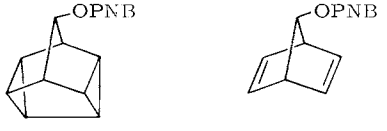
[43] *S. Winstein*, *E. C. Friedrich*, *R. Baker*, and *Y. Lin*, Tetrahedron Suppl. *8* [II], 621 (1966), and literature cited there.

Recently, work on the synthesis and solvolysis of 9-deuteriopentacyclo[4.3.0.0^{2,4}.0^{3,8}.0^{5,7}]nonyl *p*-nitrobenzoate *(134)* was carried out by *Coates* and *Kirkpatrick* [44]. The synthetic scheme is outlined below. The most important steps in the synthesis are the acid-catalyzed rearrangement of the epoxide *(129)* to the bromohydrin *(130)* and the photochemical valence isomerization of the tetracyclic alcohol *(131)* to the desired pentacyclic alcohol *(132)*.

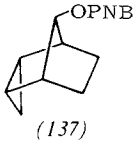


The solvolysis of the unlabeled *p*-nitrobenzoate *(135)* in 65% aqueous acetone at 125.0 °C exhibited good first order kinetics with a rate constant of $7.0 \times 10^{-5}\ s^{-1}$. Under the same conditions 7-norbornadienyl *p*-nitrobenzoate *(136)* solvolyzed with a first-order rate constant of $5.8 \times 10^{-4}\ s^{-1}$ [45]. Therefore, k_1 *(135)*/K_1 *(136)* equals 0.12 [16].

The large rate enhancement observed for *(135)* cannot be attributed to an overall relief of strain upon cyclopropane ring opening since *(132)* is the major reaction product. The acceleration most probably is a result of the geometry in this system which is particularly favorable for homocyclopropyl-carbinyl participation in the solvolysis transi-



tion state. This hypothesis was previously advanced for the similar *endo-anti*-8-tricyclo[3.2.1.0^{2,4}]octyl *p*-nitrobenzoate *(137)* [16], which solvolyzes approximately 80 times faster than *(135)*.



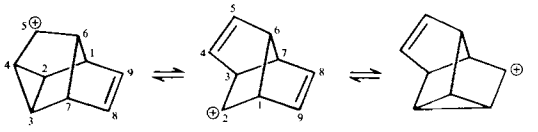
[44] *R. M. Coates* and *J. L. Kirkpatrick*, J. Amer. Chem. Soc. *90*, 4162 (1968); *92*, 4883 (1970).

[45] *S. Winstein* and *C. Ordronneau*, J. Amer. Chem. Soc. *82*, 2084 (1960).

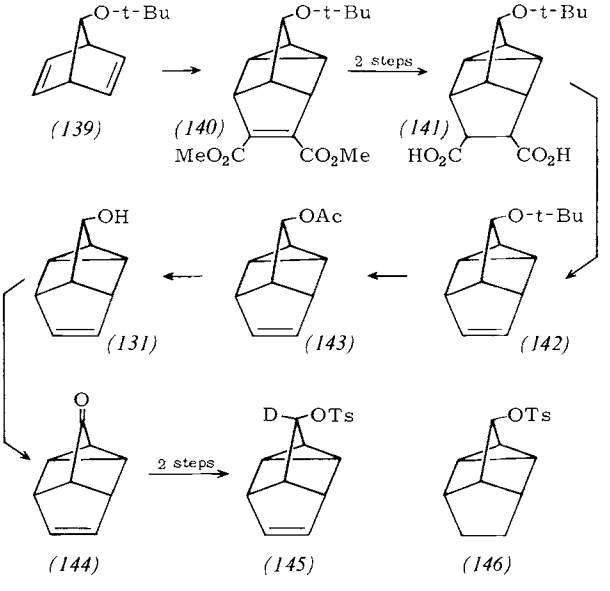
Solvolysis of *(134)* for 4–5 half lives regenerated *(132)* in which ^{1}H-NMR absorption at position C-9 had reappeared. The extent of the deuterium scrambling was determined by the ^{2}H- and ^{1}H-NMR spectrum of the product. The ^{2}H-NMR spectrum showed two peaks at τ 5.8 and 8.2 in a ratio of 1:2.05. This indicated that one-third of the deuterium label remained at C-9 and the other two-thirds were distributed between two other equivalent positions. Quantitative integration of the ^{1}H-NMR spectrum of scrambled *(132)* showed the presence of 0.67 proton at C-9. Also, the signal at τ 8.2 was reduced from an area of 2 to 1.3 protons while the remainder of the spectrum was essentially unchanged. These results provide evidence for the triply degenerate carbonium ion intermediate *(19')*. Further rearrangement through participation of the second cyclopropane ring did not occur under conditions employed.

3.4.3. Tetracyclo[4.3.0^{2,4}.0^{3,7}]non-8-en-5-yl Cation

The tetracyclo[4.3.0.0^{2,4}.0^{3,7}]non-8-en-5-yl cation *(15)* is capable of partial carbon degeneracy through a combination of cyclopropylcarbinyl and homoallylic rearrangements. Transformation of *(15)* into ion *(138)* is readily conceivable; *(138)*, with a C_2 symmetry axis through C-2



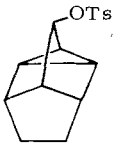
and the midpoint of the C-6–C-7 bond, should be convertible into *(15')* or back into *(15)* by homoallylic rearrangement. If ion *(15)* contains a deuterium label at C-5, continuous operation of the above mechanism will eventually result in deuterium scrambling to the four positions C-4, C-5, C-8, and C-9 because of the equivalence of these four carbon atoms. The five carbon atoms of the central five-membered ring, C-1, C-2, C-3, C-6, and C-7, would also become equivalent by such a process, but would bear no deuterium label.



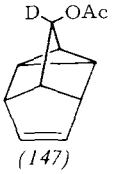
Schleyer and *Leone* were the first investigators to study cation *(15)* [46]. The synthesis is primarily based on the homo Diels-Alder reaction of dimethyl acetylenedicarboxylate with *(139)* to form *(140)*, which contains the desired tetracyclic ring system. Acid cleavage of the *tert*-butyl ether *(142)* to form acetate *(143)* is also an important step. Alcohol *(131)* is the same as that synthesized independently by *Coates* and *Kirkpatrick* (see Section 3.4.2) [44]. The saturated derivative *(146)* was also prepared for comparison purposes.

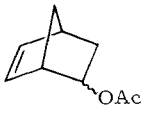
The solvolysis of *(145)* in acetic acid buffered with an excess of sodium acetate at 110 °C for three hours (over 10 half-lives) led to the formation of 5-deuterioacetate *(147)* as the sole product with the deuterium completely unscrambled. Attempts to study the solvolysis under more vigorous conditions with unbuffered acetic or formic acid failed due to solvent addition to the double bond. A summary of the acetolysis rate constants for the undeuterated tosylate *(148)*, the saturated derivative *(146)*, and nortricyclyl tosylate *(149)* are shown below in Table 6.

Table 6. Acetolysis of *(148)*, *(146)*, and *(149)* (from ref. [46]).

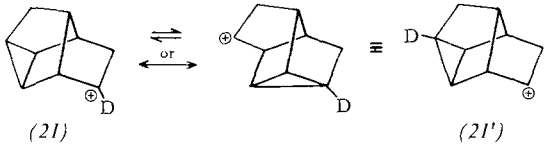
Compound	 *(148)*	 *(146)*	 *(149)*
k (s^{-1}) (75 °C)	1.85×10^{-4}	7.38×10^{-3}	1.62×10^{-3}
k_{rel}	0.11	4.6	1.0
ν_{CO} (cm^{-1})	1755	–	1762

The results obtained are somewhat surprising since the solvolysis of nortricyclyl tosylate *(149)* produces some rearranged product, norborn-2-en-5-yl acetate *(150)* [47].


(147)

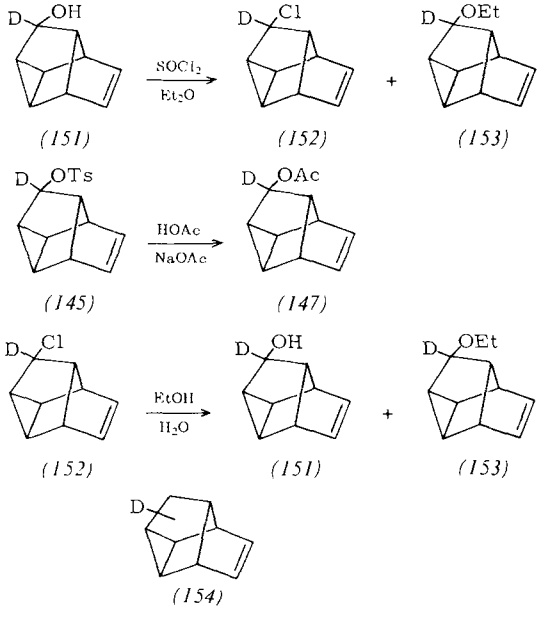

(150)

Also, work by *Freeman* and *Balls* on the related 8-tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonyl cation *(21)* indicated facile rearrangement of the type shown below (see Section 4.11) [48].


(21) *(21')*

The fact that no deuterium scrambling occurred in the solvolysis of *(145)* shows that "leakage" to *(138)* and subsequent homoallylic rearrangement was unfavorable. Apparently cyclopropyl ring opening in *(15)* does not occur because the added two-carbon bridge (C-8 – C-9) causes more strain in the norbornene than in the nortricyclene system. Both the inductive effect and the steric effect of the carbon-carbon double bond may cause the solvolysis rate of *(148)* to be significantly slower than that of *(146)*. The carbonyl frequency of ketone *(144)* indicates that there is a significant rate acceleration in the ionization of *(148)*, probably due to cyclopropylcarbinyl delocalization.

Work by *Klumpp* serves to independently verify the results obtained above on cation *(15)* [49]. By employing a synthesis related to that of *Schleyer* and *Leone*, the tetracyclic compounds *(151)*, *(145)*, and *(152)* were prepared. The solvolytic studies indicated were carried out in an attempt to generate a degenerate cation corresponding to *(15)*. No deuterium scrambling was observed in any of the cases studied. *Klumpp* feels that the cause for nonrearrangement is a high activation energy for the transfer of positive charge between two equivalent cyclopropylcarbinyl-homoallyl configurations within the same molecule [*(15)* and *(15')*]. The Grignard reagent of *(152)* was also prepared, hydrolyzed, and worked up for *(154)*. Interestingly enough, it was found that some deuterium (≈35%) scrambled to C-8 and C-9 under these conditions. An exact interpretation of this result still requires further investigation.


(151) *(152)* *(153)* *(145)* *(147)* *(152)* *(151)* *(153)* *(154)*

The results obtained by both workers clearly show that the tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]non-8-en-5-yl cation *(15)* is another example of a nondegenerate ion despite its possibilities for degenerate rearrangement. The fact that the Grignard reagent of this system rearranged (presumably through a carbanion type intermediate) may be significant, but further studies to determine the mechanism of deuterium scrambling are necessary.

3.4.4. Bicyclo[3.2.2]nona-3,6,8-trien-2-yl Cation

The bicyclo[3.2.2]nona-3,6,8-trien-2-yl cation *(14)*, a vinylog of the 7-norbornadienyl cation, can potentially exhibit degenerate properties through 1,2-vinyl shift mechanisms or through the equivalent homoallylic barbaralyl cations

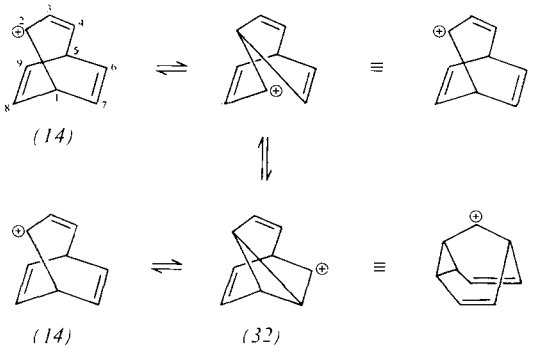
[46] *P. von R. Schleyer* and *R. E. Leone*, J. Amer. Chem. Soc. *90*, 4164 (1968).

[47] *S. J. Cristol, M. K. Seifert, D. W. Johnson*, and *J. B. Juvale*, J. Amer. Chem. Soc. *84*, 3918 (1962).

[48] *P. K. Freeman* and *D. M. Balls*, Tetrahedron Lett. *1967*, 437; *P. K. Freeman, D. M. Balls*, and *J. N. Blazevich*, J. Amer. Chem. Soc. *92*, 2051 (1970).

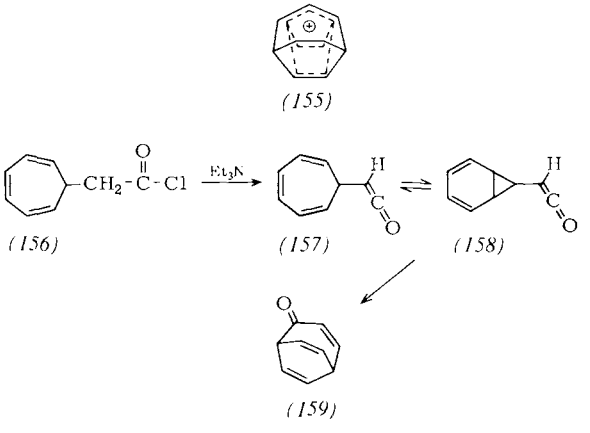
[49] *G. W. Klumpp*, Recl. Trav. Chim. Pays-Bas *87*, 1053 (1968).

(32). Combination of either of these rearrangement processes with allyl resonance (which delocalizes the positive charge between C-2 and C-4) would result in the eventual distribution of a deuterium at C-2 to all nine carbon atoms of the ion.



(14) *(14)* *(32)*

Goldstein and *Odell* sought to determine whether cation *(14)* might exhibit unusual stability or instability as a six π-electron "bicyclotropylium" ion *(155)* [50]. To this end bicyclo[3.2.2]nona-3,6,8-trien-2-one *(159)* was first synthesized. Reduction of *(159)* afforded bicyclo[3.2.2]nona-3,6,8-trien-2-ol *(160)*, which when treated with ethereal $AlCl_3$ gave a 58% yield of tricyclo[3.3.1.$0^{2,8}$]nona-3,6-dien-9-ol or "barbaralol" *(161)*. Similarly, reduction of *(159)* with $LiAlH_4$-$AlCl_3$ gave 30% barbaralol *(161)*, 30% barbaralane *(162)*, and 13% indan *(163)*. No bicyclo[3.2.2]-

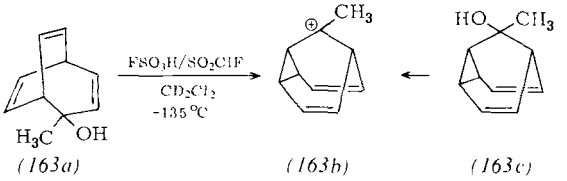


(155)

(156) *(157)* *(158)* *(159)*

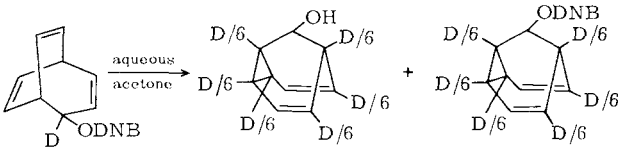
nona-2,6,8-triene *(164)* was found in the product mixture. These observations suggested not only that the barbaralane skeleton is more stable than the bicyclo[3.2.2.]nona-2,6,8-trienyl skeleton, but also that the barbaralyl cation *(32)* is preferred over the bicyclononatrienyl cation *(14)*.

Recent, extensive investigations have confirmed this conclusion. 2-Methyl-2-bicyclo[3.2.2]nona-3,6,8-trienol *(163a)*, easily prepared from ketone *(159)*, gives the 9-methyl-9-barbaralyl cation *(163b)* at −135 °C in FSO_3H-SO_2ClF-CD_2Cl_2; the same ion can be obtained directly from *(163c)* [50a, 50b]. Similarly, under the same conditions *(160)* gives the 9-barbaralyl cation *(32)* [50c]. (The behavior of ions *(32)* and *(163b)* is discussed in Section 3.4.7.)



(163a) *(163b)* *(163c)*

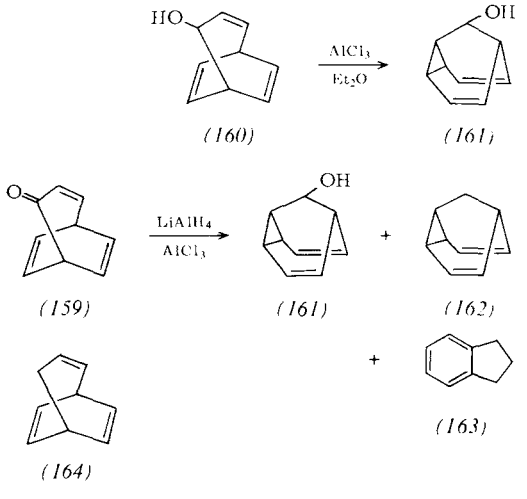
Additional information is revealed by solvolysis of deuterium labeled bicyclo[3.2.2]nona-3,6,8-trien-2-yl 3,5-dinitrobenzoate *(163d)* [50d] and the corresponding *p*-nitrobenzoate [50e]. From *(163d)* only 9-barbaralol *(163e)* and



(163d) *(163e)* *(163f)*

the return product *(163f)* are obtained; in both these products the deuterium label has become virtually statistically scrambled to *six but to only six* of the *nine* available positions, as shown [*]. This demonstrates that the conversion of cation *(14)* to *(32)* is not a simple, direct process. (The possible mechanism whereby the observed scrambling takes place is discussed in Section 3.4.7.)

Experimental results seem to indicate that cation *(14)* possesses no unusual stability as might be depicted by formulation *(155)*. The solvolysis rates of bicyclo[3.2.2]-nona-3,6,8-trien-2-yl derivatives, *e.g.(163d)*, are not accelerated, and, perhaps, are even slower than one might anticipate for allyl-stabilized systems [50d, 50e]. *Goldstein* has attempted to give a theoretical justification for cation *(14)* not possessing exceptional stability in terms of "bicycloaromaticity" [51]. By using MO symmetry arguments,



(160) *(161)* *(159)* *(161)* *(162)* *(163)* *(164)*

[50] *M. J. Goldstein* and *B. G. Odell*, J. Amer. Chem. Soc. *89*, 6356 (1967).

[50a] *P. Ahlberg, D. L. Harris*, and *S. Winstein*, J. Amer. Chem. Soc. *92*, 2146 (1970).

[50b] *P. Ahlberg, J. B. Grutzner, D. L. Harris*, and *S. Winstein*, J. Amer. Chem. Soc. *92*, 3478 (1970).

[50c] *P. Ahlberg, D. L. Harris*, and *S. Winstein*, J. Amer. Chem. Soc. *92*, 4454 (1970).

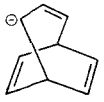
[*] It should be kept in mind that barbaralyl derivatives undergo rapid degenerate Cope rearrangements[58]which contribute to the extent of deuterium scrambling observed in the solvolysis products *(163e)* and *(163f)*.

[50d] *J. C. Barborak* and *P. von R. Schleyer*, J. Amer. Chem. Soc. *92*, 3184 (1970).

[50e] *J. B. Grutzner* and *S. Winstein*, J. Amer. Chem. Soc. *92*, 3186 (1970).

[51] *M. J. Goldstein*, J. Amer. Chem. Soc. *89*, 6357 (1967).

it was shown that the 2-bicyclo[3.2.2]nonatrienyl cation *(14)* should be *destabilized* and *antibicycloaromatic*, but that the corresponding anion *(165)* should be *stabilized* and *bicycloaromatic*. As an experimental verification of this prediction, anion *(165)* was recently prepared by *Winstein* and *Grutzner* and shown by its NMR spectrum to be a delocalized structure *(166)* [52].

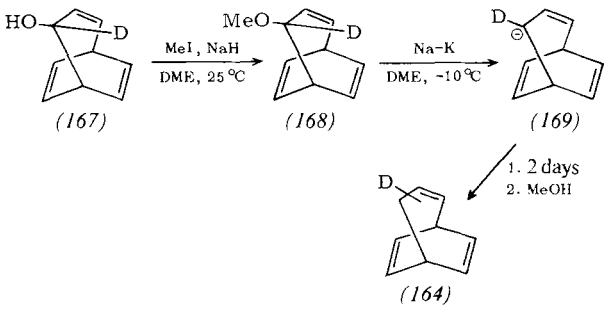


(165)

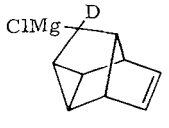


(166)

Another interesting observation was obtained in the work of *Winstein* and *Grutzner* concerning anion *(165)*. Their preliminary experiments indicated the occurrence of a degenerate nine-carbon rearrangement in *(165)* [52]. The sequence outlined below was carried out. The hydrocarbon *(164)* exhibited essentially complete deuterium scrambling to all carbon atoms. The NMR spectrum of *(169)* immediately after preparation showed no scrambling. This carbon degeneracy could be formulated as in the case of cation *(14)* as proceeding through a series of 1,2-vinyl shifts or through a barbaralyl intermediate. This degeneracy is still under investigation, but, together with the work of *Klumpp* on the rearrangements of *(17)* [49], it may indicate that the anions of certain potentially degenerate cation systems can exhibit degenerate properties although the cations do not.



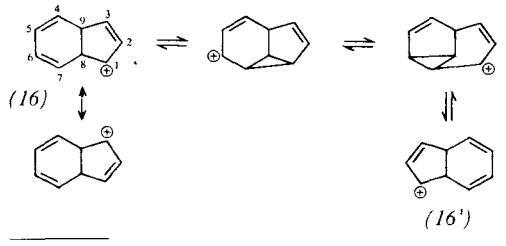
(167) *(168)* *(169)* *(164)*



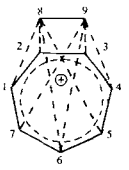
(170)

3.4.5. *cis*-8,9-Dihydro-1-indenyl Cation

The *cis*-8,9-dihydro-1-indenyl cation *(16)* could show degenerate properties through a homoallylic rearrangement followed by a cyclopropylcarbinyl-cyclopropylcarbinyl rearrangement. The combination of these processes with allyl resonance in *(16)* and *(16')* would result in the equivalence of carbon atoms C-1, C-2, C-3, C-4, C-5, C-6, and C-7. This is perhaps best represented by ion intermediate *(171)*, in which the seven equivalent carbons form a tropylium ion type ring with a two carbon bridge rotating above the ring.

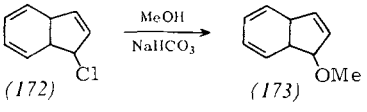


(16) *(16')*

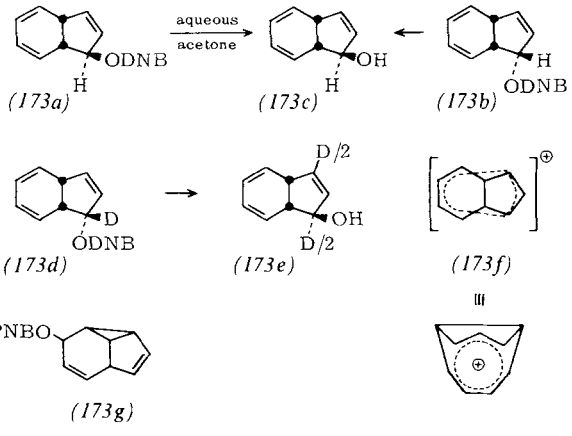


(171)

The above predictions for cation *(16)* have not yet been fully tested experimentally. The methanolysis of 1-chloro-8,9-dihydroindene *(172)* has been carried out, and the product was 1-methoxy-8,9-dihydroindene *(173)* [53]. More recently solvolysis of both *exo (173a)* [54a, 54b] and *endo (173b)* [54a] derivatives of 1-hydroxy-*cis*-8,9-dihydroindene have been studied. In aqueous acetone the product is 1-*exo*-hydroxy-*cis*-8,9-dihydroindene *(173c)*. Studies of labeled *(173d)* under the same conditions give a scrambling pattern in the product *(173e)* which indicates no degeneracy in the intermediate ion *(16)* other than that expected on the basis of allylic resonance [54a].



(172) *(173)*



(173a) *(173c)* *(173b)*

(173d) *(173e)* *(173f)*

(173g)

In particular, no evidence for the formation of the bishomotropylium ion *(173f) on solvolysis* is found, and the same is true for the solvolysis of *(173g)* [54b]. However, ion *(173f)* is formed in $FSO_3H/SO_2ClF/CD_2Cl_2$ solution at −125 to −135 °C from both *(173c)* and the alcohol related to *(173g)* [54b]. Under these conditions, *(173f)* appears to be one of the most stable $C_9H_9^+$ cations and it is the product of rearrangement of the 9-barbaralyl cation *(32)* [50c]. Even the tertiary 9-methyl-9-barbaralyl cation *(163b)* rearranges to a methyl-substituted bishomotropylium ion [50a, 50b].

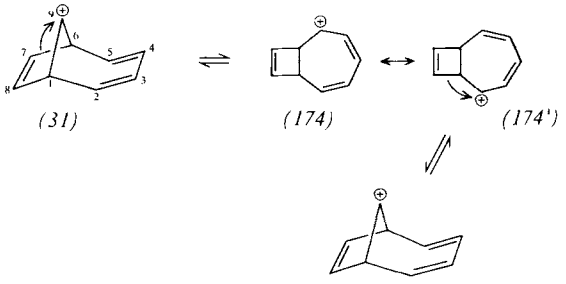
[52] *J. B. Grutzner* and *S. Winstein*, J. Amer. Chem. Soc. *90*, 6562 (1968).

[53] *T. J. Katz* and *P. J. Garratt*, J. Amer. Chem. Soc. *86*, 5194 (1964).

[54] a) *J. C. Barborak* and *P. von R. Schleyer*, unpublished; b) *D. Cook* and *S. Winstein*, personal communication.

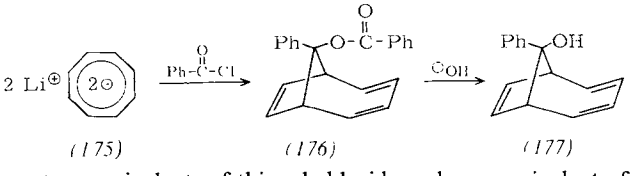
3.4.6. Bicyclo[4.2.1]nona-2,4,7-trien-9-yl Cation

The bicyclo[4.2.1]nona-2,4,7-trien-9-yl cation *(31)*, another vinylog of the 7-norbornadienyl cation, may undergo two types of rearrangement processes which could lead to degeneracy. One of these would be the 1,2-vinyl shift of C-7 or C-8 to form intermediate ion *(174)*. Cation *(174)* after resonance interconversion to *(174')* could then ring expand back to cation *(31')*. Continuous operation of this



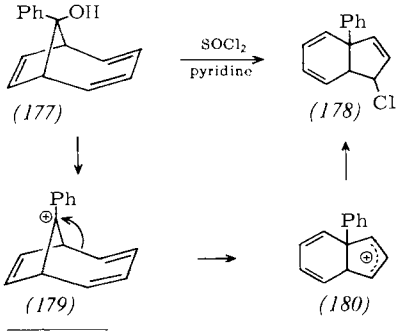
(31) *(174)* *(174')* *(31')*

process, in direct analogy with the mechanism of degeneracy observed for the 7-norbornadienyl cation (see Section 3.3.2), would result in the equivalence of carbon atoms C-1, C-2, C-3, C-4, C-5, C-6, and C-9. A second type of rearrangement in *(31)* would be a 1,2-vinyl shift of C-2 or C-5. This would result in the formation of the dihydroindenyl cation *(16)* which can exhibit degenerate properties as described in Section 3.4.5. The dihydroindenyl rearrangements mix carbon atoms C-2, C-3, C-4, C-5, C-6, C-7, and C-8. Work on the parent bicyclo[4.2.1]nona-2,4,7-trien-9-yl cation *(31)* has not yet been carried out. However, some experiments have been done with the 9-phenyl substituted system, which has been synthetically accessible through the work of *Cantrell* and *Shechter*. These workers prepared compound *(176)* from the reaction of dilithium cyclooctatetraenediide *(175)* with benzoyl chloride[55]. *Kende* and *Bogard* obtained alcohol *(177)* by alkaline hydrolysis of *(176)*[56].Alcohol *(177)* when treated with



(175) *(176)* *(177)*

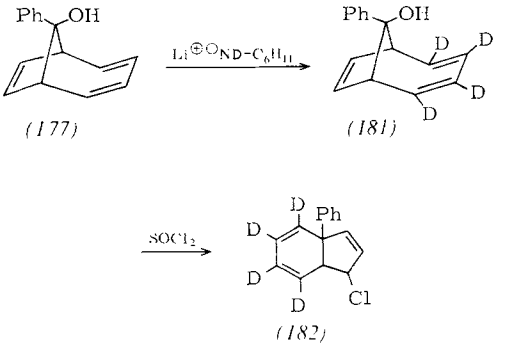
two equivalents of thionyl chloride and one equivalent of pyridine gave a high yield of 1-chloro-9-phenyl-*cis*-8,9-di-



(177) *(178)* *(179)* *(180)*

[55] *T. S. Cantrell* and *H. Shechter*, J. Amer. Chem. Soc. *87*, 3300 (1965).

hydroindene *(178)*[56]. Presumably, the mechanistic path through ions *(179)* and *(180)* is involved. This hypothesis was verified by a labeling experiment[57]. The results seem to indicate that the bicyclo[4.2.1]nonatrienyl cation *(31)*

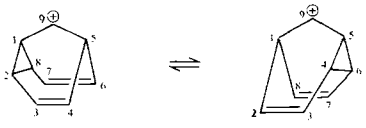


(177) *(181)* *(182)*

would rearrange to the dihydroindenyl cation *(16)*, but that the reverse process is not favorable. No deuterium scrambling was observed in product *(182)*, which indicates that the potential degenerate rearrangements in the dihydroindenyl cation *(16)* may not occur. The interconversion of two $C_9H_9^+$ type ions is also demonstrated by the above experiments.

3.4.7. Barbaralyl or Tricyclo[3.3.1.$0^{2,8}$]nona-3,6-dien-9-yl Cation

The barbaralyl cation *(32)* is unique among the potentially degenerate carbonium ions within the $C_9H_9^+$ group. This cation has the capacity to exhibit degeneracy through a combination of degenerate carbonium ion rearrangements and degenerate Cope rearrangements. The latter possibility exists because the barbaralyl cation *(32)*, like bullvalene[2], contains a homotropylidene structure. This



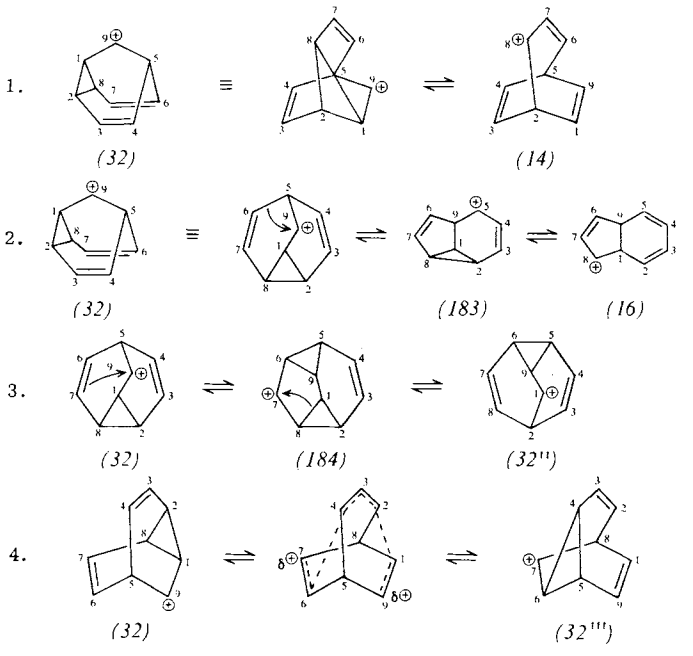
(32) *(32')*

rearrangement causes the interconversion and equivalence of carbon atoms C-1 and C-5, C-2 and C-4, and C-8 and C-6. Some of the potential carbonium ion rearrangements of *(32)* that could lead to degeneracy are shown in Scheme 1.

Mechanism 1) involves the interconversion of the 9-barbaralyl *(32)* and the bicyclo[3.2.2]nonatrienyl *(14)* cations. Since *(14)* has the potential of undergoing complete carbon degeneracy as described in Section 3.4.4, this mechanism would predict complete carbon scrambling in *(32)* also. Such degeneracy may be even easier to achieve. Because of symmetry in the allylic ion *(14)*, many of the carbons are equivalent. If the degenerate Cope rearrangement in *(32)* is rapid, the mere conversion of *(32)* into *(14)* and back again will lead eventually to complete degeneracy.

Mechanism 2) employs a 1,2-vinyl shift to form ion *(183)* which could give rise to either the dihydroindenyl *(16)* or the bishomotropylium *(184)* cations. If this process were reversible, *(32)* would eventually become completely de-

[56] *A. S. Kende* and *T. L. Bogard*, Tetrahedron Lett. *1967*, 3383.
[57] *A. S. Kende*, personal communication.



Scheme 1

generate. This mechanism seems unlikely since precursors to *(16)* and to *(183)* give no barbaralyl products either under solvolysis [53, 54a, 54b] or stable ion conditions [50c, 54b]. Mechanism 3) involves direct formation of the bishomotropylium ion *(184)* by homoallylic rearrangement from *(32)*. As shown [and as implied by *(171)*], ion *(184)* has the potential of extensive automerization, but this process is not rapid under stable ion conditions at $-125\,^{\circ}C$ [50c]. Furthermore, experimental observations show that *(184)* is more stable than *(32)* and does not reconvert, at least in super acid media [50a, 50c]. Thus, even though mechanism 3) can, in principle, give rise to complete scrambling in the 9-barbaralyl cation *(32)*, it does not, in fact, seem to take place.

Mechanism 4) is a synchronous process involving the concerted migration of three bonds. This results in the direct reformation of the 9-barbaralyl cation *(32''')*, but with some of the carbon atoms mixed. After several such rearrangements, carbons 3,7, and 9 would become equivalent, as would the six remaining carbon atoms [keeping the degenerate Cope rearrangement *(32)* $\rightleftharpoons$ *(32')* in mind]. Only recently has the experimental picture of the barbaralyl cation *(32)* become clear. The first evidence was obtained by solvolysis [59]. Contrary to an earlier suggestion [58], 9-barbaralyl tosylate *(185)* was found to be quite reactive; in acetic acid at 16.5 °C it solvolyzed with a first order rate constant of $2.28 \times 10^{-3}\ s^{-1}$ [59]. Solvolysis of



(185) *(186)*

deuterated tosylate *(186)* in acetic acid (sodium acetate buffer, thirty minutes at 25 °C) and in aqueous acetone (80% acetone, one hour at 18 °C) gave barbaralyl acetate *(187)* and barbaralol *(161)*, respectively, as the main products with the deuterium label scrambled to every position [59]. Multiple integrations of the NMR spectra of the products from several solvolytic runs gave the average percentage deuterium distributions as shown in Table 7.

The results obtained show that the potential for carbon degeneracy in the barbaralyl cation *(32)* can be realized. However, the label distributions are not uniquely consistent

Table 7. Solvolysis products of barbaralyl tosylate *(186)* (mean values from several experiments).

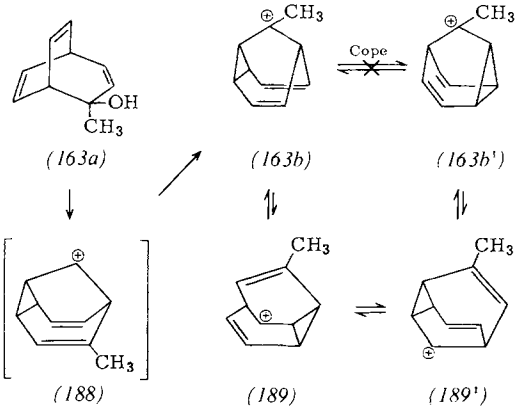


(187), R = Ac
(161), R = H

Position	Solvolysis with HOAc D (%)	Solvolysis with aq. acetone ± 3 %	Statistical D distribution D (%)
9	28.4	53.2	11.1
1,5	7.4	5.2	22.2
2,8,4,6	18.2	1.7	44.4
3,7	46.1	39.9	22.2

with any one mechanism postulated above. The first three mechanisms would predict a statistical deuterium distribution after many rearrangements. Mechanism 4) would predict 33.3% D at C-9 and 66.6% D at C-3, C-7 after many rearrangements. The observed experimental values do indicate a high proportion of deuterium at C-3, C-7, and C-9, particularly in the product derived from solvolysis in aqueous acetone. Thus, the results seem best explained by a combination of mechanism 4), or its equivalent, as the primary process responsible for deuterium scrambling with another mechanism that allows complete label scrambling.

The existence of the three-fold degenerate rearrangement process [mechanism 4)] in the 9-barbaralyl cation *(32)* has been confirmed in two additional ways. As described in Section 3.4.4, solvolysis of deuterium-labeled bicyclo-[3.2.2]nonatrien-2-yl derivatives, *e.g. (163d)*, gave rise to 9-barbaralyl products with the deuterium scrambled to six, but only to six positions, *e.g. (163e)* and *(163f)*, in accord with mechanism 4) [50d, 50e].



The "methyl-labeled" bicyclononatriene *(163a)* behaves somewhat differently in FSO_3H-SO_2ClF solution at low temperature [50a, 50b]. The expected ion *(188)* is not observed; rather the more stable tertiary species *(163b)* is first produced. This ion undergoes a degenerate rearrangement ($\Delta G^{\neq} = 7.3$ kcal/mole at $-121\,^{\circ}C$) which renders the "left-hand" and "right-hand" sides of the molecule equivalent [50b]. Although this equivalence might easily be

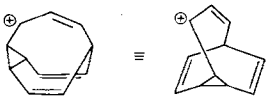
[58] *W. von E. Doering, B. M. Ferrier, E. T. Fossel, J. H. Hartenstein, M. Jones, Jr., G. Klumpp, R. M. Rubin,* and *M. Saunders,* Tetrahedron *23*, 3943 (1967).

[59] *J. C. Barborak, J. Daub, D. M. Follweiler,* and *P. von R. Schleyer,* J. Amer. Chem. Soc. *91*, 7760 (1969).

pictured as a degenerate Cope rearrangement, *(163b)* ⇌ *(163b')*, analysis of the NMR spectrum shows that this is not actually taking place. Rather, the interconversion probably occurs *via (189)* and *(189')*, *i.e.*, mechanism 4) [50b]. At slightly higher temperatures ($\Delta G^{\neq}$ = 11 kcal/mole at −116 °C) ion *(163b)* rearranges irreversibly to a methyl-substituted bishomotropylium ion [50a, 50b].

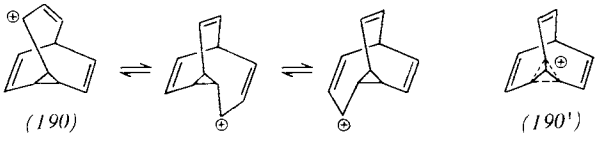
The crowning achievement is the direct observation of a single-line NMR spectrum for the 9-barbaralyl cation *(32)* [50c]. This demonstrates that even at −135 °C the degenerate rearrangements leading to complete scrambling of all nine (CH) units are fast on the NMR time scale! For bullvalene, the same result is not achieved until the temperature ist 200 °C higher [2]. Mechanism 1) [*via* the less stable ion *(14)*] is the process implicated for complete degeneracy; the process suggested by mechanism 4) must be even faster. At −125 °C, *(32)* rearranges irreversibly to *(184)*.

In connection with the barbaralyl cation *(32)* the carbonium ion *(190)* derived from homobullvalene is of interest. Cation *(190)*, a $C_{11}H_{11}^{+}$ vinylog of the barbaralyl cation



(190)

(32), also has the potential to combine degenerate carbonium ion rearrangements with degenerate Cope rearrangements to make *(190)* completely degenerate. Through cyclopropylcarbinyl-cyclopropylcarbinyl rearrangements, cation *(190)* could be viewed as structure *(190')*, or its equivalent, which has C_{3v} symmetry. This formulation makes cation *(190)* a carbonium-ion equivalent of bullvalene, which also has C_{3v} symmetry [2]. Combination of this charge delocalization with allyl resonance and the three-fold degenerate Cope rearrangement would distribute the positive charge to every carbon atom of cation *(190)*. The monohalocarbene adducts of bullvalene could presumably serve as solvolytic precursors to cation *(190)*.



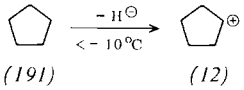
(190) *(190')*

4. Other Degenerate Carbonium Ions

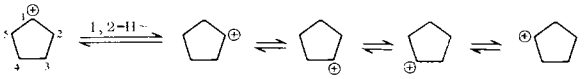
There are a number of degenerate carbonium ions not having a $(CH)_n^{+}$ empirical formula which have been studied in detail. These ions can exhibit forms of carbon degeneracy, hydrogen degeneracy, and combinations of both. Most ions of this type do not have the potential for complete degeneracy, and in this sense they contrast with ions of the $(CH)_n^{+}$ series. Also, there is no apparent systematization within this group of ions. Many of these cations have been generated in highly acidic solvents and studied directly by NMR.

4.1. Cyclopentyl Cation

Olah and *Lukas* investigated the cyclopentyl cation *(12)* by examining the NMR spectrum of the ion generated in highly acidic solvents [60]. They found that when cyclopentane *(191)* was dissolved in FSO_3H-SbF_5 or HF-SbF_5 diluted with SO_2ClF below −10 °C, the cyclopentyl cation *(12)* was formed by hydride abstraction. The ion exhibited a single peak at δ 4.75 and the NMR spectrum remained unchanged down to −130 °C. This indicated that *(12)* was undergoing a series of rapid 1,2-hydride shifts that resulted in complete hydrogen degeneracy. No study of possible carbon degeneracy in ion *(12)* has been reported.

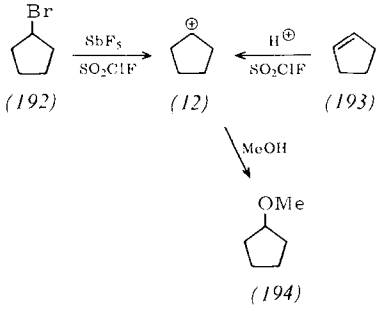


(191) *(12)*



(12)

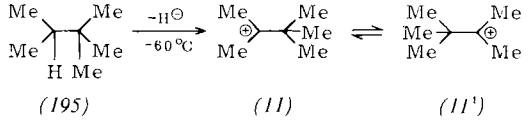
Cation *(12)* was also generated from cyclopentyl bromide *(192)* and cyclopentene *(193)* as shown below [60]. Quenching of these solutions of *(12)* with methanol gave cyclopentyl methyl ether *(194)* in high yield.



(192) *(12)* *(193)* *(194)*

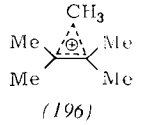
4.2. Dimethyl-*tert*-butylcarbonium Ion

Olah and *Lukas* observed that when 2,2,3-trimethylbutane *(195)* was dissolved in $FSO_3H-SbF_5-SO_2ClF$ at −60 °C, the dimethyl-*tert*-butylcarbonium ion *(11)* was generated [61]. The NMR spectrum of *(11)* showed a single sharp singlet at δ 2.86. The equivalence of all five methyl groups in *(11)* was attributed to fast 1,2-methyl shifts. This carbonium ion serves as a good example of twofold partial



(195) *(11)* *(11')*

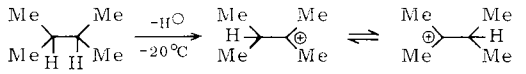
carbon degeneracy. The fact that only one peak was observed in the spectrum of *(11)* rules out a static nonclassical ion structure such as *(196)* which would exhibit two distinct methyl resonances.



(196)

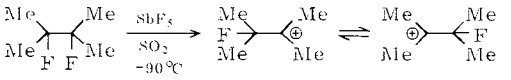
[60] *G. A. Olah* and *J. Lukas*, J. Amer. Chem. Soc. *90*, 933 (1968).
[61] *G. A. Olah* and *J. Lukas*, J. Amer. Chem. Soc. *89*, 4739 (1967).

The dimethylisopropylcarbonium ion *(197)* and the dimethylfluoroisopropylcarbonium ion *(199)* both are similar to cation *(11)*. Ion *(197)*, generated from 2,3-dimethylbutane *(198)* in FSO_3H-SbF_5 exhibited only a doublet at δ 3.32 (J = 4.2 Hz) for the four methyl groups [61]. The equivalence of all methyl groups was best interpreted in



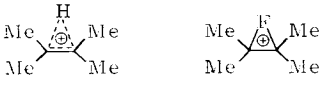
(198) *(197)* *(197')*

terms of the rapidly equilibrating ions *(197)* and *(197')* in which the single hydrogen undergoes a degenerate 1,2-shift. Ion *(199)*, obtained from 2,3-difluoro-2,3-dimethylbutane *(200)*, showed a single doublet at δ 3.10 (J = 11 Hz) for the



(200) *(199)* *(199')*

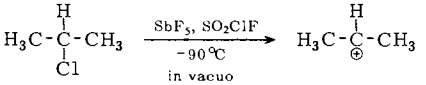
proton resonance spectrum [62]. This observation is compatible with ion *(199)* existing as the doubly degenerate equilibrating cation pair *(199)* and *(199')*. Rapid 1,2-fluorine shifts are responsible for the equivalence of the four methyl groups. Structures *(201)* and *(202)* were ruled out on the basis of chemical shift comparisons of the hydrogen and fluorine in *(197)* and *(199)* with known species of similar structure.



(201) *(202)*

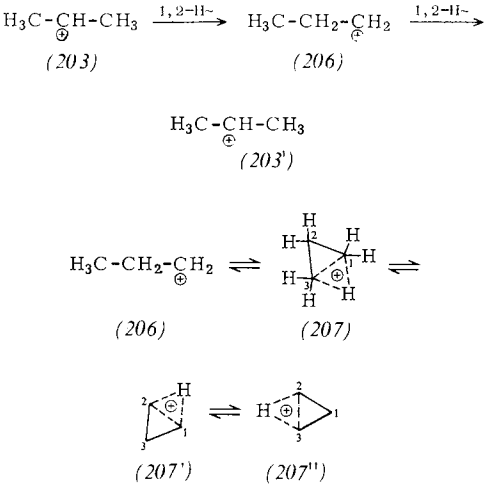
4.3. Isopropyl Cation and *sec*-Butyl Cation

Saunders and *Hagen* have studied the isopropyl cation *(203)* and found that this ion exhibited degenerate properties in NMR solvents [63]. The cation was prepared from isopropyl chloride *(205)* as shown below. At temperatures below 0 °C ion *(203)* showed two peaks, a doublet for the



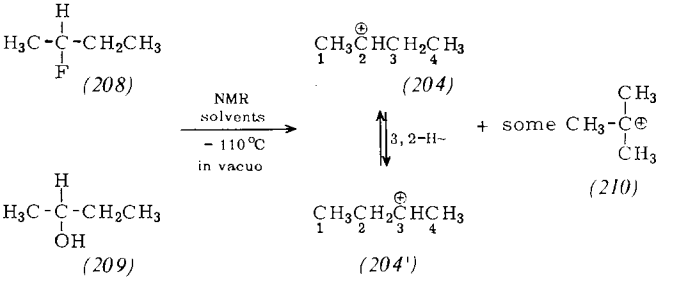
(205) *(203)*

methyl groups at high field and a septet for the methine hydrogen at lower field strength. Over the range from 0 to 40 °C the spectrum changed in a manner indicating interchange between the two types of protons present. The simplest mechanism for this interchange is reversible rearrangement to *n*-propyl cation *(206)*. The activation energy determined for this mechanism was 16.4 ± 0.4 kcal/mole. A further process which might be involved is rearrangement of the intermediate *n*-propyl cation *(206)* to protonated cyclopropane *(207)* before return to *(203)*. Proton scrambling in protonated cyclopropane *(207)* is well documented, so complete mixing of all protons could occur before return to *(206)* [64].



(203) *(206)* *(203')* *(206)* *(207)* *(207')* *(207'')*

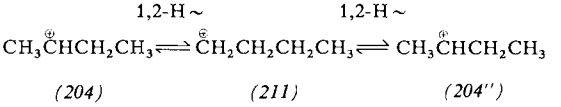
Saunders and his co-workers also studied the *sec*-butyl cation *(204)*, prepared by reaction of 2-fluorobutane *(208)* or 2-butanol *(209)* with strongly acidic NMR solvents at −110 °C in a vacuum line [65]. The NMR spectrum at low temperature consisted of two peaks (plus a sharp singlet due to *tert*-butyl cation *(210)* impurity, formed in the preparation). These two peaks were assigned to the 1 and



(208) *(204)* *(209)* *(204')* *(210)*

4 and 2 and 3 protons of *(204)* averaged by rapid degenerate 3,2-hydride shifts (see above). The activation energy for this process was estimated as approximately 6 kcal/mole. As the cation *(204)* sample was warmed from −110 to −40 °C the two peaks broadened and then coalesced to a sharp singlet. The *tert*-butyl peak remained unchanged in this temperature range. Above −40 °C conversion of *(204)* into *(210)* occurred fairly rapidly.

The single absorption peak for all positions in *(204)* at higher temperatures indicates complete equivalence of all hydrogens. One process for this could be reversible rearrangement to the primary *n*-butyl cation *(211)*; this is one of the possible mechanisms advanced for the isopropyl cation *(203)*. However, the energy barrier for the complete proton equivalence in *(204)* is much lower than in



(204) *(211)* *(204'')*

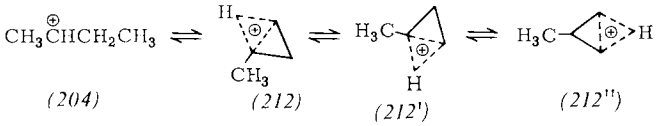
[62] *G. A. Olah* and *J. M. Bollinger*, J. Amer. Chem. Soc. *89*, 4744 (1967).

[63] a) *M. Saunders* and *E. L. Hagen*, J. Amer. Chem. Soc. *90*, 6881 (1968); see also b) *G. A. Olah* and *A. M. White*, J. Amer. Chem. Soc. *91*, 5801 (1969).

[64] For a review on protonated cyclopropanes see *C. J. Collins*, Chem. Rev. *69*, 543 (1969); see also ref. [12].

[65] *M. Saunders*, *E. L. Hagen*, and *J. Rosenfeld*, J. Amer. Chem. Soc. *90*, 6882 (1968).

(203); this tends to disfavor such a mechanism for *(204)*. A better mechanism appears to be cyclization to a protonated methylcyclopropane *(212)*, followed by proton scrambling and reopening to *(204)*. This mechanism

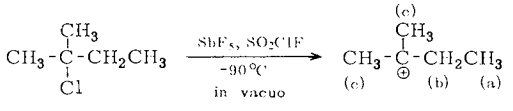


(204) *(212)* *(212')* *(212'')*

would predict an activation energy of approximately 7.5 ± 0.1 kcal/mole for complete mixing of all hydrogens (compare to value of 16.4 ± 0.4 kcal/mole obtained for the process of complete hydrogen mixing in the isopropyl cation).

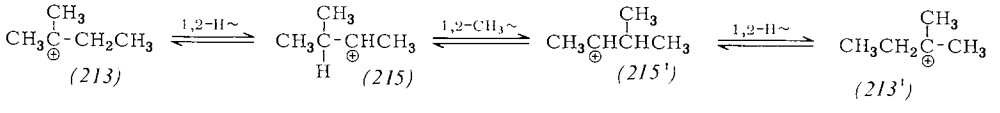
4.4. *tert*-Amyl Cation

Saunders and *Hagen* studied the temperature dependent NMR spectrum of the *tert*-amyl cation *(213)* and observed that this ion exhibited partial degeneracy [66]. Cation *(213)* was prepared by allowing 2-chloro-2-methylbutane *(214)* to react with an excess of antimony pentafluoride in sulfuryl chlorofluoride in a vacuum line at −90 °C. Below −40 °C the NMR spectrum consisted of peaks at τ 7.70 (triplet), 5.58 (triplet), and 5.25 (multiplet) assigned to protons a, c, and b, respectively. As the cation solution was warmed above −40 °C, the triplets for the methyl protons



(214) *(213)*

broadened and then coalesced, but the multiplet for the methylene protons remained unchanged. Upon recooling the sample, the original spectrum was reobtained. The spectral changes demonstrated interchange of the two types of methyl groups without mixing in the CH_2 protons. This is best explained by a mechanistic scheme in which first a 1,2-hydride shift occurs, then a degenerate 1,2-methyl shift followed by another hydride shift. Mechanisms

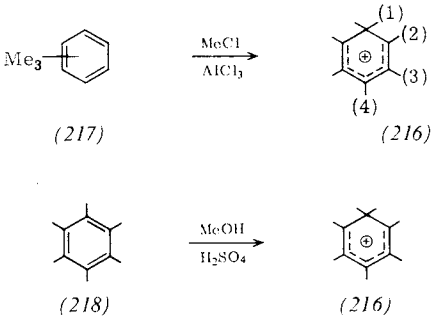


(213) *(215)* *(215')* *(213')*

involving primary carbonium ions are considered less likely and could also involve complete mixing of all types of hydrogens. *Brouwer* and *Mackor* also studied the *tert*-amyl cation *(213)* in $HF-SbF_5$ solution and observed the same reversible line broadening at temperatures above −20 °C for the different methyl groups [67a]. *Brouwer* [67b] examined the system in detail and independently came to the same conclusions as *Saunders* and *Hagen* concerning the nature of the equilibrium process. Recently, higher-temperature studies have shown that above 130 °C the methyl and methylene signals coalesce [68].

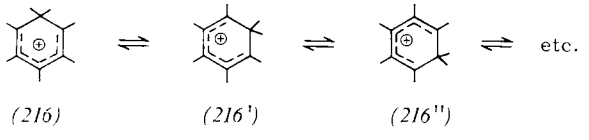
4.5. Heptamethylbenzenonium Ion

The heptamethylbenzenonium ion *(216)* represents one of the earliest studied examples of a degenerate carbonium ion. Cation *(216)* was originally synthesized over ten years ago by the exhaustive methylation of trimethylbenzenes *(217)* with methyl chloride in the presence of aluminum chloride or by the reaction of hexamethylbenzene *(218)* with methanol in the presence of concentrated sulfuric acid [69]. The NMR spectrum of ion *(216)* at 25 °C showed



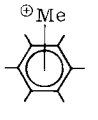
(217) *(216)* *(218)* *(216)*

four resonance signals in the ratio of 1:2:2:2 with the three lowest field peaks assigned to the methyl groups labeled (4), (3), and (2), respectively, and the highest field peak due to the gem dimethyl groups labeled (1). *Saunders* studied the NMR spectrum of *(216)* at higher temperatures and observed that the three low field peaks coalesced into a broad singlet while the high field peak remained a singlet, although broadened, at ≈70 °C [70]. This was interpreted in terms of *(216)* undergoing a series of rapid degenerate 1,2-methyl shifts.



(216) *(216')* *(216'')*

Alternatively, a "random" shift mechanism could be imagined in which a methyl group leaving the saturated carbon might jump from one ring carbon to another in a series of steps before becoming reattached to one of the ring carbons. The intermediate for such a process is represented by *(219)*. Recently, *Derendyaev*, *Mamatyuk*, and *Koptyug* studied the NMR spectrum of *(216)* with the aid



(219)

of multiple resonance techniques and established that the "random" migration of a methyl group did not play a

[66] *M. Saunders* and *E. L. Hagen*, J. Amer. Chem. Soc. *90*, 2436 (1968).

[67] a) *D. M. Brouwer* and *E. L. Mackor*, Proc. Chem. Soc. *1964*, 147; b) *D. M. Brouwer*, Recl. Trav. Chim. Pays-Bas *87*, 210 (1968).

[68] *M. Saunders* and *J. Rosenfeld*, J. Amer. Chem. Soc. *91*, 7756 (1969).

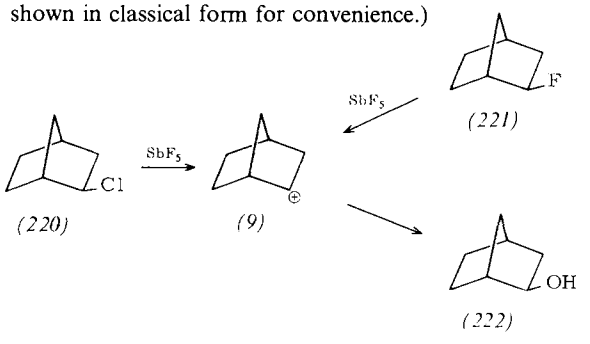
[69] *W. von E. Doering*, *M. Saunders*, *H. G. Boyton*, *H. W. Earhart*, *E. F. Wadley*, *W. R. Edwards*, and *G. Laber*, Tetrahedron *4*, 178 (1958).

[70] *M. Saunders* in *A. Ehrenberg*, *B. G. Mahmström*, and *T. Vänngard*: Magnetic Resonance in Biological Systems. Pergamon Press, New York 1967, p. 90.

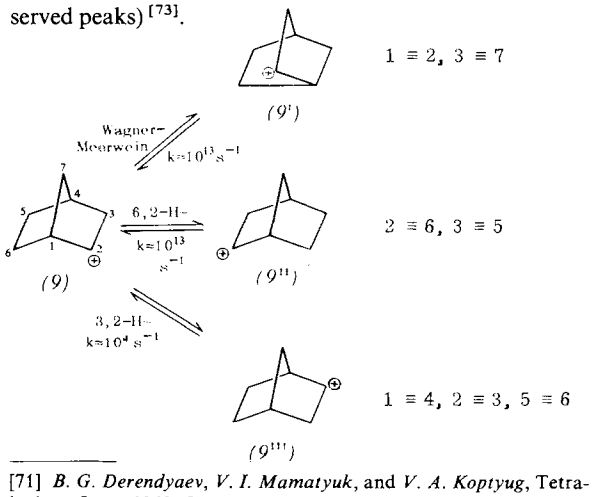
significant role in the rearrangement of *(216)* [71]. It was concluded that the intramolecular 1,2-methyl shift mechanism was responsible for the observed spectral changes. Analogous 1,2-hydride shifts have recently been demonstrated in the parent benzenonium ion [71a].

4.6. 2-Norbornyl Cation

Schleyer, Watts, Fort, Comisarow, and *Olah* were the first workers to report the direct observation of the NMR spectrum (60 MHz) of the 2-norbornyl cation *(9)* [72]. The ion was prepared by dissolving either 2-*exo*-norbornyl chloride *(220)* or 2-*exo*-norbornyl fluoride *(221)* in SbF_5 or in SbF_5-liquid SO_2. The NMR spectrum in the temperature range -5 to $+37\,°C$ consists of a single broad band at δ 3.75, indicating that all the protons (and probably all the carbons) are equivalent. At $-60\,°C$ the spectrum separates into three bands of relative areas 4 (δ 5.35), 1 (δ 3.15), and 6 (δ 2.20). Further cooling to $-120\,°C$ produced no other changes in the spectrum of *(9)*. Evidence for *(9)* in solution was obtained by quenching the cation solution with water; this produced 2-*exo*-norbornanol *(222)*. (The ion *(9)* is shown in classical form for convenience.)

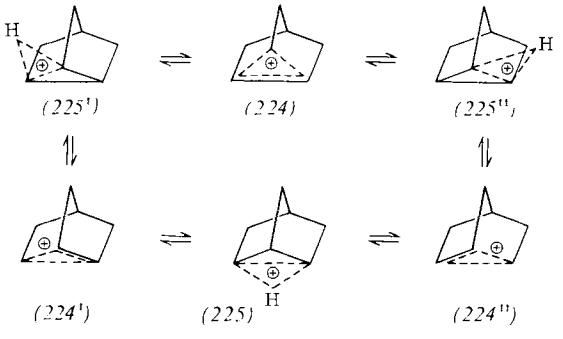


The above results were interpreted in terms of the 2-norbornyl cation *(9)* undergoing three reaction processes: (a) a Wagner-Meerwein rearrangement *(9)* $\rightarrow$ *(9')*, occurring rapidly over the temperature range studied; (b) a 6,2-hydride shift *(9)* $\rightarrow$ *(9'')*, also occurring rapidly over the temperature range studied; and (c) a 3,2-hydride shift *(9)* $\rightarrow$ *(9''')*, which is fast at room temperature but slow below $-23\,°C$ (temperature of coalescence of the 3 observed peaks) [73].



At $-60\,°C$ the 3,2-hydride shift is not occurring rapidly enough to be significant. The three peak NMR spectrum can be interpreted in terms of positions made equivalent by the Wagner-Meerwein rearrangement and the 6,2-hydride shift. The peak of area 4 is due to protons at C-1, C-2, and C-6; the peak of area 1 is due to the one proton at C-4; the peak of area 6 is due to protons at C-3, C-5, and C-7. Addition of the 3,2-hydride shift at higher temperatures makes all positions equivalent by interchanging C-1 with C-4, C-2 with C-3, and C-5 with C-6. Thus, by this interpretation the 2-norbornyl cation *(9)* represents an example of combined carbon and hydrogen degeneracies which results in the equivalence of all carbon and hydrogen atoms.

Jensen and *Beck* observed that the best defined NMR spectrum (60 MHz) of the 2-norbornyl cation *(9)* was obtained by treating 2-norbornyl bromide *(223)* with gallium tribromide in SO_2 solvent [74]. The NMR spectrum of *(9)* obtained by these workers exhibited a fine structure not recorded by *Schleyer, Olah*, and co-workers. The spectrum recorded by *Jensen* and *Beck* at $-80\,°C$ consisted of resonance signals at δ 5.2, 3.1, and 2.1 with relative intensities of 4:1:6 and observed multiplicities of 7,1, and 6 respectively. These workers feel that the observed slow 3,2-hydride shifts are not consistent with a classical ion *(9)* being the stable species observed in the NMR studies, since secondary, secondary-hydride shifts should occur in classical *(9)* with a lower activation energy than that observed. They believe the observed spectrum and rates of proton exchange can be adequately accounted for on the basis that alkyl and hydrogen bridged ions *(224)* and *(225)* occur in the system as stable forms, or one of these forms is a transition state and the other a stable species.



Olah, Commeyras, and *Lui* generated the norbornyl cation in strong acid solutions from the precursors shown in Scheme 2 [75].

These workers obtained a 100 MHz NMR resonance spectrum of this cation which showed the fine structure reported by *Jensen* and *Beck*. They also obtained a Raman spectrum of the cation in strong acid solution and concluded that the ion was best represented as a protonated nortricyclene [75]. These authors felt that either a corner-protonated nortricyclonium ion *(224)* or an edge-protonated nortricyclonium ion *(225)* was most compatible with the NMR and Raman spectra. On this basis the observed high energy barrier for a 3,2-hydride shift in the 2-norbornyl cation *(9)* arises from the necessary transition of either ion

[71] *B. G. Derendyaev, V. I. Mamatyuk*, and *V. A. Koptyug*, Tetrahedron Lett. *1969*, 5.

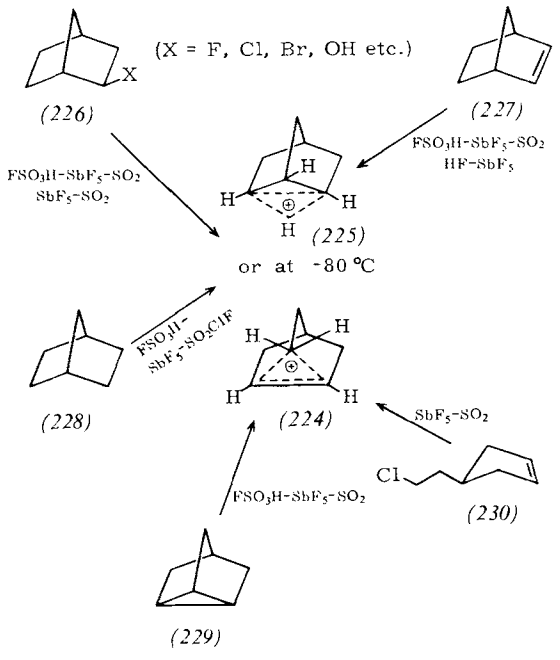
[71a] *G. A. Olah, R. H. Schlosberg, D. P. Kelly*, and *G. D. Mateescu*, J. Amer. Chem. Soc. *92*, 2546 (1970).

[72] *P. von R. Schleyer, W. E. Watts, R. C. Fort, Jr., M. B. Comisarow*, and *G. A. Olah*, J. Amer. Chem. Soc. *86*, 5679 (1964).

[73] *M. Saunders, P. von R. Schleyer*, and *G. A. Olah*, J. Amer. Chem. Soc. *86*, 5680 (1964).

[74] *F. R. Jensen* and *B. H. Beck*, Tetrahedron Lett. *1966*, 4287.

[75] *G. A. Olah, A. Commeyras*, and *C. Y. Lui*, J. Amer. Chem. Soc. *90*, 3882 (1968).



(224) or (225) to the classical 2-norbornyl cation (9) before the 3,2-hydride shift occurs. Ion (224) or (225) at low temperatures would then represent what was originally assigned for the 2-norbornyl cation (9) as the result of a combination of Wagner-Meerwein rearrangements and 6,2-hydride shifts.

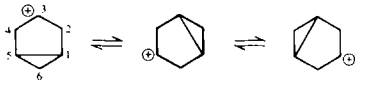
Recently *Olah* and *White* examined the ^{13}C-NMR spectrum of the norbornyl cation generated in SbF_5-SO_2 from 2-*exo*-norbornyl chloride (220) at $-70\,^{\circ}C$[76,77]. This spectrum consisted of three peaks: 1) a pentuplet (J = 53.3 Hz) at 101.8 ppm (from $^{13}CS_2$) for three equivalent carbons associated with four equivalent protons; 2) a triplet (J = 140.2 Hz) at 162.5 ppm for three equivalent carbons each associated with two equivalent protons; and 3) a doublet (J = 153 Hz) at 156.1 ppm for one carbon associated with one proton.

This spectrum is most consistent with rapidly interconverting edge-protonated nortricyclonium ions [(225), (225'), and (225'')] or with rapidly interconverting corner-protonated nortricyclonium ions [(224), (224'), and (224'')]. The equilibrating classical 2-norbornyl cation (9) is not in accord with the low-temperature Raman, proton, and carbon NMR spectra.

To determine whether the edge-protonated ion (225) or the corner-protonated species (224) is the more stable cation, *Olah* and *White* recorded the 100 MHz proton NMR spectrum of the norbornyl cation at temperatures down to $-156\,^{\circ}C$[76,77]. At $-120\,^{\circ}C$, the spectrum was identical with that described previously. In the temperature range -128 to $-150\,^{\circ}C$ the low-field peak due to the four equilibrating protonated cyclopropane ring protons broadened and then separated into two resonances each of relative area 2 at δ 3.05 and 6.59. The high-field resonance, due to the six methylene protons, also broadened, developing a shoulder at δ 1.70. The peak at δ 2.82 due to the single bridgehead proton remained unchanged. This spectrum is best explained (in conjunction with the data above) in terms of the nonclassical corner-protonated ion (224) structure. Cation (224) represents the most stable ion in strong acid solution with ions like (225) as transition states between forms of (224).

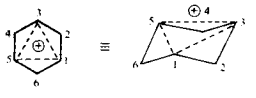
4.7. 3-Bicyclo[3.1.0]hexyl Cation

The 3-bicyclo[3.1.0]hexyl cation (231) could exhibit threefold carbon degeneracy by means of homocyclopropylcarbinyl rearrangements as shown below. Alternatively, this ion could exist in the trishomocyclopropenyl cation



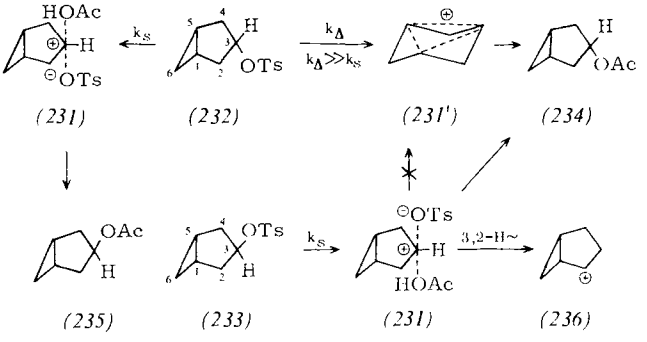
(231)

form (231'), in which positions 1, 3, and 5 as well as 2, 4, and 6 are equivalent to each other due to the charge delocalized structure. According to the definition advanced in Section 1, the 3-bicyclo[3.1.0]hexyl cation can only exhibit true degenerate rearrangements if it exists as the rapidly equilibrating set of ions. Structure (231') is a homoaromatic analog of the cyclopropenyl cation and would simply exhibit threefold equivalence of positions.



(231')

Winstein and his co-workers have studied thoroughly the solvolysis of *cis*-3-bicyclo[3.1.0]hexyl tosylate (232) and *trans*-3-bicyclo[3.1.0]hexyl tosylate (233)[43,78]. These investigations provide strong evidence that the acetolysis of the *cis* isomer proceeds primarily through the trishomocyclopropenyl cation (231'), while that of the *trans* isomer proceeds primarily through cation (231), which is not a rapidly equilibrating species.



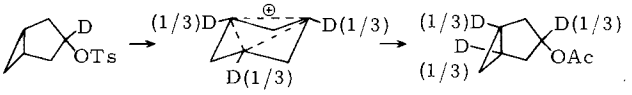
Evidence for this mechanistic scheme is the following: 1) The rate of solvolysis of (232) is faster that that of (233). 2) The value of k_Δ is approximately 50 times that of k_s for the solvolysis of (232). 3) The solvolysis of (232) exhibits a special salt effect, while that of (233) does not. 4) The exclusive product of solvolysis of (232) is the *cis*-acetate (234) with essentially complete retention of configuration.

[76] *G. A. Olah* and *A. M. White*, J. Amer. Chem. Soc. *91*, 3954 (1969).

[77] *G. A. Olah, A. M. White, J. R. DeMember, A. Commeyras*, and *C. Y. Liu*, J. Amer. Chem. Soc. *92*, 4627 (1970).

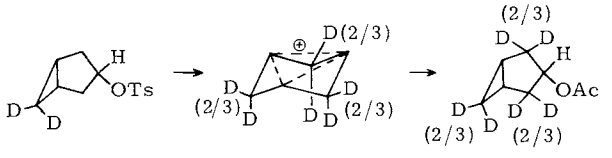
[78] *S. Winstein*, Aromaticity, Internat. Symp. in Sheffield. The Chemical Society, London, Special Publ. No. 21, p. 16.

The solvolysis of *(233)* gives several products, some of which are derived from ion *(236)*. 5) Solvolysis of *cis*-3-deuteriobicyclo[3.1.0]hexyl tosylate *(237)* gives product *cis*-acetate *(238)* with one-third of a deuterium distributed at positions 3, 5, and 1.

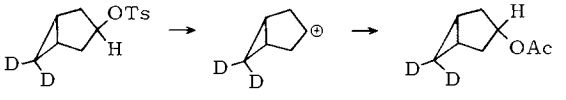


(237) *(238)*

Similarly, solvolysis of the 6,6-dideuterated isomer *(239)* gives a product *cis*-acetate with 1.35 cyclopropane methylene protons. This result is within experimental error of the value 1.33 predicted for the trishomocyclopropenyl intermediate. The *trans* isomer product *(242)* showed no cyclopropane methylene protons.

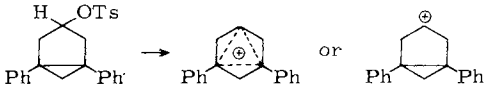


(239) *(240)*



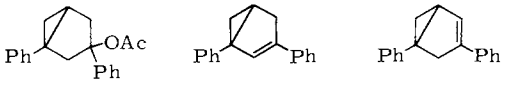
(241) *(242)*

Corey and *Uda* have studied the solvolysis of *cis*-1,5-diphenylbicyclo[3.1.0]hex-3-yl tosylate *(243)* to form either cation *(244)* or *(245)* [79]. Acetolysis of *(243)* gave a rate slower than that of *(232)* with the formation of *(246)*,



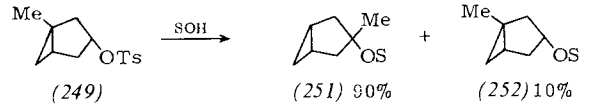
(243) *(244)* *(245)*

(247), and *(248)* as products. These authors feel that these results are inconsistent with the trishomocyclopropenyl



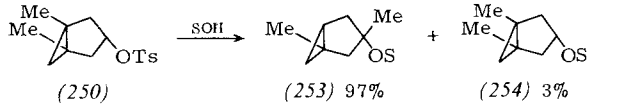
(246) *(247)* *(248)*

cation formulation *(244)*. However, phenyl substituent rate effects are notably complicated by opposing inductive and resonance effects [80]. *Winstein* has reported the solvolysis and products of the *cis*-monomethyl and *cis*-dimethyl-substituted bicyclo[3.1.0]hex-3-yl tosylates *(249)* and *(250)* [78]. The stereochemistry of the products and the relative rate increases of these methyl-substituted compounds compared to the parent system *(232)* were said to be consistent with the formation of the trishomocyclopropenyl cations *(255)* and *(256)* as intermediates in



(249) *(251)* 90% *(252)* 10%

$k(249)/k(232) = 5.1$



(250) *(253)* 97% *(254)* 3%

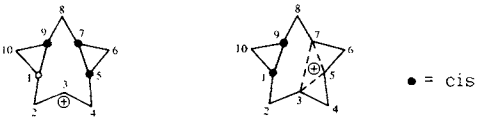
$k(250)/k(232) = 7.0$



(231') *(255)* *(256)*

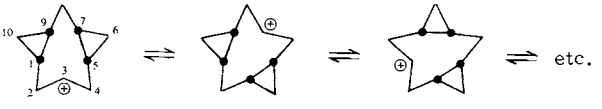
these solvolyses. However, based on previous examples for rate enhancements due to methyl substituents on charged delocalized structures [15,81], the value of 7.0 for $k(250)/k(232)$ is considerably lower than expected. The value should be closer to $(5.1)^2 = 26.1$ for the intermediate *(256)*.

In connection with the 3-bicyclo[3.1.0]hexyl cation, the 3-tricyclo[7.1.0.0^{5,7}]decyl cation *(257)* is also of interest [78].



(257) *(258)*

Ion *(257)* contains two *cis*-3-bicyclo[3.1.0]hexyl moieties within the same cation. If delocalization similar to that observed in the trishomocyclopropenyl cation *(231')* were to take place, ion *(258)* would be formed with positions 6 and 4 equivalent. On the other hand, if *(257)* were to exist as a rapidly equilibrating set of ions as shown then the positions 2, 4, 6, 8, and 10 would be equivalent and this would constitute an example of fivefold degeneracy. *Winstein*, *Bruck*, *Radlick*, and *Baker* studied the solvolysis of the tetradeuterated 3-tricyclo[7.1.0.0^{5,7}]decyl tosylate *(259)* and isolated the products [82].



(257)

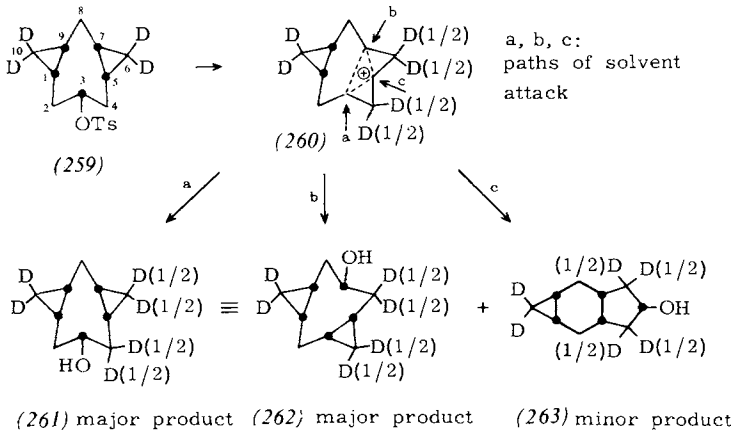
The fully protonated starting tosylate shows 2.0 cyclopropane methylene protons at τ 10.3 in the NMR spectrum, while the tetradeuterated tosylate *(259)* gives acetolysis products *(261)* and *(262)* with 0.52 protons at τ 10.3. This is in accord with ion intermediate *(260)* shown above, but is not consistent with a rapidly equilibrating set of ions arising from *(257)*. The latter mechanism would predict 1.20 cyclopropane methylene protons at τ 10.3. These results indicate participation of only one cyclopropane ring in the 3-tricyclo[7.1.0.0^{5,7}]decyl cation even though participation by both rings would seem to be possible. This is a situation similar to that observed by *Coates* and *Kirkpatrick* for the 9-pentacyclo[4.3.0.0^{2,4}.0^{3,8}.0^{5,7}]nonyl cation *(19)* [44].

[79] *E. J. Corey* and *H. Uda*, J. Amer. Chem. Soc. *85*, 1788 (1963).

[80] *G. D. Sargent*, Quart. Rev. Chem. Soc. *20*, 367 (1966).

[81] *P. D. Bartlett* and *G. D. Sargent*, J. Amer. Chem. Soc. *87*, 1297 (1965); *P. G. Gassman* and *D. S. Patton*, *ibid. 91*, 2160 (1969).

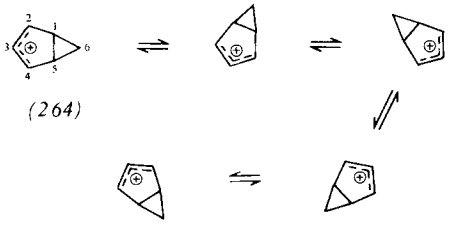
[82] *S. Winstein*, *P. Bruck*, *P. Radlick*, and *R. Baker*, J. Amer. Chem. Soc. *86*, 1867 (1964).



(259) (260) (261) major product (262) major product (263) minor product

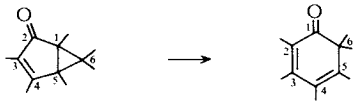
4.8. Bicyclo[3.1.0]hex-3-en-2-yl Cation

Swatton and *Hart* were the first to recognize the possibility that an appropriately substituted ion with the bicyclo-[3.1.0]hex-3-en-2-yl cation *(264)* structure could exhibit fivefold carbon degeneracy as shown below [83]. These investigators reported experiments that were best interpreted



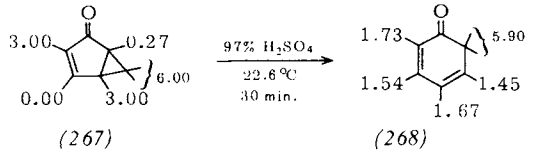
(264)

in terms of carbonium ions like *(264)* in which four or five such structures rapidly equilibrate [83]. When a solution of hexamethylbicyclo[3.1.0]hex-3-en-2-one *(265)* in 97% sulfuric acid was allowed to stand at 22.6 °C for 30 minutes and then hydrolyzed, a nearly quantitative yield of hexamethyl-2,4-cyclohexadienone *(266)* was obtained. To study the mechanism of this reaction the compound with two CD_3 groups *(267)* was rearranged to give *(268)* with the



(265) *(266)*

proton integrations for each methyl group as shown. This result is consistent with Scheme 3 in which *(270)* and *(270')* are rapidly equilibrated and each can collapse by proton loss to *(271)* and *(271')* ($-CD_3$ groups marked by an asterisk). Rapid equilibration of *(270)* and *(270')* prior

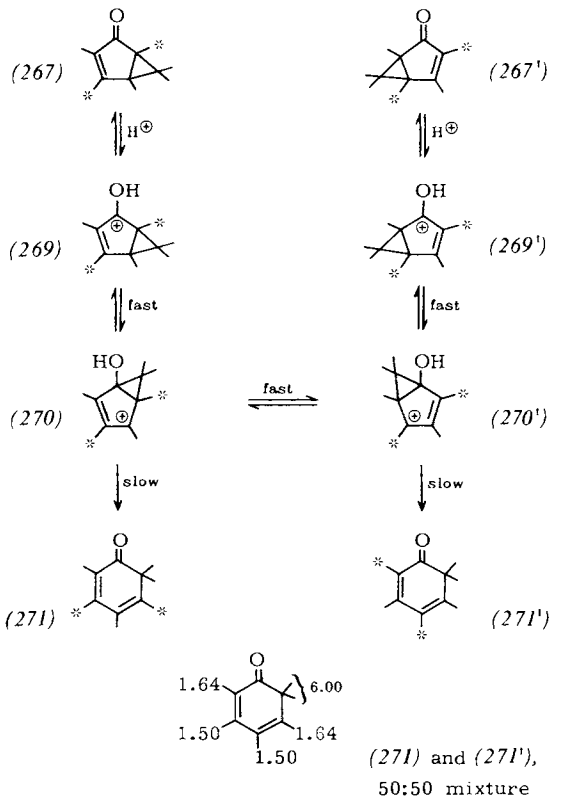


(267) *(268)*

The figures indicate the numbers of protons at the respective positions.

to collapse should lead to a 1:1 mixture of *(271)* and *(271')* with the label distribution as indicated. This is in good agreement with the values obtained for product *(268)*.

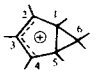
[83] *D. W. Swatton* and *H. Hart*, J. Amer. Chem. Soc. *89*, 5075 (1967).



Scheme 3. Perdeuterated methyl groups are asterisked.

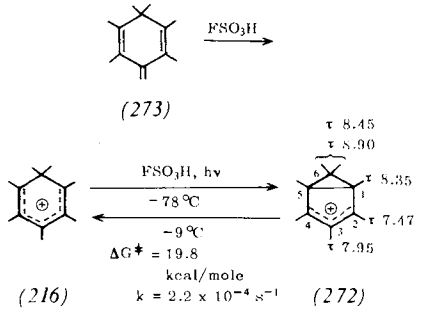
The rapid migration of the cyclopropane ring around four of the five sides of the cyclopentenyl ring is thus established.

Childs and *Winstein* studied the heptamethylbicyclo[3.1.0]-hexenyl cation *(272)* and observed fivefold degenerate



(272)

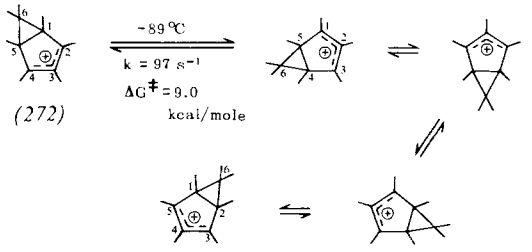
scrambling as predicted by *Swatton* and *Hart* [84]. Cation *(272)* was prepared by the irradiation of a solution of the heptamethylbenzenonium ion *(216)* in FSO_3H at −78 °C.



The reverse process, *(272)* to *(216)*, occurs smoothly on warming the solution of ion *(272)* up to −9 °C. Cation *(272)* displays a temperature-dependent NMR spectrum, and to permit lower temperature observations *(272)* was formed photochemically in a 2:1 $SO_2ClF-FSO_3H$ mixture. In this solvent the NMR spectrum of *(272)* could be observed over the temperature range −110 to −9 °C.

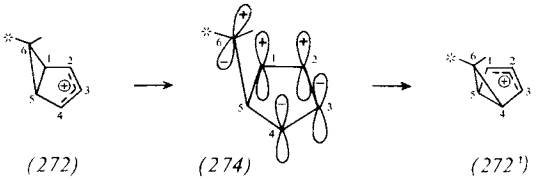
[84] *R. F. Childs* and *S. Winstein*, J. Amer. Chem. Soc. *90*, 7146 (1968).

Below −100 °C the spectrum is that shown above. At higher temperatures the signals for the five methyl groups on the cyclopentenyl ring broaden, then coalesce at about −87 °C and eventually become a sharp statistically averaged singlet (τ 7.90) at −48 °C. Although these five methyl groups become averaged at elevated temperatures, the two methyl groups on the cyclopropane methylene carbon atom C-6 remain distinct and show no sign of averaging up to −9 °C.



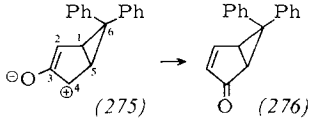
(272)

The observed fivefold degenerate scrambling in *(272)* involves migration of the cyclopropane methylene carbon C-6 around the cyclopentene ring as indicated. The key step is a concerted sigmatropic 1,4-shift of C-6 which, in the ring system *(272)*, must be suprafacial [85].

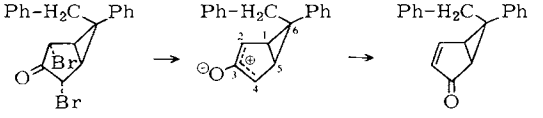


(272) (274) (272')

The symmetry of the highest occupied MO of this system, shown in *(274)*, predicts inversion of the anti-symmetric p orbital in each shift. Thus, the starred methyl group should always remain "outside" and the unstarred methyl group remain "inside" during the fivefold degenerate rearrangement. This agrees with the experimental observation that the two C-6 methyl groups maintain their identities when the other five methyl groups average rapidly. Recent work by *Hart*, *Rodgers*, and *Griffiths* on the stereochemistry of the rapid equilibration of protonated bicyclo[3.1.0]hexenones (see above) also indicates that these interconversions occur without interchange in the positions of substituents at C-6 [86]. Similarly, investigations by *Zimmerman* and *Crumrine* on the interconversion of *(275)* into *(276)* [87]



(275) (276)



(277) (278) (279)

[85] *R. B. Woodward* and *R. Hoffmann*, J. Amer. Chem. Soc. *87*, 2511 (1965).

[86] *H. Hart*, *T. R. Rodgers*, and *J. Griffiths*, J. Amer. Chem. Soc. *91*, 754 (1969).

[87] *H. E. Zimmerman* and *D. S. Crumrine*, J. Amer. Chem. Soc. *90*, 5612 (1968).

and by *Brennan* and *Hill* on the interconversion of *(278)* into *(279)* [88] indicate that these 1,4-sigmatropic rearrangements proceed with inversion of configuration at C-6. The 1,2,3,4,5,6-*anti*-hexamethylbicyclo[3.1.0]hex-3-en-2-yl cation (but not the 6-*syn* isomer) undergoes a fivefold degenerate rearrangement similar to *(272)* [88a]. The parent bicyclo[3.1.0]hex-3-en-2-yl cation also behaves similarly [88b].

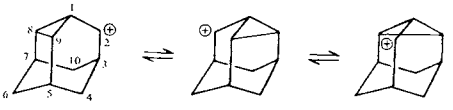
4.9. 8,9-Cyclo-2-adamantyl Cation

The degenerate cyclopropylcarbinyl-cyclopropylcarbinyl rearrangement, *(18)* ⇌ *(18')* [18], also takes place in more elaborate systems.



(18) (18')

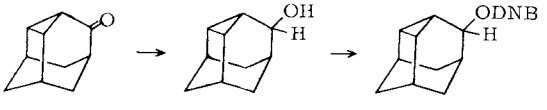
The 8,9-cyclo-2-adamantyl cation *(280)* contains the proper symmetry such that continuous cyclopropylcarbinyl-cyclopropylcarbinyl rearrangements could lead to threefold carbon degeneracy as indicated below (classical ions shown for convenience). *Baldwin* and *Foglesong*



(280) (280') (280'')

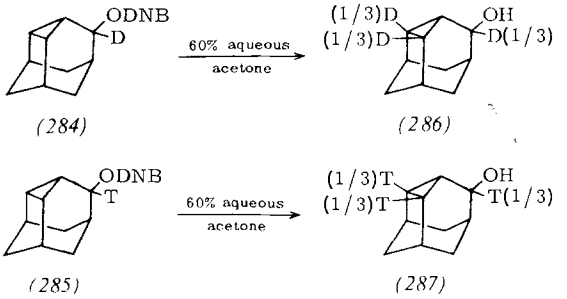
studied the solvolysis of derivatives leading to the formation of cation *(280)* and observed the nearly complete equivalence of positions 2, 8, and 9 [89,90]. This provides evidence for the occurrence of degenerate cyclopropylcarbinyl-cyclopropylcarbinyl rearrangements within this system.

Reduction of 8,9-cyclo-2-adamantanone [90] *(281)* with sodium borohydride gave alcohol *(282)* which was converted to its 3,5-dinitrobenzoate *(283)*. Solvolysis of *(283)*



(281) (282) (283)

in 60% aqueous acetone afforded a 95% yield of *(282)*. The 2-deuterio and 2-tritio analogs of *(282)* were prepared with $NaBD_4$ and $NaBT_4$. Solvolysis of the labeled 3,5-dinitro-



(284) (286)

(285) (287)

[88] *T. M. Brennan* and *R. K. Hill*, J. Amer. Chem. Soc. *90*, 5614 (1968).

[88a] *V. A. Koptyug*, *L. I. Kuzubova*, *I. S. Isaev*, and *V. I. Matyuk*, Chem. Commun. *1969*, 389.

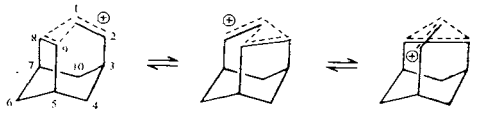
[88b] *P. Vogel*, *M. Saunders*, *N. Hasty*, and *J. A. Berson*, unpublished.

[89] *J. E. Baldwin* and *W. D. Foglesong*, J. Amer. Chem. Soc. *89*, 6372 (1967).

[90] *J. E. Baldwin* and *W. D. Foglesong*, J. Amer. Chem. Soc. *90*, 4303 (1968).

benzoates *(284)* and *(285)* gave product alcohols *(286)* and *(287)* with the label distributions as shown. The deuterium contents were determined by mass spectrometry and the tritium activities were determined by liquid scintillation counting.

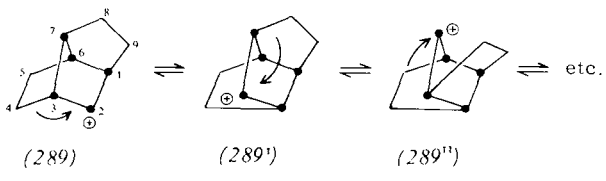
These results indicate that the 2, 8, and 9 positions of the 8,9-cycloadamantyl system attain a high degree of equivalence during the solvolysis reaction. The solvolysis rate constant for *(283)* indicates a substantial rate acceleration above that expected for classical ion *(280)*. Based on these two observations, the authors feel that the 8,9-cyclo-2-adamantyl cation is best represented as a set of rapidly equilibrating, charge delocalized, "bisected" [15] cyclopropylcarbinyl cations *(288)*, *(288')*, and *(288'')*.



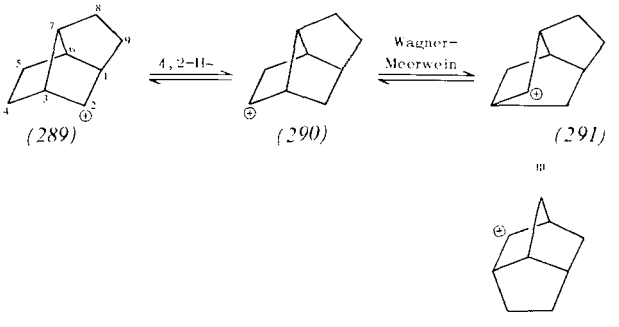
(288) *(288')* *(288'')*

4.10. 2-Brexyl or 2-Tricyclo[4.3.0.0^{3,7}]nonyl Cation

Nickon and co-workers pointed out the possibility that the 2-brexyl cation *(289)* could exhibit multiple degenerate properties [91]. Ion *(289)*, by consecutive Wagner-Meerwein rearrangements, could transfer the positive charge originally at C-2 to all five carbons of the central five-membered ring, which is identified in *(289)* by heavy dots. Repetition of this process many times would result in carbon atoms 1,2,3,6, and 7 becoming equivalent to each other and in carbon atoms 4,5,8, and 9 becoming equivalent to each other also. Thus, the theoretical NMR spectrum of cation *(289)* would contain two peaks of areas 5 and 8 if the above mechanism were operative. A second rearrangement possibility exists for *(289)*, that of a 4,2-hydride shift, which would lead to the 4-brexyl cation *(290)*, an ion not capable of multiple degeneracy. Wagner-Meerwein rearrangement in *(290)* produces the 2-brendyl cation *(291)* which can undergo no further rearrangement.

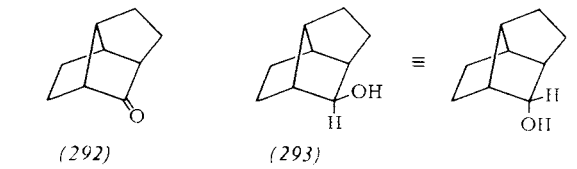


(289) *(289')* *(289'')*

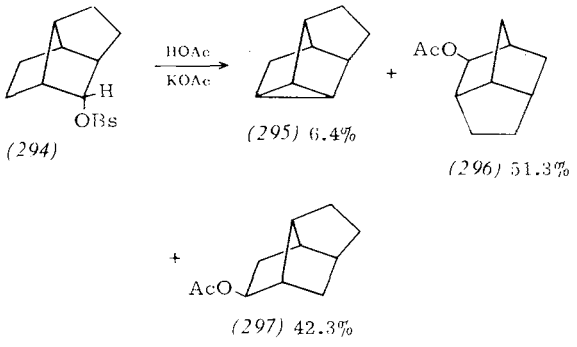


(289) *(290)* *(291)*

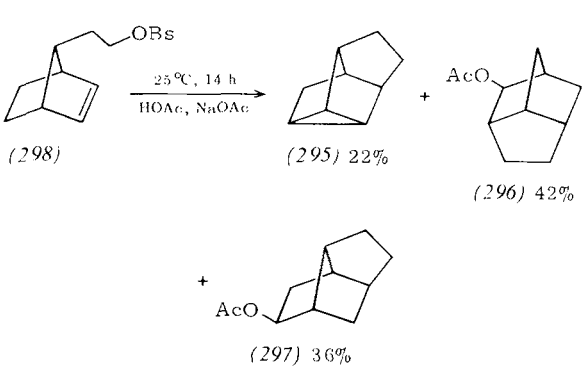
Nickon and his associates have synthesized brexan-2-one *(292)* and brexan-2-ol *(293)* [91]. The solvolysis of 2-brexyl brosylate *(294)* was carried out to give the product mixture shown below [92]. *Bly* and co-workers have reported the solvolysis of β-(*syn*-7-norbornenyl)ethyl brosylate *(298)* to give the same set of products [93]. Both sets of results are best explained in terms of initial formation of the 2-brexyl cation *(289)*, which then rapidly undergoes the 4,2-hydride shift to form cation *(290)*; *(290)* then yields *(291)* by Wagner-Meerwein rearrangement. The two acetate products arise from these ions. Lack of formation of acetate *(299)*, which would arise from the 2-brexyl cation *(289)*, indicates that this cation is not as stable as ions *(290)* and *(291)*.



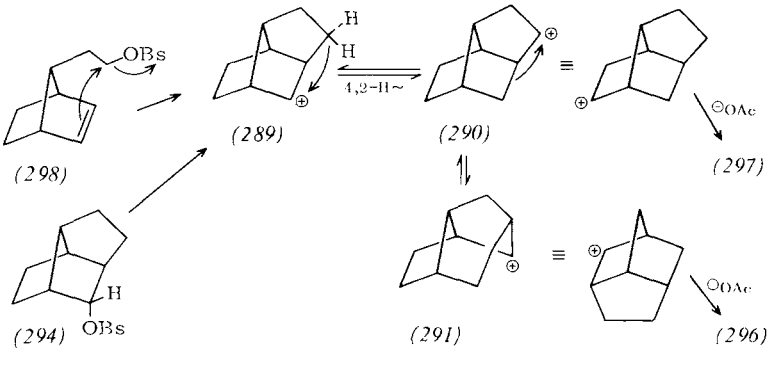
(292) *(293)*



(294) *(295)* 6.4% *(296)* 51.3% *(297)* 42.3%



(298) *(295)* 22% *(296)* 42% *(297)* 36%

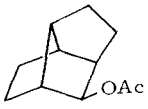


(298) *(289)* *(290)* *(297)* *(294)* *(291)* *(296)*

[91] *A. Nickon, H. Kwasnik, T. Swartz, R. O. Williams*, and *J. B. Di Giorgio*, J. Amer. Chem. Soc. *87*, 1613, 1615 (1965).

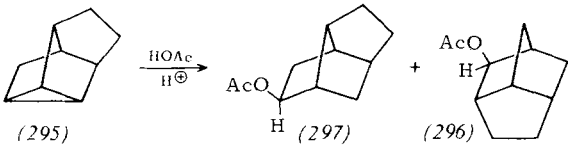
[92] *A. Nickon*, personal communication of unpublished results.

[93] *R. S. Bly, R. K. Bly, A. O. Bedenbaugh*, and *O. R. Vail*, J. Amer. Chem. Soc. *89*, 880 (1967).



(299)

Nickon, *Pandit*, and *Williams* studied the acid catalyzed acetolysis of deltacyclane *(295)* and found only products *(296)* and *(297)* also [94]. The brendyl acetate *(296)* is the more stable of the two products and predominates almost exclusively if the acetolysis mixture is allowed to equili-

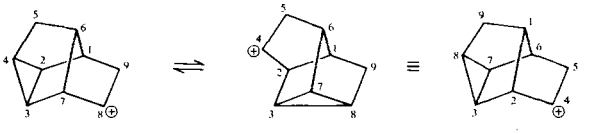


(295) (297) (296)

brate. Once again no product *(299)* due to the 2-brexyl cation was observed. This tends to indicate that the proposed degeneracy for the 2-brexyl cation *(289)* may never be observed due to the instability of the ion relative to other tricyclic cation isomers.

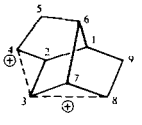
4.11. 8-Tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonyl Cation

The 8-tetracyclo[4.3.0.0^{2,4}0.^{3,7}]nonyl cation *(21)* is capable of twofold carbon degeneracy if homocyclopropylcarbinyl rearrangements of the type shown below occur. Alternatively, it is possible that this cation could exist in



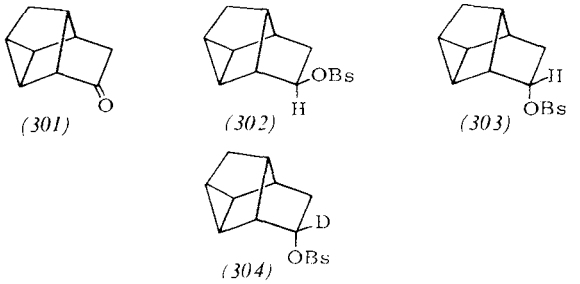
(21) (21')

the nonclassical form *(300)*, in which carbon atoms 8 and 4 are simply equivalent due to charge delocalization.



(300)

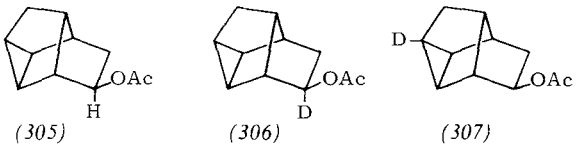
Freeman and *Balls* synthesized the tetracyclic ketone *(301)* and were able to prepare the derivatives *(302)*, *(303)*, and *(304)* for solvolysis [48]. The acetolysis of *(302)* and *(303)* gave only one acetate product *(305)*. Acetolysis of the



(301) (302) (303) (304)

[94] *A. Nickon, G. D. Pandit*, and *R. O. Williams*, Tetrahedron Lett. *1967*, 2851

labeled compound *(304)* produced *exo*-acetate which according to infrared and NMR spectroscopy contained one-half of a deuterium at C-8 and one-half a deuterium in the cyclopropane ring. These results are consistent with

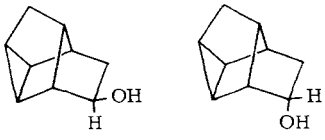


(305) (306) (307)

the formation of an equimolar mixture of acetates *(306)* and *(307)* in which the deuterium is distributed between C-8 and C-4.

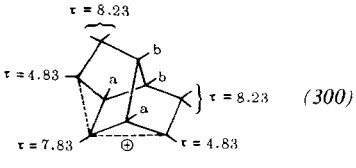
The rate constants for the acetolysis of *(302)* and *(303)* at 25 °C are 2.79 × 10^{-4} s^{-1} and 4.74 × 10^{-6} s^{-1}, respectively. From these values anchimeric assistance factors of $10^{5.9}$ for *(302)* and $10^{3.7}$ for *(303)* were calculated. Since the rate factor for anchimeric assistance in the 2-*exo*-norbornyl cation is only $10^{3.3}$, it appears that both the *exo* and *endo* isomers *(302)* and *(303)* of the tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonyl system solvolyze with anchimeric assistance. It can be argued that this disfavors a rapid equilibration of classical cations *(21)* and *(21')* as the mechanism for the deuterium label scrambling since a classical ion derived from the *endo* compound *(303)* should show little anchimeric assistance. However, it is not clear why the *endo* isomer shows an accelerated rate; the nature of the participation has not been identified.

When either alcohol *(308)* or *(309)* is dissolved in FSO_3H-SO_2 at −78 °C, the same carbonium ion



(308) (309)

solution is observed. The NMR spectrum of this solution does not change significantly from −55 to −10 °C, and is characteristic of a cation showing absorptions at τ 4.83, 7.08, 7.50, 7.83, and 8.23 in the ratio 2:2:2:1:4, respectively. Quenching the cation solution with aqueous potassium hydroxide produces *(308)*. This spectrum is best interpreted in terms of ion structure *(300)* with the proton resonance signals assigned as shown. Based on the rate data, the deuterium label scrambling, and the NMR spectrum



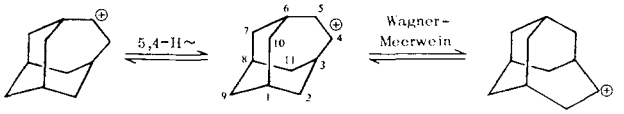
(300)

a protons τ = 7.08 or 7.50
b protons τ = 7.50 or 7.08

of the carbonium ion above, it appears that ion *(300)* best represents the structure of the carbonium ion derived from the solvolysis of 8-tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonyl precursors.

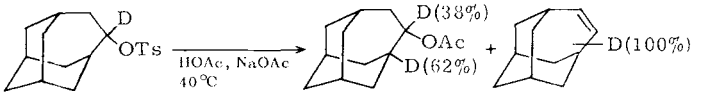
4.12. 4-Homoadamantyl or 4-Tricyclo[4.3.1.1^{3,8}]-undecyl Cation

The 4-homoadamantyl cation *(310)*, as noted by *Nordlander*, is capable of exhibiting combined carbon and hydrogen degeneracy [95]. Cation *(310)* can be degenerate with respect to both Wagner-Meerwein rearrangement and vicinal hydride shifts. These two processes can be distinguished on the basis of deuterium label redistribution; a deuterium label originally at C-4 in *(310)* would appear at C-5 in *(310')*, but at C-3 in *(310'')*. Combination of both 1,2-carbon shifts and 1,2-hydride shifts could lead to elevenfold (complete) degeneracy in *(310)* if classical cations are involved. The degeneracy may be limited by ion pairing or by bridged cation formation.



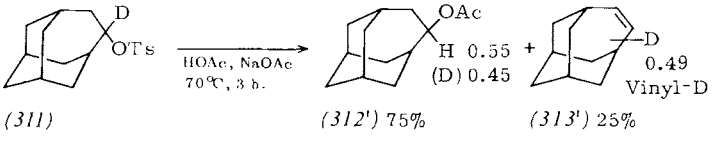
(310') *(310)* *(310'')*

Nordlander and his associates have synthesized the deuterated 4-homoadamantyl tosylate *(311)* and solvolyzed it with the results indicated [95]. These results tend to indicate a 1,2-carbon shift as the primary process responsible for label redistribution (this predicts 50% D at C-3 and C-4), but intervention of hydride shifts could be responsible for part of the label scrambling. Work within these laboratories has involved an independent synthesis of *(311)* and a solvolysis with the results shown in Scheme 4 [96]. These data indicate a deuterium labeling distribution which is quite close to the predicted values for a degenerate 1,2-carbon shift occurring in *(310)*. The formolysis of *(311)* has also been carried out and the results are in accord with the acetolysis above [97]. The acetolyses of the dideuterated and trideuterated tosylates *(315)* and *(316)* were studied within these laboratories, and the acetate and olefin products showed label scrambling results which are inconsistent with a mechanism involving only a 1,2-carbon shift [97]. Tentatively, it has been concluded that hydride shifts are involved in the rearrangements of cation *(310)* although studies on *(310)* are still in progress.



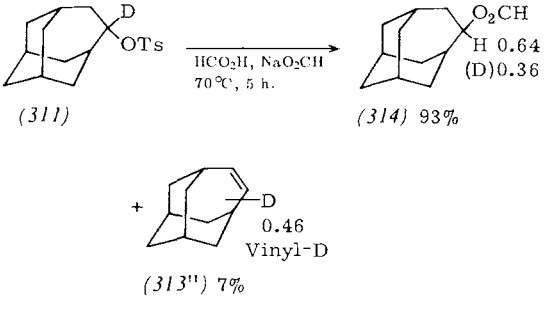
(311) *(312)* 75% *(313)* 25%

Deuterium distribution determined by mass spectrometry.



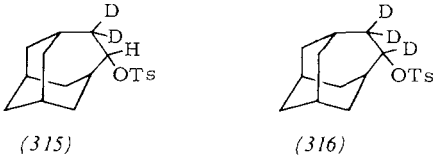
(311) *(312')* 75% *(313')* 25%

Scheme 4. Deuterium distribution as determined by NMR.



(311) *(314)* 93% *(313'')* 7%

Deuterium distribution determined by NMR.



(315) *(316)*

5. Conclusion

At the beginning of this paper it was mentioned that the interest in studying degenerate carbonium ions revolved around three questions:

1) Can degeneracy be achieved, and if so, to what extent?
2) What is the mechanism whereby the degeneracy is achieved?
3) Are there any special properties resulting from degeneracy?

After surveying the work which has already been completed on degenerate cations, it is instructive to consider these questions once again.

Degeneracy in carbonium ions can obviously be achieved, as indicated by the many examples discussed in this paper. Degenerate cations have been generated under solvolytic conditions from appropriate precursors and in highly acidic NMR solvents. The latter conditions enhance cation stabilities and lifetimes and often enable the observation of degenerate rearrangements which might not occur during solvolysis in more nucleophilic solvents. The extent of degeneracy varies considerably; numerous carbonium ions exhibit twofold degeneracy, but only a few like the 9-homocubyl cation *(10)* show extensive degeneracy over several carbon atoms. Extensive degeneracy cannot be achieved easily, particularly under solvolytic conditions, and examples of this phenomenon will probably always be limited. Highly acidic NMR solvents increase the probability of multiple degeneracy, but the cation under consideration may not always be formed under these conditions. For example, attempts to form the 9-homocubyl cation *(10)* from 9-homocubanol *(109)* in such solvents have not been successful, evidently because of ring opening and degradation or polymerization [98]. However, the 9-barbaralyl cation *(32)* has been observed directly as a fully degenerate species [50d].

[95] *J. E. Nordlander, F. Ying-Hsiueh Wu, S. P. Jindal*, and *J. B. Hamilton*, J. Amer. Chem. Soc. *91*, 3962 (1969).

[96] *P. von R. Schleyer, E. Funke*, and *S. H. Liggero*, J. Amer. Chem. Soc. *91*, 3965 (1969).

[97] *S. H. Liggero*, unpublished results.

[98] *G. A. Olah*, personal communication.

The basic mechanisms for degeneracy do not seem to be exceptional. Wagner-Meerwein rearrangements, hydride shifts, double bond participation, cyclopropane ring participation (homocyclopropylcarbinyl rearrangement and cyclopropylcarbinyl-cyclopropylcarbinyl rearrangement), allyl resonance, and combinations of these appear to account for the degeneracy of almost all the carbonium ions studied thus far. Barbaralyl cation *(32)* is unusual in that its most rapid automerization does not correspond to any normally predicted mechanism. Certain of the above processes are more prone to yield specific types of degeneracy. For example, hydride shifts and Wagner-Meerwein rearrangements often give rise to twofold degeneracy. Participation of a cyclopropane ring often gives rise to threefold degenerate cations.

Degeneracy within a carbonium ion does not seem in general to confer any special properties upon the cation involved aside from possible nonclassical resonance stabilization. Of the cations which have been studied, none appears conclusively to be destabilized by virtue of possessing degenerate properties. However, all evidence obtained thus far does indicate that the bicyclo[3.2.2]nona-3,6,8-trien-2-yl cation *(14)* is destabilized, but the available evidence cannot be regarded as conclusive. Some degenerate cations, such as the 9-homocubyl cation *(10)* and the 9-pentacyclo[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]nonyl cation *(19)*, appear to be stabilized by nonclassical resonance. The tetracyclo-[4.3.0.$0^{2,4}$.$0^{3,7}$]non-8-en-5-yl cation *(15)* also possesses nonclassical stabilization, but exhibited no degenerate properties. Thus, it cannot be inferred that degeneracy must be accompanied by nonclassical ion formation. The nonclassical stabilization in the 7-norbornadienyl cation *(13)* is evidenced by the distorted geometry of the ion and the energy barrier to bridge flipping. The anions of the bicyclo[3.2.2]nona-3,6,8-trien-2-yl and the tetracyclo-[4.3.0.$0^{2,4}$.$0^{3,7}$]non-8-en-5-yl systems appear more prone to degenerate rearrangement than the corresponding cations.

Further study is needed in the area of stability of degenerate carbonium ions, since this may provide information that is useful in predicting when degeneracy may or may not occur [*].

This work was supported by grants from the National Institutes of Health (AI-07766), the National Science Foundation, and the Petroleum Research Fund, administered by the American Chemical Society. We would like to thank Dr. H. Quast, Dr. G. Seybold, and Professor K. Mislow for suggestions and assistance with the manuscript.

Received: October 30, 1969 [A 781 IE]
German version: Angew. Chem. *82*, [illegible] (1970)

[*] *Note added in proof*: The following cations, which exhibit degenerate properties, have also been studied recently: 2-Methylpentyl cation (*D. M. Brouwer*, Recl. Trav. Chim. Pays-Bas *88*, 9 (1969)); 3-methylpentyl cation (ref. [63b]); 2,4-dimethylpentyl cation (*D. M. Brouwer* and *J. A. Van Doorn*, Recl. Trav. Chim. Pays-Bas *88*, 573 (1969)); methylcyclobutyl cation (*M. Saunders* and *J. Rosenfeld*, J. Amer. Chem. Soc. *92*, 2548 (1970)); methylcyclopentyl cation (ref. [68]); 1,3-dimethyl-1-cyclopentyl cation (*H. Hogeveen* and *C. J. Gaasbeek*, Recl. Trav. Chim. Pays-Bas *88*, 1305 (1969)); 1,3,4,4-tetramethylcyclohexenyl cation (*T. S. Sorensen* and *K. Ranganayakulu*, J. Amer. Chem. Soc. *92*, 6539 (1970)); pentamethylcyclopentenyl cations and hexamethylcyclopentenyl cations (*D. M. Brouwer* and *J. A. Van Doorn*, Recl. Trav. Chim. Pays-Bas *89*, 333 (1970); *D. M. Brouwer* and *H. Hogeveen*, *ibid. 89*, 211 (1970)); 1-*tert*-butyl-1,3,3-trimethylallyl cation (*T. S. Sorensen* and *K. Ranganayakulu*, Tetrahedron Lett. *1970*, 659); 1,2,3,4,5,6-hexamethyl[2.1.1]hexenyl cations (*H. Hogeveen* and *H. C. Volger*, Recl. Trav. Chim. Pays-Bas *88*, 353 (1969)); 4-protoadamantyl cation (*D. Lenoir* and *P. v. R. Schleyer*, Chem. Commun. *1970*, 941; see also *Z. Majerski, S. H. Liggero*, and *P. v. R. Schleyer*, Chem. Commun., in press).

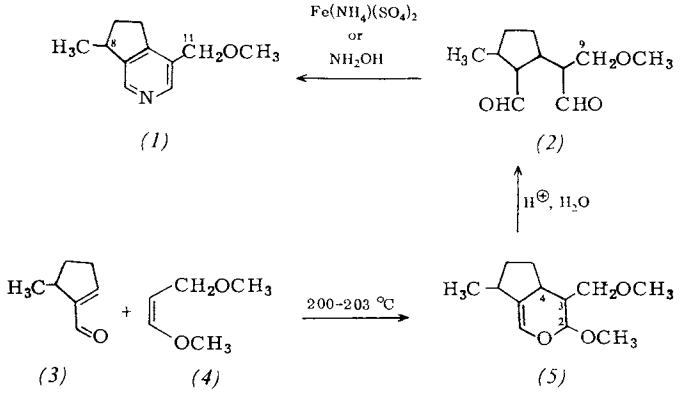
Valerianine, a Tertiary Monoterpene Alkaloid from Valerian[1]

By *Burchard Franck*, *Uwe Petersen*, and *Fritz Hüper*[*]

Dedicated to Professor Kurt Mothes on the occasion of his 70th birthday

Although it has long been known that valerian (*Valeriana officinalis* L.), which is used medicinally because of its sedative action, contains alkaloids[2], it is only recently that two quaternary pyridine bases have been isolated from it and their structures determined[3].

We now report a new, sedative, tertiary, monoterpene alkaloid *(8)* from *Valeriana officinalis* and its total synthesis, which also opens a simple route to a group of related alkaloids from Actinidiaceae and Bignoniaceae[4].



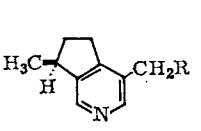
(1) *(2)* *(3)* *(4)* *(5)*

Chromatographic separation (basified silica gel; $CHCl_3$/CH_3OH 10:1) of the tertiary base fraction of a methanol extract of fresh *Valeriana* roots gave an alkaloid valerianine, m.p. 134 °C, $[\alpha]_D^{20} = -10.5°$ (c = 0.370 in CH_3OH), which crystallizes as hydrochloride. The base has molecular formula $C_{11}H_{15}NO$, which together with its IR band (1585 cm^{-1} in KBr), UV absorption (λ_{max} = 261, 269 nm in CH_3OH), and NMR multiplet at δ = 8.37 ppm ($CDCl_3$, TMS = 0, —CH=N—CH=) indicate a pyridine derivative unsubstituted at positions 2 and 6. Since the NMR spectrum indicates also groups CH_3—CH< (1.32 ppm) and CH_3—O—CH_2—C< (3.40, 4.46 ppm), formula *(1)* can be assumed for valerianine subject to the proviso that the position of the methyl group on C-8 has only a biogenetic basis. This structure has been confirmed by synthesis.

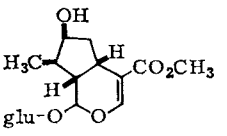
A key compound for the synthesis was 9-methoxyiridodial *(2)*, which like glutardialdehyde should be susceptible to pyridine ring closure[5]. 5-Methyl-1-cyclopentenecarbaldehyde *(3)* is easily obtained from 4-methylpyrocatechol[6] and on diene condensation with 1,3-dimethoxypropene *(4)*[7] at 200—203 °C affords a 47% yield of the dihydropyranyl ether *(5)* which consists of three diastereoisomers. Since the chirality centers at C atoms 2, 3, and 4 disappear when the ether is converted into a pyridine derivative, it is unnecessary to separate the *cis/trans*-isomers *(4)* or the diastereoisomers *(5)* obtained by diene condensation. The ether *(5)* is hydrolyzed by acid to the desired 9-methoxyiridodial *(2)*, which, without isolation, is condensed to give *(1)* in 19% or 20% yield by $Fe(NH_4)(SO_4)_2$[5a] or by NH_2OH[5b], respectively.

The racemic hydrochloride of *(1)*, $C_{11}H_{16}NOCl$, m.p. 143 °C, is identical with valerianine hydrochloride in R_F value, and IR, NMR, and mass spectra.

The (—)-antipode obtained by resolution with dibenzoyltartaric acid also agrees with the alkaloid in its optical rotation ($[\alpha]_D^{20} = -11.6°$, c = 1.13 in CH_3OH). Since valerianine *(1)* corresponds in its chiral chromophore and optical rotation with actinidine *(6)* ($[\alpha]_D^{11} = -7.2°$, c = 17.54 in $CHCl_3$)[8] and tecostidine *(7)* ($[\alpha]_D^{22} = -4°$, c = 1.221 in $CHCl_3$)[9], it, like these two alkaloids, probably has the



(6), R = H
(7), R = OH
(8), R = OCH_3



(9)

S-configuration, and thus the complete formula *(8)* is proved. It is thus not improbable that loganin *(9)* is a biosynthetic precursor of valerianine *(8)* as it is for numerous monoterpene, isoquinoline, and indole alkaloids[10].

The synthesis of (—)-valerianine is also the first preparation of a derivative of (—)-tecostidine *(7)*[11]. Actinidine *(6)* can also be simply prepared in this way[13].

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[1] Part 6 of Pyridine Alkaloids. — Part 5: *B. Franck* and *M. Schiebel*, Naturwissenschaften *48*, 717 (1961).

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[7] 1,3-Dimethoxypropene *(4)* was obtained from the *p*-toluenesulfonate of 1,3-dimethoxy-2-propanol by means of CH_3ONa/DMSO in 71% yield with *cis/trans* = 2.1:1.

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[10] *K. Mothes* and *H. R. Schütte*: Biosynthese der Alkaloide. Deutscher Verlag der Wissenschaften, Berlin 1969, pp. 602, 480.

[11] Only the dextrorotatory, unnatural antipode of tecostidine has previously been prepared, in a multi-stage partial synthesis from (+)-pulegone [12], after attempts to hydroxylate actinidine *(6)* at C-11 had failed [8, 12].

[12] *C. W. K. Cavill* and *A. Zeitlin*, Austr. J. Chem. *20*, 349 (1967).

[13] *E.g.*, the solution obtained after treatment of *(5)* with $Fe(NH_4)(SO_4)_2$ is made alkaline with NaOH and distilled in steam. The valerianine *(8)* is then completely reduced to actinidine *(6)* which passes over in the steam.

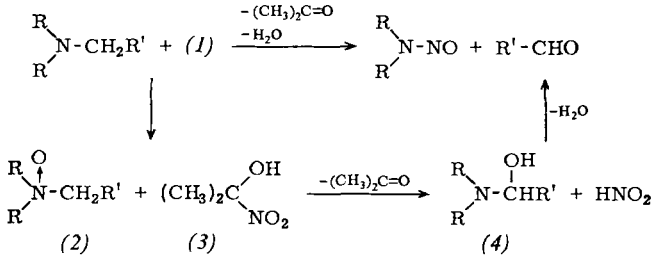
A New Degradation of Amines

By *Burchard Franck, Jens Conrad,* and *Peter Misbach*[*]

We have found a simple procedure for converting tertiary into secondary amines that consists of a combination of degradations by peroxide[1,2] and by nitrous acid[1,3] and gives good yields under very mild conditions.

$$(CH_3)_2CH\text{-}NO_2 + O_2 \xrightarrow{CuCl} (CH_3)_2C(OOH)(NO_2)$$

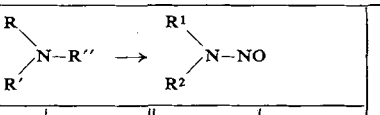
(1)



(2) *(3)* *(4)*

2-Nitroprop-2-yl hydroperoxide *(1)*, which is formed as intermediate during autoxidation of 2-nitropropane[4] and can be considered as an adduct of the hypothetical "peroxynitrous acid" to acetone, reacts with tertiary aliphatic amines with removal of one alkyl group as aldehyde or ketone and formation of a nitrosamine. To carry out the reaction it is only necessary to shake the tertiary amine in pyridine with 2-nitropropane and CuCl under oxygen. The nitrosamine formed can be easily separated and reduced to secondary amine. The tertiary amine remains unchanged in the absence of 2-nitropropane. Investigations of the reaction mechanism show that *(1)* oxidizes the amine to the amine oxide *(2)*, being converted itself into 2-nitro-2-propanol *(3)* which decomposes to acetone and HNO_2. The HNO_2 traps the secondary amine formed from the amine oxide *(2)* after rearrangement to the carbinol-amine *(4)* as nitrosamine.

The relative rates of removal of alkyl groups are k_{CH_3}: $k_{C_2H_5}$: $k_{n\text{-}C_3H_7}$: $k_{i\text{-}C_3H_7}$: $k_{tert\text{-}C_4H_9}$ = 100:62:57:(6—25):0, and correspond approximately to the relative numbers of protons in α-positions. It is remarkable that



R	R′	R″	R¹	R²	Yield (%)
C_2H_5	C_2H_5	C_2H_5	C_2H_5	C_2H_5	50
CH_3	CH_3	C_3H_7	CH_3	C_3H_7	59
			CH_3	CH_3	17
CH_3	$i\text{-}C_3H_7$	$i\text{-}C_3H_7$	CH_3	$i\text{-}C_3H_7$	7
			$i\text{-}C_3H_7$	$i\text{-}C_3H_7$	60
C_2H_5	$i\text{-}C_3H_7$	$i\text{-}C_3H_7$	C_2H_5	$i\text{-}C_3H_7$	21
			$i\text{-}C_3H_7$	$i\text{-}C_3H_7$	65
CH_3	CH_3	$t\text{-}C_4H_9$	CH_3	$t\text{-}C_4H_9$	60
C_2H_5	$i\text{-}C_3H_7$	$t\text{-}C_4H_9$	C_2H_5	$t\text{-}C_4H_9$	15
			$i\text{-}C_3H_7$	$t\text{-}C_4H_9$	59
CH_3	$-(CH_2)_5-$		$-(CH_2)_5-$		58

strongly hindered amines such as ethyldiisopropylamine (the Hünig base) and even *tert*-butylethylisopropylamine[5] which resist degradation by cyanogen bromide are dealkylated in particularly good yield. Amines whose nitrogen forms part of a five-membered ring are not degraded, and ring nitrosation is the predominant reaction of aromatic amines.

General procedure:

A solution of a tertiary amine (0.1 mole) in pyridine (100 ml) and CuCl (5 g, 0.05 mole) are placed in a double-walled flask that can be heated by connecting it with a thermostat and the mixture is saturated with O_2. The 2-nitropropane (30 ml, *ca.* 0.3 mole) is added and the mixture is shaken under O_2 at 50 °C. After 2—3 h (O_2 uptake 0.1—0.15 mole) the contents of the flask are poured on a mixture of ice (1 kg) and concentrated HCl (180 ml) and extracted with $CHCl_3$. The extract is dried over Na_2SO_4 and the residue obtained on evaporation is distilled from a bulb-tube and separated by layer chromatography on silica gel G. The quantitative composition of the nitrosamine mixture was determined by gas chromatography.

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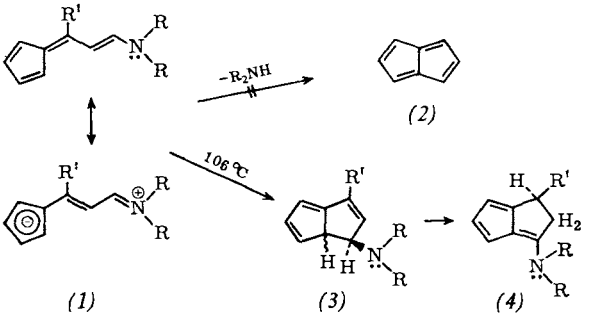
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A Simple Synthesis of 1,2-Dihydropentalene and its Substitution Products

By *Reinhard Kaiser* and *Klaus Hafner*[*]

Whereas thermolysis of 6-(4-amino-1,3-butadienyl)fulvenes yields azulenes[11], it is not unexpected that the corresponding reaction of 6-(2-aminovinyl)fulvenes *(1)* does not lead to the desired but presumably highly thermolabile pentalene *(2)*[2]. Surprisingly, however, fulvenes of type *(1)* undergo ready cyclization to give 1,2-dihydropentalenes, of which only a few, multiply substituted representatives have hitherto been known[3].

During attempts to prepare stabilized pentalenes[4,5] from substituted 6-vinylfulvenes[4] we found that *N,N*-dialkyl derivatives of *(1)* are converted into 3-dialkylamino-1,2-dihydropentalenes *(4)* in boiling piperidine [*(4a)*, pale

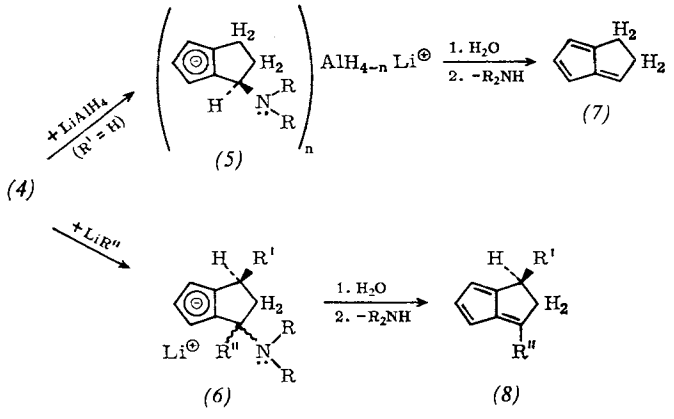


(1) *(3)* *(4)*

	2 R	R′	M.p. (°C)	Yield (%)
(4a)	$2\ CH_3$	H	121—122	71
(4b)	$-(CH_2)_5-$	H	99—100	75
(4c)	$-(CH_2)_2-O-(CH_2)_2-$	CH_3	102—103	62
(4d)	$-(CH_2)_5-$	CH_3	83—84	70

yellow needles, λ_{max} = 314 nm (log ε = 4.43) in *n*-hexane; NMR spectrum (in $CDCl_3$): multiplets centered at τ = 3.09 (H-5), 3.79 (H-4), 4.09 (H-6), broad singlet at τ = 6.75 ($N(CH_3)_2$), multiplet centered at τ = 6.97 (H_2-1, H_2-2)]. Intramolecular Michael addition is followed by base-catalyzed isomerization of the intermediate *(3)* to the thermodynamically more stable 6-aminofulvene derivatives (1,2-dihydropentalenes) *(4)*.

Like 6-dimethylaminofulvene[6], the bicyclic fulvenes *(4)* also add lithium tetrahydridoaluminate and alkyl- or aryllithiums in ether at 20 °C to give the organometallic compounds *(5)* and *(6)* respectively. On hydrolysis at 0 °C followed by amine elimination at 25 °C, compound *(5)* affords 1,2-dihydropentalene *(7)* [yellow, air-sensitive and thermolabile oil, b.p. 15 °C/10^{-2} torr; λ_{max} = 378 (2.68), 272 (3.70), 263 (4.04), 258 (4.08), 255 (4.09), 250 (4.04) nm (log ε) in *n*-hexane; NMR spectrum (in CCl_4): multiplets centered at τ = 3.29 (H-3, H-5), 3.96 (H-4), 4.18 (H-6), 6.93 (H_2-2), 7.39 (H_2-1)] and *(6)* gives the corresponding 1,2-dihydropentalene *(8)*.



	R'	R''	M.p. (°C)	B.p. (°C/torr)	Yield (%)
(8a)	H	CH_3	—	30—33/10^{-2}	84
(8b)	H	C_6H_5	61—62	—	82
(8c)	CH_3	CH_3	—	45—47/10^{-2}	81
(8d)	CH_3	C_6H_5	36—37	—	81

The composition and structure of the isolated compounds *(4)*, *(7)*, and *(8)* were confirmed by elemental analysis and by UV, NMR, and mass spectrometry. Experiments on the conversion of *(3)*, *(7)*, and *(8)* into the corresponding pentalenes are in progress.

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[1] *K. Hafner*, Liebigs Ann. Chem. *606*, 79 (1957).

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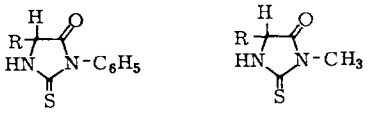
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Gas Chromatographic Identification of the Thiohydantoins of Degradation Products of Peptides and Proteins[**]

By *Harald Tschesche*, *Rainer Obermeier*, and *Sigrid Kupfer*[*]

Although the Edman degradation has been developed for the stepwise sequential determination of peptides and proteins and has been extensively schematized and even automated[1], a simple method (cf.[2]) for the identification of the cleaved amino acids — mainly in the form of phenylthiohydantoins *(1)* — has not yet been reported. The compounds *(1)* are not well suited for identification by gas chromatography[3] because of their decomposability and low volatility, which can only be overcome in part by silylation[4].



(1) *(2)*

We have found, however, that the methylthiohydantoins *(2)* are suitable for gas chromatographic identification. With the exception of arginine and histidine all the naturally occurring amino acids, including Phe, Asn, Gln, Tyr, and Trp, can be chromatographed in the form of their methylthiohydantoins; Asp, Glu, and His can be chromatographed after methylation or silylation; and the separation and identification of leucine and isoleucine do not present any difficulties. The dehydrated derivatives of Ser and Thr were prepared and identified (see Table). Preliminary experiments indicate the possibility of coupling with automatic sequenators[6].

Mass spectra were used for the characterization of methylthiohydantoins *(2)* (see Table).

Table. Detection of naturally occurring amino acids in the form of their methylthiohydantoins *(2)*. Varian gas chromatograph 1520 with linear temperature programming of 4 °C/min, starting temperature 130 °C, 2 m column 1/4", 5% OV-1 on Chromosorb W-AW-DMCS, 50 ml He/min.

Amino acid	Effusion temp. (°C)	Rel. retention time (min)	*m/e* [5]
Ala	152	6.3	144
Gly	157	7.6	130
Ser [a]	157	7.65	142
Val	164	10.0	172
Thr [a]	178	12.7	156
Ile	190	15.4	186
Leu	190	16.0	186
Pro	206	19.6	170
Met	208	19.9	204
Phe	208	20.1	220
Asn	231	24.5	187
Gln	241	26.8	201
Tyr	252	28.5	236
Trp	277	34.8	259

[a] Dehydrated compound.

Experimental

The peptide (1—5 μmole), dissolved in pyridine (0.5 ml, spectral grade) or pyridine/water (1:1), was coupled with methyl isothiocyanate (10 mg) under nitrogen at 0 or 40 °C for 60—90 min in a microflask in a rotary evaporator; solvent and unreacted reagent were removed under vacuum. After repeated extraction with toluene the residue was rubbed with ethyl acetate for separation of the dimethylthiourea and the carbamoyl peptide was centrifuged off. This procedure was repeated once. Trifluoroacetic acid or heptafluorobutyric acid were used for the cleavage and cyclization (50 °C, 45 min). Although the methylthiohydan-

toins of Ser and Thr are partially dehydrated with trifluoroacetic acid, with heptafluorobutyric acid we have obtained only the dehydrated derivative. After removal of acid and repeated extraction with toluene, the cleaved derivatives *(2)* were dried in vacuum and extracted with ethyl acetate. The residual peptide can be used for the next degradation.

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[**] *Note added in proof*: A paper on the same subject has recently come to our knowledge: *M. Waterfield* and *E. Haber* Biochemistry *9*, 832 (1970).

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Fourier Transform ^{13}C-NMR Spectroscopy of Biologically Active Cysteine Peptides[**]

By *Günther Jung*, *Eberhard Breitmaier*, *Wolfgang Voelter*, *Toni Keller*, and *Christian Tänzer*[*]

Nuclear magnetic resonance was hitherto unable to provide direct information concerning the carbon skeleton of large organic molecules owing to the low natural abundance of the ^{13}C isotope (1.1%). The Fourier transformation of accumulated pulse interferograms solves this problem, since it provides assignable ^{13}C-NMR spectra within a short time despite the small nuclear concentration.

The results of our Fourier transform ^{13}C measurements on amino acid derivatives[1] with natural abundance of ^{13}C, in conjunction with earlier measurements on ^{13}C-enriched amino acids[2] relative to tetramethylsilane as external standard, permit the following conclusions:

1) The ^{13}C-carbonyl signals of carboxyl, ester, amide, hydrazide, and peptide groups appear between —185 and —170 ppm. Acyl protecting groups such as benzyloxycarbonyl and *tert*-butyloxycarbonyl are characterized by signals between —160 and —150 ppm.

2) The $^{13}C_\alpha$ signals of amino acids appear between —65 and —40 ppm. They depend characteristically on the side chain.

3) The $^{13}C_\beta$ signals of amino acids appear between —70 and —15 ppm and are strongly influenced by hetero substituents such as SH and OH.

4) The ^{13}C signals of aromatic rings in the side chain are observed between —140 and —120 ppm.

The ^{1}H-noise-decoupled 22.63-MHz Fourier transform ^{13}C-NMR spectra (Fig. 1) of glutathione and its oxidized form in 0.2 M aqueous solution were measured relative to external TMS on a Bruker HX-90 multinuclear spectrometer at 25 °C. 4000 scans each of 0.4 s were accumulated using a pulse width of 40 μs, resulting in an overall measuring time of less than 30 min. The two examples (Fig. 1) illustrate how easily the ^{13}C spectra of polypeptides can be assigned from the ^{13}C data of amino acids.

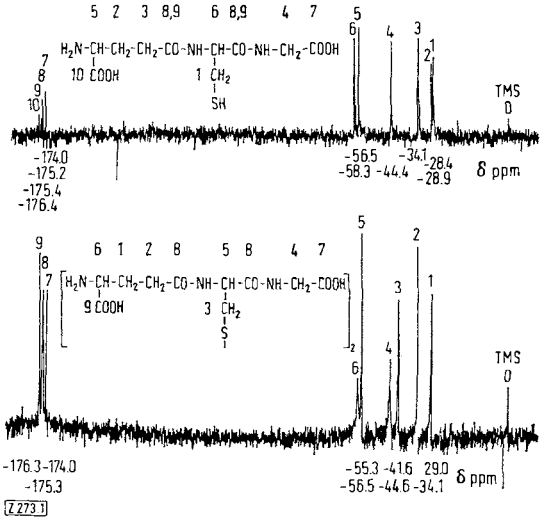


Fig. 1. ^{13}C-NMR spectra of glutathione (above) and its oxidized form (below).

In this way the carboxyl signals of the two peptides can be assigned by comparison with glutamic acid (—175.6 ppm) and glycine (—173.5 ppm). Further, the carbonyl resonance region contains the signals of the two peptide groups, which are split for glutathione (—175.2 and —175.4 ppm) but are superimposed for the oxidized form (—175.3 ppm). By a further comparison of the spectra of glutathione and its oxidized form it is shown that the ^{13}C signals of the methylene groups of glutamic acid (C_β —29.0, C_γ —34.1 ppm) and glycine (—44.6 ppm) are almost identical for the two peptides.

The most important results of our measurements are the large differences between the $^{13}C_\alpha$ and $^{13}C_\beta$ shifts of cysteine and cystine in glutathione and its oxidized form. The ^{13}C signal of C_β next to sulfur is shifted by 13 ppm to lower field on transition from glutathione (—CH_2SH) to the oxidized form (—CH_2SSCH_2—), and the ^{13}C signal of C_α is shifted by 3 ppm to higher field. Further increase in the oxidation state causes even greater shifts: thus the ^{13}C signal of C_β of cysteic acid (—CH_2SO_3H) at —52 ppm is shifted downfield by about 24 ppm in comparison with that of cysteine; the $^{13}C_\alpha$ signal of cysteic acid, however, appears about 5 ppm upfield.

These differences open up new pathways to the elucidation of the structure of cysteine peptides without loss of material. For example, we have also been able to recognize the ^{13}C signal of the —CH_2SSCH_2— group at —41.6 ppm in the Fourier transform ^{13}C-NMR spectra of the peptide hormones oxytocin, vasopressin, and insulin.

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Preparation and Properties of a Crystalline Compound $Na_4Sn_9 \cdot 6$–8 Ethylenediamine[**]

By *Dieter Kummer* and *Lothar Diehl*[*]

About 40 years ago *Zintl* and his co-workers[1] discovered a class of salt-like intermetallic compounds that are soluble in liquid ammonia. This class includes Na_4Sn_9, Na_4Pb_9, and Na_3Sb_7 which exist in solution as Na^+ cations and complex anions such as Pb_9^{4-}. At that time *Zintl* proposed the designation polyanionous salts for such compounds.

In spite of the interest that these compounds aroused by their composition and properties, they have not previously been further characterized because it proved impossible to isolate them from their ammoniacal solutions in solid crystalline form. When the ammonia was removed, decomposition occurred giving metallic alloy phases of the same composition but no longer containing the (unknown) complex structure of the polyanions that exist in solution.

We have now prepared the compound Na_4Sn_9 in solid crystalline form by using various amines as solvents. Our experiments have shown that alloys of sodium and tin in atomic proportions 2:4 to 2:5 (obtained by melting the components together) dissolve not only in NH_3 but also (with a deep reddish-brown color) in ethylenediamine (en), *N,N'*-dimethylethylenediamine, diethylenetriamine, and triethylenetetramine. They do not dissolve in $N(CH_3)_3$, $NH(CH_3)_2$, $N(C_2H_5)_3$, $NH(C_2H_5)_2$, $NH_2C_2H_5$, or *N,N,N',N'*-tetramethylethylenediamine. The solutions are similar in color and metal composition (always Na_4Sn_9) to the ammonia solutions described by *Zintl*. In the absence of air and moisture they are stable almost indefinitely.

Ethers precipitate the metal compounds from the amine solutions. Thus diethylene glycol monoethyl ether (monoglyme) precipitates from an ethylenediamine solution reddish-brown crystals of composition $Na_4Sn_9 \cdot 6$–8 en, which give a characteristic X-ray diagram containing many reflections.

The degradation isotherm of this compound at 58 °C shows steps at the compositions $Na_4Sn_9 \cdot 8$ en (p = 24 torr), $Na_4Sn_9 \cdot 6$ en (p = 7 torr), $Na_4Sn_9 \cdot 4$ en (p = 4 torr), and Na_4Sn_9. Two of the diamine molecules in $Na_4Sn_9 \cdot 8$ en are so loosely bound that they are partially washed out on precipitation of the product by the ether; thus the diamine content of various preparations lies between 6 and 8. The products corresponding to these steps all give characteristic X-ray diagrams. It is interesting that the dark gray Na_4Sn_9 obtained free from ethylenediamine produces a different diffraction pattern from that of the starting alloy; careful removal of the ethylenediamine thus does not regenerate the starting material. If, however, this new Na_4Sn_9 is melted, its structure collapses and the metallic starting material (with its X-ray diagram) is again obtained, comprising a mixture of phases and containing, *inter alia*, metallic tin.

Magnetic measurements support these findings. The initial alloy shows paramagnetism, but the Na_4Sn_9 containing ethylenediamine and that freed from the diamine are diamagnetic. After melting, the diamagnetic Na_4Sn_9 has become paramagnetic again.

	χ_g [cm³/g] ± 0.10 × 10^{-6} at 25 °C [2]
Na/Sn alloy 4:10	+4.337 × 10^{-6}
$Na_4Sn_9 \cdot 6.4$ en	−0.604 × 10^{-6}
Na_4Sn_9	−0.488 × 10^{-6}
Na_4Sn_9 (melted)	+1.183 × 10^{-6}

The differences between the values for the initial alloy and the melted Na_4Sn_9 are to be ascribed to differences in composition.

The ^{119}Sn Mössbauer spectrum[2] of $Na_4Sn_9 \cdot 6$ en (absorber, exposure temperature 4.2 °K) contains one absorption line (isomeric shift δ = +0.15 mm/sec against α-Sn, halfwidth Γ = 1.90 mm/sec, source Mg_2Sn δ = −0.25 mm/sec against α-Sn). Quadrupole splitting could not be detected. This does not permit any unique determination of structure because other compounds of tin are known for which (contrary to expectation) no quadrupole splitting can be detected and which show only one Mössbauer line in spite of possessing chemically different tin atoms[3]. Our attempts to obtain structural information about Na_4Sn_9 by ^{119}Sn nuclear resonance measurements of its solutions in ethylenediamine failed because we could detect no absorption.

The facts given above, and particularly the relatively high diamagnetism, are in accord with the assumption of a Sn_9^{4-} polyhedron (a trigonal prism with pyramids set on each of its square faces). This structure has been found for the electronically equivalent unit Bi_9^{5+} of $Bi_{24}Cl_{28}$[4], and has also been suggested by analogy for Na_4Sn_9 and Na_4Pb_9[5]. Final solution of this problem will only come from an X-ray determination of structure, which is in progress (X-ray data for the unit cell: monoclinic, space group C2/c, Z = 8 on the assumption of Sn_9^{4-} units in connection with the observed density 2.05 ± 0.2 g/cm³; lattice constants a = 20.17, b = 11.64, c = 39.36 Å, β = 90.61 °)[6].

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X-Ray Structure Analysis of 1,2,3,4-Tetrathiadecalin[**] [***]

By *Franz Fehér, Aloys Klaeren*, and *Karl-Heinz Linke*[*]

1,2,3,4-Tetrathiadecalin[1], which has been synthesized from cyclohexanedithiol and disulfur dichloride by the dilution technique, crystallizes as triclinic crystals with lattice constants a = 9.28₇ Å, b = 8.60₆ Å, c = 6.30₉ Å, α = 107.7 °, β = 102.4 °, and γ = 98.6 °. The observed pycnometric density is 1.55 g cm^{-3}, corresponding to a unit cell of two molecules ($d_{calc.}$ 1.528 g cm^{-3}). The space group $P\bar{1}$ has been derived from the statistics of the intensity distribution[2] and the external habit of the crystals.

For three-dimensional X-ray structure analysis the intensities of 962 independent reflections were determined from precession photographs. The sign was determined for 43 reflections of the *hk*0 projection and for 30 reflections of the *h*0*l* projection by means of the Harker-Kasper inequalities, and thence by a series of successive Fourier projections the initial parameters were obtained for three-dimensional refinement by the method of least squares, the sulfur atoms being treated anisotropically and the carbon atoms isotropically. The hydrogen atoms were left out of consideration. In these conditions the R value converged at 0.129. In the last cycle of refinement the change in all the atomic parameters was less than half the corresponding standard

deviation. Fig. 1 shows the bond lengths and bond angles found for 1,2,3,4-tetrathiadecalin.

1,2,3,4-Tetrathiadecalin exists in a chair-chair conformation. The sulfur atoms bound to C-1 and C-6 are trans-equatorial with respect to the cyclohexane ring. The intermolecular separation of the sulfur-carbon skeletons is in all

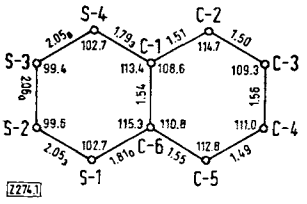


Fig. 1. Bond lengths (Å) and bond angles (°) in 1,2,3,4-tetrathiadecalin. Standard deviations of bond lengths and bond angles: σ_{S-S} 0.008 Å, σ_{S-C} 0.020–0.023 Å, σ_{C-C} 0.025–0.033 Å; σ_{S-S-S} 0.3°, σ_{S-S-C}, σ_{S-C-C}, σ_{C-C-C} 0.7–1.8°.

cases greater than 3.8 Å, so that crystal packing cannot exert any appreciable influence on the molecular conformation.

Deviations from two-fold symmetry of the molecule are not significant. Within the experimental error all the bond lengths lie within the values given in the literature. The relatively small values of the bond angles at sulfur, and particularly at S-2 and S-3 are due to incorporation of C-1 and C-6 in the sulfur ring. Noteworthy are the dihedral angles (C-6)—(S-1)—(S-2)—(S-3) = 66.1°, (S-1)—(S-2)—(S-3)—(S-4) = 69.1°, and (S-2)—(S-3)—(S-4)—(C-1) = 68.3°, which are significantly smaller than the corresponding angle in S_6-sulfur. *Pauling*[3] ascribed the difference between the bonding energies of the sulfur-sulfur bond in cyclohexa- and cycloocta-sulfur at a first approximation to the differing dihedral angles, and if we apply this view to the six-membered ring containing four sulfur atoms we can calculate from a mean dihedral angle of 68° that the bonding energy should be 1.9 kcal/mole per S—S bond greater than for cyclooctasulfur.

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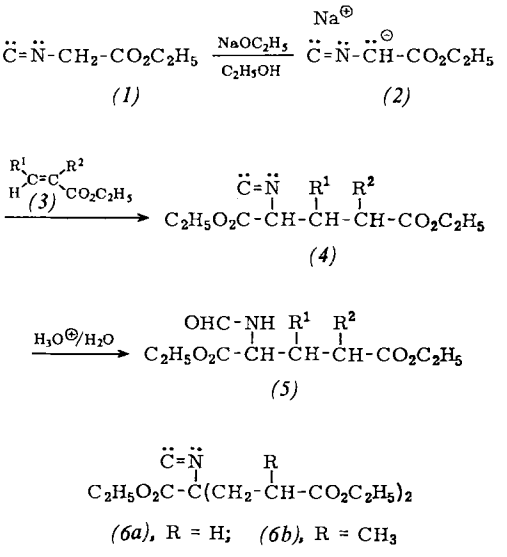
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Preparation of Glutamic Acid Derivatives from α-Metalated Ethyl Isocyanoacetate and Acrylic Esters[1]

By *Ulrich Schöllkopf* and *Kurt Hantke*[*]

When ethyl isocyanoacetate *(1)*[2] is allowed to react with ethyl acrylate and its derivatives *(3)* in ethanol containing catalytic amounts of sodium ethoxide, ethyl α-isocyanoglutarate and its derivatives *(4)* can be isolated in satisfactory yields.

The decisive intermediate in this synthesis is the α-metalated ethyl isocyanoacetate *(2)* which adds to the activated double bond of the acrylic ester in a Michael addition.



(6a), R = H; *(6b)*, R = CH_3

Treating 3 equivalents of acrylic or methacrylic ester with one of the ester *(1)* at 50 °C in presence of 0.14 equivalent of the catalyst affords a 72% or 75% yield of the diadduct *(6a)* or *(6b)*, respectively.

Compounds of type *(4)* can be converted into ethyl *N*-formylglutamates *(5)* by treatment with *ca.* 2% ethanolic hydrochloric acid for *ca.* 1.5 hours.

(4), R^1 =	R^2	B.p. (°C/torr)	Yield (%)
H	H	150/10	48
CH_3	H	151/10	65
C_6H_5	H	165/1.5	42
$COOC_2H_5$	H	128/0.1	31
H	CH_3	80/0.1	40

Diethyl 2-isocyano-3-methylglutarate:

A mixture of ethyl isocyanoacetate (4.54 g, 40 mmoles) and ethyl crotonate (4.56 g, 40 mmoles) is added dropwise with stirring during *ca.* 0.5 h to a solution of sodium (0.15 g, 6.5 mmoles) in anhydrous ethanol (20 ml), the temperature rising to about 50 °C. The mixture is set aside for 24 h, then the ethanol is distilled off, and the residue is neutralized with 0.2 N-hydrochloric acid and extracted with ether (100 ml). The extract is dried over magnesium sulfate and evaporated, and the residue is fractionated, which affords diethyl 2-isocyano-3-methylglutarate, b.p. 151 °C/10 torr (*ca.* 60:40 mixture of diastereoisomers). — IR spectrum (film): 2145 cm^{-1} ($\nu_{N\equiv C}$), 1740 cm^{-1} ($\nu_{C=O}$). NMR spectrum (CCl_4, τ): 5.58 (d, $J \approx 3.5$ Hz), 5.42 (d, $J \approx 3$ Hz) for the proton α to the isocyano group.

A variant of this process is used for synthesis of the unsubstituted diethyl 2-isocyanoglutarate and diethyl 2-isocyano-4-methylglutarate. To avoid formation (very easy in this case) of the diadduct *(6a)* or *(6b)*, 2 equivalents of *(1)* are placed in ethanol containing sodium ethoxide, and 1 equivalent of *(3)* is added dropwise.

Diethyl N-formyl-β-methylglutamate:

Diethyl 2-isocyano-3-methylglutarate (4.59 g, 20 mmoles) is treated with ethanol (20 ml) and 35% hydrochloric acid (1 ml) and set aside at room temperature for 1.5 h, then neutralized with powdered potassium hydroxide (0.56 g, 10 mmoles), filtered from the precipitated potassium chloride, and fractionally distilled, yielding diethyl *N*-formyl-β-methylglutamate, b.p. 125 °C/0.07 torr. — IR

spectrum (film): 1690 cm^{-1} ($\nu_{C=O}$ amide), 1730 cm^{-1} ($\nu_{C=O}$ ester), 1520 cm^{-1} (ν_{NH}), and 3300 cm^{-1} (ν_{NH}). NMR spectrum (CCl_4, τ): 1.82 (HC=O).

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Free Radical Additions to Dicyclopentadienylcobalt[1] [**]

By *Gerhard E. Herberich* and *Johann Schwarzer*[*]

A two-step radical mechanism has been proposed[3] for the reaction of dicyclopentadienylcobalt *(1)* with organic halides[2–4], in which *(1)* acts both as one-electron donor [eq. (a)] and as radical trap [eq. (b)]:

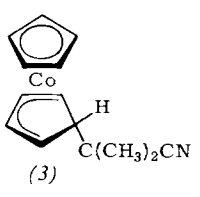
$$Co(C_5H_5)_2 + RX \xrightarrow{slow} [Co(C_5H_5)_2]X + \{R\cdot\} \quad (a)$$
(1)

$$\{R\cdot\} + Co(C_5H_5)_2 \xrightarrow{fast} Co(C_5H_5)(C_5H_5R) \quad (b)$$

R = *e.g.* CCl_3 [2], $C_6H_5CH_2$ [3], CH_2I [4], or $CHBr_2$ [4]
X = Cl, Br, or I

We have found direct proof of the addition of a radical to *(1)*. Thermal decomposition of an excess of azoisobutyronitrile (AIBN) in boiling toluene containing *(1)* affords cyclopentadienyl-[5-*exo*-(1-cyano-1-methylethyl)cyclopentadiene]cobalt *(3)* almost quantitatively. This product forms red prisms, stable in air and melting at 93—94 °C; $\tilde{\nu}_{CN}$ = 2230 cm^{-1}; ^{1}H-NMR spectrum in C_6D_6: τ = 5.02 [$H_{(2)}$, $H_{(3)}$; "triplet"], τ = 5.54 (C_5H_5; singlet), τ = 7.32 [$H_{(endo)}$; triplet], τ = 7.46 [$H_{(1)}$, $H_{(4)}$; "quartet"], τ = 9.39 (2 CH_3; singlet); cf.[2,4]. As shown by the ^{1}H-NMR data for *(3)*, the addition occurs stereospecifically:

(1) + $\{\cdot C(CH_3)_2CN\}$ → *(3)*



The mechanistic alternative of an initial one-electron transfer from *(1)* to *(2)* with subsequent nucleophilic addition of $[C(CH_3)_2CN]^-$ to $[Co(C_5H_5)_2]^+$ can be excluded because *(3)* is also obtained in very good yield using 1-butanol as solvent at 100 °C.

On thermolysis of AIBN in styrene, only 50% of the radicals *(2)* formed are incorporated into the polymer chain[5]; the extensive dimerization is ascribed to a cage effect. However, decomposition of AIBN in presence of a small excess of *(1)* in dilute benzene solution affords more than 80% of the adduct *(3)*. These findings support the mechanism cited above and make it probable that *(1)* could add a variety of C-radicals in accord with eq. (b).

Experimental:

A solution of AIBN (148 mg, 0.90 mmole) and $Co(C_5H_5)_2$ (249 mg, 1.32 mmoles) in anhydrous toluene (5 ml) is refluxed (oil-bath temperature 130 °C) for 15 min with rigorous exclusion of O_2 (*ca.* 97% decomposition of AIBN[6]). The mixture is then cooled rapidly, filtered through a G4 frit, and freed from solvent and organic impurities at 20 °C in a high vacuum. Sublimation of the residue in a high vacuum then gives analytically pure *(3)* [330 mg, 97% based on *(1)*].

A solution of AIBN (117 mg, 0.71 mmole) and $Co(C_5H_5)_2$ (327 mg, 1.73 mmoles) in benzene (20 ml) is heated for 15 h under reflux (> 99% decomposition of the AIBN[6]). The excess of $Co(C_5H_5)_2$ is extracted with aqueous NH_4Cl solution, and the benzene phase is dried over $CaCl_2$. Further working up as above affords *(3)* (297 mg, 81% based on AIBN).

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Hexathio-digermanates and -distannates: A New Type of Dimeric Tetrahedral Ion

By *Bernt Krebs, Siegfried Pohl*, and *Willy Schiwy*[*]

The only statements so far made about the nature of the thiogermanates(IV) that are formed from aqueous solution have been mutually contradictory[1]. Characterization of definite phases has been made difficult by formation of various hydration stages. The formal analogs of the anhydrous thiogermanates and ternary sulfides[2] that can be obtained by high-temperature methods are hydrated salts of probable fundamental composition $M^I_4GeS_4$, $M^I_2GeS_3$, and $M^I_2Ge_2S_5$ (each $\cdot xH_2O$; M^I = alkali metal)[1]; nothing is known about the structure of thiogermanate ions except for tetrahedral GeS_4^{4-} (*e.g.*[3,6]).

We have now obtained definite alkali metal salts containing the ion $Ge_2S_6^{4-}$ by dissolving GeS_2 in a concentrated aqueous solution of the alkali sulfide and precipitating the extremely water-soluble salts by a large excess of acetone (cf.[1a]) at constant pH (7—8). Higher members $(Ge_nS_{2n+2})^{4-}$ can also be prepared by altering the ratio M^I_2S : GeS_2 and the pH.

$Na_4Ge_2S_6 \cdot 14\,H_2O$ *(1)* was characterized by analysis, vibration spectra, and a complete X-ray structure analysis. These showed that "trithiogermanates" ("metathiogermanates") contain dimeric isolated $Ge_2S_6^{4-}$ anions with the structure shown in Fig. 1. This unexpected structure, which is novel for thio- and oxo-anions and consists of edge-sharing tetrahedra, corresponds to the structure of, *e.g.*, Al_2Cl_6 (in the gas phase), Al_2Br_6, and the thiohalides $(SCX_2)_2$ and $(SSiX_2)_2$ (X = halogen). Of the sulfides, only the chain-polymeric SiS_2 has this edge junction; GeS_2 does not[2].

(1) crystallizes in the triclinic system ($P\bar{1}$) with a = 9.978(6) Å, b = 7.020(5) Å, c = 9.601(6) Å, α = 108.41(4)°, β = 92.39(4)°, γ = 91.69(4)°, $d_{obs.}$ = 1.80, $d_{X\text{-ray}}$ = 1.778 g cm^{-3}, Z = 1. The $Ge_2S_6^{4-}$ ion in *(1)* has exact C_i sym-

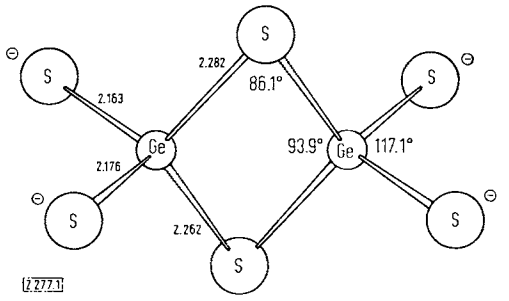


Fig. 1. Structure of the ions $Ge_2S_6^{4-}$ and $Sn_2S_6^{4-}$; bond lengths (in Å) and bond angles for $Ge_2S_6^{4-}$ in solid $Na_4Ge_2S_6 \cdot 14\ H_2O$.

metry, deviations from D_{2h} being very small. The terminal bonds have definite π-content, while the bridging Ge—S bonds correspond approximately to single bonds (sum of the covalent radii 2.26 Å). The bond angles S(terminal)-Ge-S(bridge) range between 110.1 and 111.8 °. The Raman spectrum of the solid, in which D_{2h} symmetry would require that 9 of the 18 fundamental vibrations be active, has lines at 457 (rel. int. 8), 452 (sh, 4), 402 (1), 378 (1), 350 (10), 221 (1), 191 (5), 180 (2), 143 (8), 101 (1), 81 (1), and 58 (1) cm^{-1}.

The "thiopyrogermanates" described by *Schwarz* and *Giese*[1a] do not exist as homogeneous phases — they consist of mixtures of $M_4^IGeS_4$ and $M_4^IGe_2S_6$.

It is especially remarkable that the same structure as shown in Fig. 1 applies to the corresponding tin ion which has been formally described as "metathiostannate" SnS_3^{2-}, but which has not been structurally characterized as yet. According to our X-ray results, the ion has to be formulated as hexathiodistannate(IV) $Sn_2S_6^{4-}$. The sodium salt, which has been isolated by *Jelley*[4] using a complicated procedure, was prepared by us analogously to the thiogermanate (pH 8—9). Li, K, Rb, and Cs form similar salts of various water contents.

$Na_4Sn_2S_6 \cdot 14\ H_2O$ (not $16\ H_2O$[4]) is isotypic with *(1)* and crystallizes with a = 10.114(6) Å, b = 7.027(5) Å, c = 9.801(6) Å, α = 108.30(4) °, β = 92.18(4) °, γ = 91.11(4) °, d_{obs} = 1.97, $d_{X\text{-ray}}$ 1.945 g cm^{-3}.

The bonding in $Sn_2S_6^{4-}$ ions is very similar to that in $Ge_2S_6^{4-}$. Raman spectrum: 391 (4), 377 (8), 341 (10), 281 (4), 190 (1), 178 (2), 151 (1), 136 (2), 118 (1), 96 (1), 59 (6), and 44 (1) cm^{-1}.

X-ray analysis of the orthothiostannate $Na_4SnS_4 \cdot 14\ H_2O$ *(2)*[5] (not $18\ H_2O$[4]) shows that here too tetrahedrally coordinated tin exists in the form of isolated SnS_4^{4-} ions (d_{Sn-S} = 2.380 Å) analogous to PS_4^{3-}, AsS_4^{3-}, SbS_4^{3-}, and GeS_4^{4-} and to the SnS_4 unit in ternary and quaternary sulfides[6]. The salt *(2)* crystallizes in the monoclinic system (C2/c) with a = 8.622(5) Å, b = 23.534(12) Å, c = 11.347(7) Å, β = 110.53(4) °, $d_{obs.}$ = 1.84, $d_{X\text{-ray}}$ = 1.835 g cm^{-3}, Z = 4.

Thus, contrary to previous assumptions[4], octahedral six-coordination [*e.g.*, as $Sn(OH)_3(SH)_3$] is unstable in solid hydrated thiostannates. Raman spectra, however, show that in aqueous solutions a pH-dependent equilibrium exists between various species, possibly including octahedrally coordinated ones.

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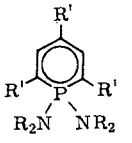
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Structure of 1,1-Bis(dimethylamino)-2,4,6-triphenylphosphorin

By *Ulf Thewalt*, *Charles E. Bugg*, and *Albert Hettche*[*]

Dimroth et al.[1] recently prepared a phosphorin with NR_2 substituents on the P atom, namely, the compound *(1)* with R = R′ = C_6H_5. The properties of the compound indicated aromatic character for the C_5P ring system.



(1)

An X-ray structure analysis of a compound of type *(1)* therefore seemed of interest, especially for comparison with *P*-alkyl and *P*-alkoxy phosphorins.

Yellow-fluorescing, plate-shaped, orthorhombic crystals of 1,1-bis(dimethylamino)-2,4,6-triphenylphosphorin *(1)*, R = CH_3, R′ = C_6H_5, were obtained by slow evaporation of an ethanolic solution. Crystal data: space group Pbca; a = 13.99 Å, b = 15.66 Å, c = 21.62 Å; Z = 8, $d_{X\text{-ray}}$ = 1.156, d_{obs} = 1.16 g/cm^3. The intensities of about 4000 independent reflections were measured on a Picker automated diffractometer using Cu—K_α radiation. The structure determination was based on the symbolic addition method[2] and was carried out with a FORTRAN program. To find the signs or symbols of the 237 strongest reflections ($E \geq 1.9$) required only a few minutes with a TR4 computer. An E map revealed the positions of all non-hydrogen atoms. Least-squares refinement of the structure — including the

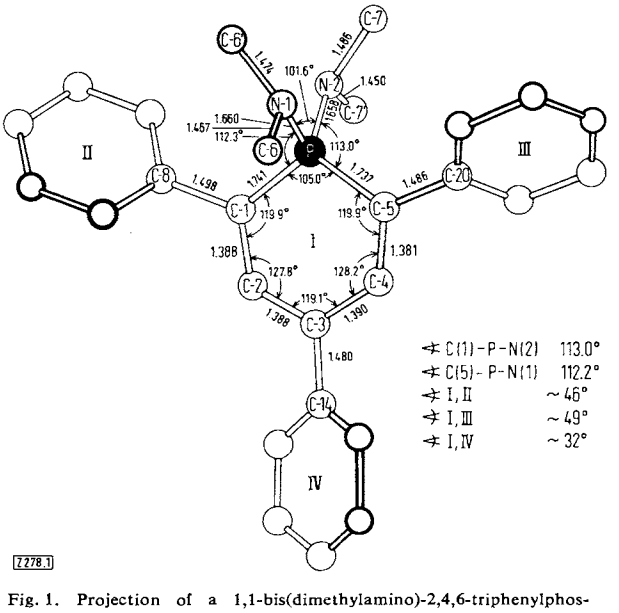


Fig. 1. Projection of a 1,1-bis(dimethylamino)-2,4,6-triphenylphosphorin molecule along the crystallographic *b*-axis. Standard deviations of the bond lengths (Å) are *ca.* 0.005 Å.

hydrogen atoms during the final cycles — led to a conventional R index of 9.1 % for all 3932 reflections. Fig. 1 shows a projection of the molecule along with selected bond distances and bond angles.

The PC_5 ring is almost planar; the deviations from the C(2)PC(4) plane are C(1) = −0.055 Å, C(3) = 0.026 Å, C(5) = 0.003 Å. The mean P—C bond length (1.739 Å) is intermediate between the lengths of P—C single and double bonds (1.82 and 1.66 Å, respectively [3]). The C—C bonds of the PC_5 ring compare well with each other (mean value 1.387 Å). This ring geometry and the coordination at the P atom [distorted tetrahedron; C—P—C and N—P—N angles distinctly smaller than the tetrahedral angle; N(1)-PN(2) plane perpendicular to the C(1)PC(5) plane] agree very well with those found for P-alkyl and P-alkoxy phosphorins [4, 5]. As in the case of these last compounds, conclusions as to the aromatic character of the PC_5 system can be drawn from bond lengths and angles within the central ring. Broadening of the ligand-P-ligand angle to 101.6° from the 93° of 1,1-dimethoxy-2,4,6-triphenylphosphorin [5] may be caused by the greater spatial demands of the NR_2 groups. The two P—N bonds of 1.66 Å are significantly shorter than a P—N single bond (1.77 ± 0.02 Å in $Na[PO_3NH_3]$ [6]). This indicates a $d_\pi p_\pi$ interaction superimposed on the single bonds. The arrangement of the three phenyl groups is propeller-like.

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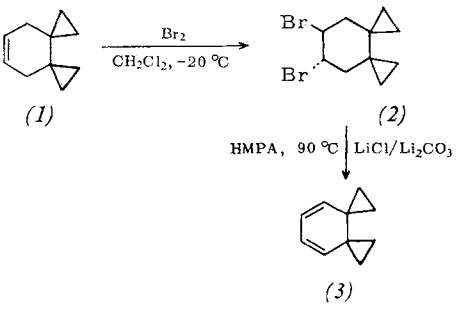
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Dispiro[2.0.2.4]deca-7,9-diene, a Bishomo-*o*-quinodimethane

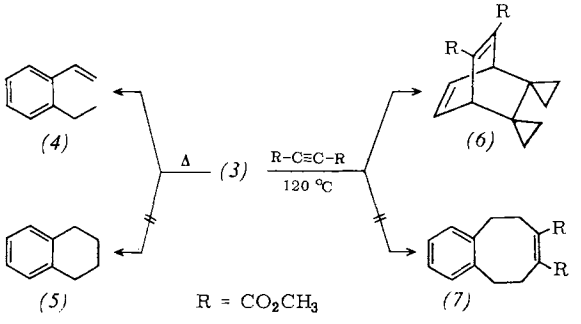
By *Armin de Meijere* [*]

The maximum electronic interaction between double bonds and cyclopropane rings occurs when the π-orbitals of the double bond are aligned parallel to the plane of the three-membered ring [1]. In the dispiro[2.0.2.4]deca-7,9-diene *(3)* such a favorable conformation is fixed, because the six-membered ring formed from six sp^2-hybridized carbon atoms [2] must be planar or nearly so. Compound *(3)* may thus be expected to show interesting chemical and physical properties.

Synthesis of *(3)* started from dispiro[2.0.2.4]dec-8-ene *(1)* [3]. Addition of bromine in methylene dichloride led to the dibromide *(2)*, and dehydrobromination of *(2)* by lithium chloride in hexamethylphosphoramide [4] then yielded *(3)* [5] [*ca.* 40 %, based on *(1)*]. The spectroscopic data are in accord with the proposed structure: In the mass spectrum the molecular ion appeared at m/e = 132. The ^{1}H-NMR spectrum (in CCl_4) showed one AA'XX' system for four olefinic protons at τ = 4.81, τ = 4.02, and another one for eight cyclopropyl protons at τ = 9.46, τ = 9.58.



Compound *(3)* resinifies on exposure to air for several days. Its thermal rearrangement, which proceeds relatively rapidly at 120 °C ($\tau_{1/2} \approx 3.5$ h), leads to *o*-ethylstyrene *(4)*. Surprisingly the bicyclopropyl-cyclohexene rearrangement [6], which is known for the parent compound and would have afforded tetralin *(5)* from *(3)*, does not occur.



Dimethyl acetylenedicarboxylate reacts smoothly with *(3)* at 120 °C in 1 hour to give the Diels-Alder adduct *(6)* [5], m.p. 93—94 °C, whose structure was proved by the ^{1}H-NMR spectrum. By analogy to the known reaction of quadricyclane [7] one might expect addition to the bicyclopropyl system in *(3)* which would lead to the benzocyclooctadiene derivative *(7)*, thus gaining aromatization energy. However, this has not yet been observed.

The NMR spectrum provided an answer to the question whether the six-membered ring in *(3)* contains a cyclically delocalized electron system. That there is no diamagnetic ring current can be concluded from the chemical shifts of the olefinic protons — on transition from the 1,3-cyclohexadiene *(8)* to *(3)*, essentially the resonances of H-1 and H-4 are moved by 0.49 ppm to higher field due to the diamagnetic anisotropy of the cyclopropane rings (Table 1). The vicinal H,H coupling constants in the olefinic AA'XX' system of *(3)* are intermediate between those of *(8)* and *(9)*

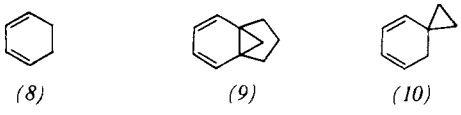


Table 1. Chemical shifts (τ values in ppm) and H,H coupling constants of the olefinic protons of some 1,3-cyclohexadiene systems.

	H-1, H-4	H-2, H-3	$J_{1,2} = J_{3,4}$	$J_{2,3}$	$J_{1,3} = J_{2,4}$	$J_{1,4}$	Ref.
(8)	4.32	4.17	9.66	5.04	1.02	1.12	[8]
(3)	4.81 [a]	4.02 [a]	9.20	5.46	0.82	1.12	[9]
(9)	3.93	4.29	9.25	5.94	0.58	1.31	[10]

[a] The assignment is supported by the observed long-range coupling of H-1, H-4 with the cyclopropyl protons.

(Table 1); this indicates that in *(3)* there is no additional equalization of bond orders due to cyclic delocalization of the π-electrons.

Compounds containing the dispiro[2.0.2.4]decadiene system have been, respectively, postulated and discussed as

intermediates in photoreactions of benzo-7-oxanorbornadiene[11] and benzonorbornadiene[12]. Therefore the UV spectrum of *(3)* is of special interest: λ_{max} = 284 nm (ε = 4800), without vibrational structure (in cyclohexane). The maximum of the longest-wavelength absorption band of spiro[2.5]octa-4,6-diene *(10)*, which was prepared for comparison[13], appears at 269 nm ($\varepsilon \approx 3000$), *i.e.* between those of *(3)* and *(8)* (λ_{max} = 250 nm[15]).

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[13] *(10)* was prepared analogously to *(3)* from spiro[2.5]oct-5-ene [14].

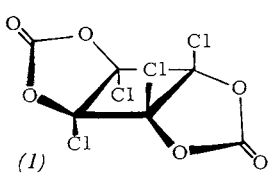
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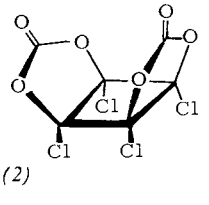
Derivatives of Tetrameric Carbon Monoxide[**]

By *Hans-Dieter Scharf* and *Helmut Seidler*[*]

Dichlorovinylene carbonate (4,5-dichloro-1,3-dioxol-2-one)[1] dimerizes when irradiated in concentrated solution in acetone by light of wavelength $\lambda \geq 290$ nm[2], affording the stereoisomeric 2+2 cycloadducts *(1)* and *(2)* in the ratio 3:1. Both products have the composition $C_6O_6Cl_4$[3].



(1)

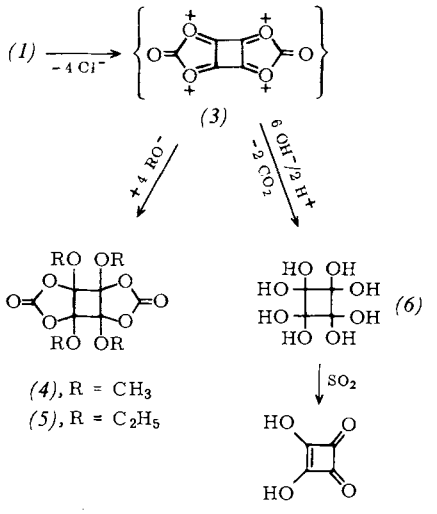


(2)

When the solvent is cyclohexane the products are formed in the same ratio but the quantum yield in acetone is higher by a factor of 5, so that triplet-sensitization is very likely. Preference for the "*anti*" isomer is in agreement with this[4].

(1) crystallizes directly from the irradiated mixtures, but *(2)* must be isolated from enriched fractions by fractional crystallization.

The thermal stability of *(1)* is surprisingly high. The compound is unchanged when its melt is refluxed (b.p. 200 °C) for a considerable time. Hydrolysis with acetone-water leads quantitatively to cyclobutaneoctaol *(6)*[5], which is identical with the product formed by oxidation of squaric acid by nitric acid[6,7].



Compound *(6)* can be reduced to squaric acid by SO_2 using the method of *West et al.*[6].

Alcoholysis of *(1)* by methanol or ethanol also under S_N1 conditions leads very rapidly to compounds *(4)* and *(5)* with replacement of all four Cl atoms by OR groups, no products of partial exchange being detectable.

(4): $C_{10}H_{12}O_{10}$[3], m.p. 200 °C (acetone); IR, CO frequency 1830 cm^{-1}; NMR[8] ([D_6]acetone), singlet at τ = 6.28.

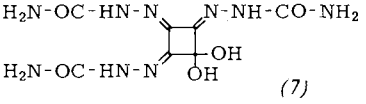
(5): $C_{14}H_{20}O_{10}$[3], m.p. 128 °C (ethanol); IR frequency 1810, 1855 (shoulder) cm^{-1}; NMR ([D_6]acetone), quartet at τ = 6.0 (2 H), triplet at τ = 8.65 (3 H), J = 6 Hz.

Surprisingly the carbonate group is not attacked under these conditions, although the alcoholic solution reacts distinctly acid[9]. To explain these facts a cation *(3)* is assumed to be formed as intermediate which is trapped by the nucleophilic OR groups.

When a 1:1 methanol-ethanol mixture is used, compound *(4)* is accompanied by two mixed substitution products, but *(5)* is not contained in the products.

Boiling *(4)* or *(5)* with dilute hydrochloric acid also leads to cyclobutaneoctaol *(6)*.

Compounds *(1)*, *(2)*, *(4)*, *(5)*, and *(6)* react with semicarbazide hydrochloride to give the same orange-colored semicarbazone, which on account of its composition $C_7H_{11}O_5N_9$ (mol. wt. 301.23) and IR-spectroscopic properties (OH and NH stretching vibrations at 3000 to 3500 cm^{-1}, ν_{CO} = 1680 cm^{-1}) is considered to be cyclobutanetetraone trissemicarbazone monohydrate *(7)*. This



(7)

substance can be recrystallized from glacial acetic acid and is shown by thin-layer chromatography[10] to be homogeneous. It deflagrates before its melting point is reached.

Preparation of (1) and (2):

4,5-Dichloro-1,3-dioxal-2-one (70 g) in anhydrous acetone (50 ml) is irradiated for 7 days at room temperature[2]. During this time product *(1)* is filtered off in portions (total 8.6 g). The mother liquor is concentrated without being heated, whereupon more *(1)* separates, and the amount can be increased by refrigeration. The mother liquor is then distilled in a high vacuum, much (*ca.* 50 g) starting material being recovered (b.p. 20—30 °C/3.5 torr). Finally there distills an oil (6 g, b.p. 110 °C/3.5 torr) that solidifies in the receiver and consists to the extent of about 80% of product *(2)*. Fractional crystallization from light

petroleum (b.p. 80–100 °C), in which *(1)* is less soluble than *(2)*, affords *(2)* in crystalline form. *(1)*: m.p. 157 °C. *(2)*: m.p. 97 °C, IR absorption ν_{CO} = 1840 and 1870 cm^{-1}.

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[**] This work was supported by the Landesamt für Forschung des Landes Nordrhein-Westfalen.

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[7] OH proton signals in the NMR spectrum ([D_5]pyridine): τ = 4.02. The OH protons of all-*cis*-cyclobutanetetraol [*W. Hartmann* and *R. Steinmetz*, Chem. Ber. *100*, 217 (1967)] in the same solvent give signals at τ = 4.15.

[8] Varian T-60 spectrometer, TMS as standard.

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[10] Al_2O_3–G and glacial acetic acid.

Lone Pair Interaction in Pyridazine, Pyrimidine, and Pyrazine[1]

By *Rolf Gleiter, Edgar Heilbronner*, and *Volker Hornung*[*]

The orbital diagram of Figure 1 correlates the energy levels $\varepsilon(\psi_J)$ of the highest occupied orbitals ψ_J of benzene *(1)*, pyridine *(2)*, pyridazine *(3)*, pyrimidine *(4)*, and pyrazine *(5)*. The orbital energies $\varepsilon(\psi_J)$ correspond to the vertical ionization potentials $I_v(J)$ (Table 1), which were determined from high-resolution photoelectron spectra[2]: $\varepsilon(\psi)_J = -I_v(J)$. (For previous measurements see, *e.g.*, ref.[4].) The designation of the orbitals ψ_J characterizes, in the usual nomenclature, the symmetry behavior of the orbital with regard to symmetry operations of the symmetry group to which the molecule belongs. The letters S and A denote the behavior of the two degenerate π orbitals $e_S = (2\Phi_1 + \Phi_2 - \Phi_3 - 2\Phi_4 - \Phi_5 + \Phi_6)/\sqrt{12}$ and $e_A = (\Phi_2 + \Phi_3 - \Phi_5 - \Phi_6)/2$ of benzene on reflection in the *x,z* plane. In Figure 1, S and A are used solely in order to correlate the orbitals of the systems *(2)* to *(5)* with the "parent orbitals" of benzene from which they are derived. Linear combination of the atomic orbitals n_1 and n_2 of the two lone pairs in *(3)*, *(4)*, and *(5)*, which are regarded as localized, yields initially the orbitals $n_+ = (n_1 + n_2)/\sqrt{2}$ and $n_- = (n_1 - n_2)/\sqrt{2}$ of correct symmetry. Those molecular orbitals ψ_J to which n_+ or n_- make the greatest contribution are marked (+) and (—) respectively in Fig. 1.

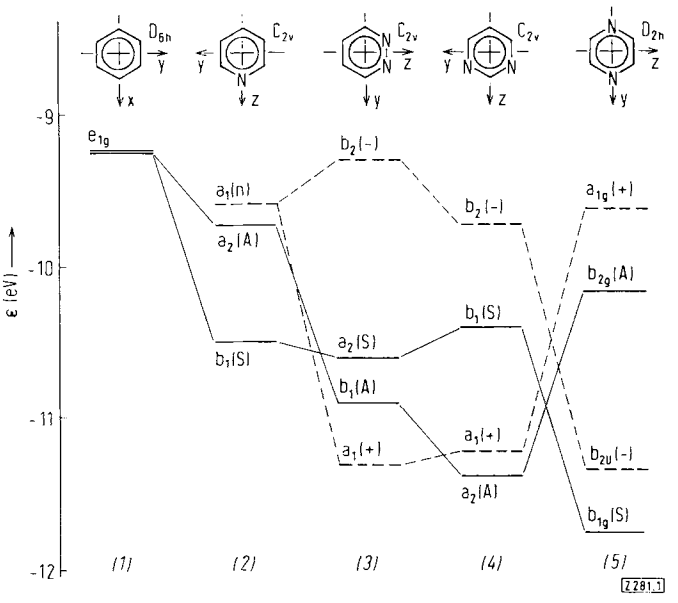


Fig. 1. Correlation diagram. It should be pointed out that (S) and (A) do *not* refer to the true symmetry of the molecule but solely to the parent orbital in *(1)* from which the respective π orbital is derived.

Assignment of the individual bands in the PE spectra to π and n/σ ionization processes is based on the characteristic shapes of π and n/σ bands as well as on model calculations. It may be deduced from the fine structure of the two n-bands of *(5)* that the first n-band ($I_v(1)$ = 9.63 eV) corresponds to an ionization process in which the photoelectron stems from an a_{1g} orbital containing the linear combination n_+, while the third band ($I_v(3)$ = 11.35 eV) must be assigned to the b_{2u} orbital containing the n_- combination[5].

Interaction between the lone pair orbitals n_1 and n_2 occurs mainly *via* two mechanisms: a) Direct overlapping, *i.e.* "through-space" interaction b) "through-bond" interaction with other bonding and/or antibonding σ orbitals of the molecule[6]. Mechanism a) always leads to the sequence $\varepsilon(\psi_-)$ above $\varepsilon(\psi_+)$, while mechanism b) leads to the same or to the reverse sequence, depending on the relative positions of the orbitals n_1 and n_2 in the molecule.

The molecules *(3)*, *(4)*, and *(5)* yield the following values for the splitting

$$\Delta_{exp} = \varepsilon(\psi_-) - \varepsilon(\psi_+) = I_v(\psi_+) - I_v(\psi_-)$$

which are compared with the theoretical values calculated from an EHT model[7].

	ψ_-	ψ_+	Δ_{exp} (eV)	Δ_{theor} (eV)
(3)	$b_2(n_-)$	$a_1(n_+)$	2.00	0.99
(4)	$b_2(n_-)$	$a_1(n_+)$	1.50	0.80
(5)	$b_{2u}(n_-)$	$a_{1g}(n_+)$	−1.72	−1.67

As can readily be understood on a qualitative basis, the contribution to the value of Δ that is attributable to mechanism a) decreases along the series *(3)*, *(4)*, *(5)* owing to

Table 1. Vertical ionization potentials $I_v(J)$ (in eV) [3].

	$I_v(1)$		$I_v(2)$		$I_v(3)$		$I_v(4)$	
(1) (D_{6h})	9.24	$e_{1g}(\pi)$						
(2) (C_{2v})	9.59	$a_1(n)$ [a]	9.73	$a_2(\pi, A)$ [a]	10.50	$b_1(\pi, S)$		
(3) (C_{2v})	9.31	$b_2(n_-)$	10.61	$a_2(\pi, S)$	10.9 [b]	$b_1(\pi, A)$	11.31	$a_1(n_+)$
(4) (C_{2v})	9.73	$b_2(n_-)$	10.41	$b_1(\pi, S)$	11.23	$a_1(n_+)$	11.39	$a_2(\pi, A)$
(5) (D_{2h})	9.63	$a_{1g}(n_+)$	10.18	$b_{2g}(\pi, A)$	11.35	$b_{2u}(n_-)$	11.77	$b_{1g}(\pi, S)$

[a] Partially resolved double band; the onset exhibits typical n band structure.
[b] Value uncertain because of overlapping with bands 2 and 4.

the increasing distance between n_1 and n_2. In contrast, mechanism b) contributes to about the same extent in all three cases. Since $\psi(n_+)$ interacts primarily with the lower-energy bonding σ orbitals of the same symmetry, and $\psi(n_-)$ mainly with the antibonding ones, mechanism b) has the effect of raising $\varepsilon(\psi(n_+))$ and lowering $\varepsilon(\psi(n_-))$. In *(5)* this leads to an inversion of the sequence of the orbitals $\psi(n_+)$, $\psi(n_-)$ relative to *(3)* and *(4)* and thus to a negative Δ value. Direct interaction between n_1 and n_2 (mechanism a)) dominates in *(3)* and *(4)*. Finally, the Δ values for *trans*-azomethane ($\Delta = -3.3$ eV)[8] and for 3,3-dimethyldiazirine ($\Delta = 3.5$ eV)[9] are given for the sake of comparison.

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Note added in proof:
After submission of the present communication, a further discussion of the PE-spectra of the diazines has appeared in print: *D. W. Turner, C. Baker, A. D. Baker*, and *C. R. Brundle*: Molecular Photoelectron Spectroscopy. Wiley-Interscience, New York 1970, p. 327. Two correlation diagrams are given, in which assignments are proposed which differ from that shown in Fig. 1.

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Lone Pair Interaction in 3,3-Dimethyldiazirine[1]

By *Edwin Haselbach, Edgar Heilbronner, Albrecht Mannschreck*, and *Werner Seitz*[*]

The photoelectron-spectroscopic determination of the interaction

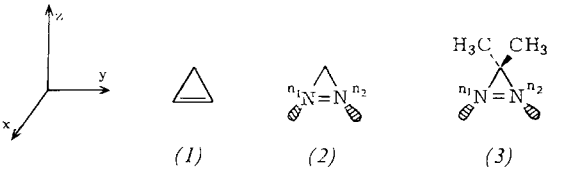
$$\Delta = \varepsilon(\psi(n_-)) - \varepsilon(\psi(n_+))$$

between the lone pairs n_1 and n_2 of the *trans* azo group in azomethane has been reported previously[2] ($\Delta = -3.3$ eV; cf. ref.[3]). The functions $\psi(n_-)$ and $\psi(n_+)$ are those molecular orbitals to which the linear combinations

	Symmetry behavior	
	C_{2h}	C_{2v}
$n_- = \frac{1}{\sqrt{2}}(n_1 - n_2)$	B_u	B_2
$n_+ = \frac{1}{\sqrt{2}}(n_1 + n_2)$	A_g	A_1

make the greatest contribution. We have now also studied the interaction of n_1 and n_2 in a diazirine derivative, which contains the *cis* azo group.

Theoretically determined orbital energies ε for the five highest occupied MOs of cyclopropene *(1)*, diazirine *(2)*, and 3,3-dimethyldiazirine *(3)* are listed in Table 1.



(1) *(2)* *(3)*

Table 1. Calculated orbital energies ($-\varepsilon$) for cyclopropene *(1)*, diazirine *(2)*, and 3,3-dimethyldiazirine *(3)* [in eV].

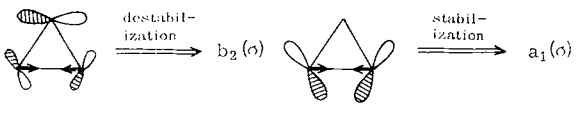
(1)		*(2)*		*(3)*
ab initio	MINDO/2	*ab initio*	MINDO/2	MINDO/2
8.97 $b_1(\pi)$	9.54 $b_1(\pi)$	10.46 $b_2(n_-)$	10.47 $b_2(n_-)$	9.72 $b_2(n_-)$
10.58 $b_2(\sigma)$	9.95 $b_2(\sigma)$	12.31 $b_1(\pi)$	11.17 $b_1(\pi)$	10.51 $b_1(\pi)$
12.39 $a_1(\sigma)$	10.86 $a_1(\sigma)$	14.46 $a_1(n_+)$	11.76 $a_1(\sigma)$	11.46 $a_1(\sigma)$
15.11 $b_1(\pi)$	14.55 $a_1(\sigma)$	16.73 $a_1(\sigma)$	13.45 $a_1(n_+)$	11.95 $a_1(n_+)$
17.12 $a_1(\sigma)$	14.72 $b_1(\pi)$	17.44 $b_1(\pi)$	15.65 $b_1(\pi)$	12.25 $b_1(\pi)$

The orbital sequence for *(2)* calculated by the MINDO/2 technique[4] differs from that obtained by *Robin, Basch, Kuebler, Wiberg*, and *Ellison*[5] from an *ab initio* model in the order of the orbitals $a_1(n_+)$ and $a_1(\sigma)$. Experience shows that for unsaturated systems MINDO/2 yields σ orbitals at too high orbital energies, so that the appearance of $a_1(\sigma)$ between $b_1(\pi)$ and $a_1(n_+)$ in the case of *(2)* and *(3)* should be regarded as an artefact of the method. For an extended Hückel model of *(2)* the reader is referred to a paper by *Hoffmann*[6] and for a detailed discussion of the electronic structure of cyclopropane, *(1)*, and *(2)* to a publication by *Kochanski* and *Lehn*[7].

Table 2. Vertical ionization potentials $I_v(J)$ of the first three bands in the photoelectron spectrum of cyclopropene *(1)* and 3,3-dimethyldiazirine *(3)* [in eV].

	$I_v(1)$	$I_v(2)$	$I_v(3)$
(1)	9.86 ($\Delta\tilde{\nu} \approx 1250\,cm^{-1}$)	11.02	12.7 ($\Delta\tilde{\nu} \approx 1100\,cm^{-1}$)
(3)	9.76	12.11	13.31

Table 2 lists the vertical ionization potentials $I_v(J)$ as determined by PE spectroscopy[8], *i.e.* the maxima of the first three bands in the spectrum of *(1)* and *(3)*. The assignment is based on the theoretical data listed in Table 1 and on the following arguments: The form of band 1 at 9.9 eV in the PE spectrum of *(1)* is typical for a π band (vibrational fine structure; mean splitting 0.15 eV corresponding to $\Delta\tilde{\nu} \approx 1200\,cm^{-1}$). The next two σ bands (at 11.0 and 12.7 eV) correspond to the orbitals $b_2(\sigma)$ and $a_1(\sigma)$ which arise from the Walsh e′ orbitals[9] of cyclopropane (D_{3h}) on removal of their degeneracy when the distance between centers 1 and 2 is reduced by introduction of a double bond:



(This qualitative consideration also explains the appearance of a vibrational fine structure of $\Delta\tilde{\nu} \approx 1100\ cm^{-1}$ in band 3 (at 12.7 eV) in the spectrum of *(1)*.) Replacement of the carbon centers in *(1)* by nitrogen centers should lead to a lowering of the π orbital by an amount comparable with that occurring in the transition *trans*-2-butene ($\varepsilon(\pi) = -9.11$ eV) $\rightarrow$ *trans*-azomethane ($\varepsilon(\pi) = -11.84$ eV)[2,3]. Thus a value of $\varepsilon(b_1(\pi)) = -9.86 - 2.73 = -12.59$ eV is predicted for *(2)*. In the case of *(3)*, this value represents an upper limit since the two methyl groups raise the level of the π orbital relative to that in *(2)*. It is therefore most likely that the band at 12.1 eV in the PE spectrum of *(3)* has to be assigned to the $b_1(\pi)$ orbital, in agreement with the theoretical prediction —. However, it should be noted that the second band in the spectrum of *(3)* does not show the fine structure typical for a N=N bond, as in the case of azomethane[2,3]. This may be due to the fact that the $b_1(\pi)$ orbital also extends over the C—CH_3-σ bonds. As a result, the low-frequency, totally symmetric normal mode of the CH_3—C—CH_3 unit is also excited on relaxation of the radical cation *(3)*$^+$ after ejection of the photoelectron from $b_1(\pi)$.

The two orbitals $b_2(\sigma)$ and $a_1(\sigma)$ in *(1)*, which are related to the Walsh e′ orbitals correspond to the orbitals $b_2(n_-)$ and $a_1(n_+)$ of *(2)* and *(3)*. In the two last-named compounds the original C—C-σ orbitals are extensively mixed with the linear combinations n_- and n_+. This factor and the reduction in the distance between centers 1 and 2 relative to *(1)* increases the splitting $\varepsilon(b_2(\sigma)) - \varepsilon(a_1(\sigma))$ found for *(1)*.

Whereas this difference amounts to 1.7 eV for *(1)*, a value

$$\Delta = \varepsilon(b_2(n_-)) - \varepsilon(a_1(n_+)) = 3.55\ eV$$

is found for 3,3-dimethyldiazirine.

Delocalization of the orbitals of the lone pairs ($a_g(n_+)$ and $b_u(n_-)$ in the case of azomethane) has already been proposed on the basis of theoretical results[3]. It may now be concluded from the results of MINDO/2 calculations that the situation is even more extreme in compounds *(2)* and *(3)*. In fact, the calculations show that the two electrons in the orbital $b_2(n_-)$ of *(3)* are localized to an extent of only 56% on the two nitrogen atoms. For the lower orbital $a_1(n_+)$ this value becomes as low as 43%. In the light of these figures, the term "lone pair" loses much of its meaning. It is therefore important when interpreting properties of such systems to bear in mind that, in keeping with modern social trends, electrons also prefer to live in a commune, rather than in pairwise isolation[10].

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Tetrakis(trimethylphosphane)nickel(0)[1]

By *Hans-Friedrich Klein* and *Hubert Schmidbaur*[*]

Present day concepts of bonding in phosphane complexes attach particular attention to the π-acceptor properties of the ligands. Thus the extensive accumulation of charge on the central atom due to the σ-donor effect of the ligands is believed to be reduced by π-back donation. The ready formation and high stability of trifluorophosphane and phosphite complexes appears to support such a concept since the inductive effect for the fluorine and oxygen atoms considerably increases the acceptor strength of the phosphorus atoms. It was consistent with this picture that metal(0) complexes having trialkylphosphanes as ligands were hitherto practically unknown[2,3]. We now report the synthesis and properties of tetrakis(trimethylphosphane)-nickel(0), which is of considerable interest in this connection.

Reduction of aqueous solutions of nickel(II) salts at pH > 7 with an excess of trimethylphosphane immediately affords the complex $Ni[P(CH_3)_3]_4$ *(1)*. Complex *(1)* is also formed on reaction of $[(CH_3)_3P]_2NiCl_2$ with an aqueous-alcoholic solution of potassium hydroxide or with sodium trimethylsilanolate in diethyl ether or tetrahydrofuran.

$$Ni^{2+} + 2\ OH^- + 5\ (CH_3)_3P \rightarrow (1) + (CH_3)_3PO + H_2O$$

$$5\ [(CH_3)_3P]_2NiCl_2 \xrightarrow{10\ OH^-} \begin{cases} 2\ (1) + 2\ (CH_3)_3PO + 3\ Ni(OH)_2 + 10\ Cl^- + 2\ H_2O \\ 2\ (1) + 2\ (CH_3)_3PO + 3\ Ni[OSi(CH_3)_3]_2 + 10\ NaCl + 2\ [(CH_3)_3Si]_2O \end{cases}$$

Compound *(1)*, which can be isolated by extraction with hexane or by sublimation under reduced pressure (80 °C/1 torr), forms pale yellow needle-like crystals (from alcohol) that decompose at 185—190 °C in a nitrogen atmosphere. The crystals are pyrophoric and deflagrate spontaneously upon admission of air. They are readily soluble in hydrocarbons, ethers, and organosilicon compounds such as tetramethylsilane or hexamethyldisiloxane; the yellow solutions become colorless on cooling to —50 °C. Cryoscopic measurements show the compound to be monomeric in benzene[4]; NMR measurements reveal its diamagnetic nature. The mass spectrum of *(1)* at 70 and at 20 eV displays only fragmentation of the ligand [$(CH_3)_3P^+ \rightarrow (CH_3)_2P^+$, $(CH_3)_2PCH_2^+$, CH_3P^+, *etc.*] but not of the intact complex which seems to decompose completely even under mild conditions in the mass spectrometer.

The ^{1}H-NMR spectrum recorded at 60 and 100 MHz contains only one proton signal whose half-width of 4 Hz remains constant between —50 and +80 °C (τ = 8.9 ppm against TMS in hexamethyldisiloxane). The ^{1}H-^{13}C coupling satellites, $^1J(HC) = 125.5$ Hz, exhibit the same signal broadening. Likewise the ^{31}P-NMR spectrum contains just a single broadened line ($\delta = +23.2$ ppm in benzene against 85% H_3PO_4 as external reference). This peak is shifted 39 ppm downfield compared with that of free $(CH_3)_3P$, thus resembling the difference found for the pair of compounds $Ni(PF_3)_4$—PF_3[5]. The forms of the signals can be regarded as arising from the complex spin-spin

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nteractions occurring in a $[A_9X]_4$-T_d system[6]. Extensive P—Ni—P interactions cause the A part (^1H) and the X part (^{31}P) to lose the first-order structures expected. An interpretation of the spectra based on the assumption of exchange processes is ruled out largely by the lack of variation of the signal with temperature.

The Raman spectrum (He—Ne laser) of crystalline *(1)* contains a strong band at 196 cm^{-1} which, in agreement with measurements on $Ni(PF_3)_4$[7], can be assigned to a stretching vibration of the NiP_4 tetrahedron. In addition, all characteristic Raman and IR frequencies of the ligands are observed between 200 and 4000 cm^{-1}; they show alternating intensities owing to the tetrahedral geometry of the molecule.

The remarkable properties of $Ni[P(CH_3)_3]_4$ serve to illustrate that strongly electronegative substituents on the phosphorus atom are *not* a necessary condition for the stability of a metal(0)-phosphane complex. It is not surprising that similar complexes of iron and cobalt have now also been prepared[8] [**].

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[1] Some of the analyses and of the spectroscopic studies described in this communication were carried out at the Department of Chemistry of the University of Edinburgh and supported by the Deutsche Forschungsgemeinschaft and the Science Research Council. H. S. is indebted to Prof. *E. A. V. Ebsworth* for permission to use departmental equipment.

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Tetrakis(trimethylphosphane)hydridocobalt(I) and -dihydridoiron(II)

By *Hans-Friedrich Klein*[*]

The unexpected stability of tetrakis(trimethylphosphane)-nickel(0)[1] gave good reason for expecting the successful outcome of attempts to synthesize analogous tetrakis(trimethylphosphane)metal hydrides of the types L_4CoH and L_4FeH_2. Such compounds, which have recently attracted particular interest on account of their stereochemical nonrigidity[2,3], were hitherto known only with phosphanes L whose phosphorus atom bore at least one electron-attracting substituent[2–5].

The cobalt compound $[(CH_3)_3P]_4CoH$ *(1)* is readily obtained when an aqueous solution of Co^{2+} is reduced under alkaline conditions in the presence of trimethylphosphane using zinc dust. Isolation of the product by extraction with light petroleum and subsequent sublimation is essentially by the same method as was employed in the case of $Ni[P(CH_3)_3]_4$[1]. An alternative method of preparation is the reduction of $[(CH_3)_3P]_2CoCl_2$ with $LiAlH_4$ in tetrahydrofuran in the presence of $(CH_3)_3P$.

Similarly, reduction of $FeCl_2$ by $LiAlH_4$ in THF in the presence of trimethylphosphane affords $[(CH_3)_3P]_4FeH_2$ *(2)* which can be sublimed *in vacuo* after extraction with light petroleum of the residue left on removal of the solvent.

At room temperature, *(1)* and *(2)* form yellow and yellowish-brown crystals that sublime without decomposition at 70 and 80—90 °C/1 torr respectively, and which decompose only above 180—190 °C when heated under nitrogen. Both compounds are readily soluble in non-polar solvents and both the solutions and the solids are oxidized only slowly by atmospheric oxygen. Thus, unlike $Ni[P(CH_3)_3]_4$[1], the new compounds are not pyrophoric. NMR measurements reveal diamagnetism.

Alongside the $(CH_3)_3P$ proton resonances, the ^1H-NMR spectra[6] contain the multiply split signals of the hydride ligands. At 20 °C compound *(1)* gives the symmetrical 1:4:6:4:1 quintet having $|J(HCoP_4)| = 32$ Hz and $\tau = 26.5$ ppm relative to ext. TMS. Rapid exchange of the axial and equatorial phosphane ligands apparently leads to complete NMR equilibration of the phosphorus atoms of the trigonal pyramid at room temperature.

In the case of *(2)*, a little below room temperature the H_2Fe resonance still appears as a doublet of triplets which does not begin to coalesce until the sample is warmed to > 30 °C. For the pairs of axial and equatorial phosphorus atoms of a *cis*-octahedral configuration which are clearly non-equivalent at 10 °C we measured the values $|J(H_2FeP_{cis})| = 72$ and $|J(H_2FeP_{trans})| = 26$ Hz ($\tau = 23.3$ ppm). Thus in *(2)* ligand exchange is much slower than in the cobalt compound *(1)* and in the analogous octahedral hydrides L_4FeH_2[2–3], primarily for steric reasons. No evidence was obtained for the existence of a *trans*-octahedral isomer.

The IR spectra of *(1)* and *(2)* both contain strong absorption bands in the metal hydride region at 1885 (νCoH) and 1795 cm^{-1} (νFeH_2) that are shifted toward lower wave numbers compared with those of the analogous PF_3 complexes[5].

Remarkably, the hydride hydrogens in *(1)* and *(2)* *do not exhibit acidic character*, unlike those of analogous carbonyl or trifluorophosphanemetal hydrides. Deprotonation to the anion $[Co(P(CH_3)_3)_4]^-$ or $[Fe(P(CH_3)_3)_4]^{2-}$ cannot be achieved by treatment with either concentrated aqueous or alcoholic alkalis or the exceptionally strong base trimethylmethylenephosphorane[7]. Even prolonged heating of a mixture of $(CH_3)_3PCH_2$ and *(1)* does not effect proton transfer.

These observations emphasize the significance of the inductive effect of the ligands attached to phosphorus as regards the reactivity of the metal hydride function.

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Novel Iminosulfur Oxydifluorides

By *Konrad Seppelt* and *Wolfgang Sundermeyer* [*]

As a rule, silicon-nitrogen bonds are readily attacked and completely cleaved by non-metallic halides and halogens [1]. However, we have now been able to prepare compound *(1)*, trimethylsilyliminosulfur oxydifluoride, one of the few exceptional cases in which an Si—N bond and an element-halogen bond are resident as immediate neighbors in the same molecule and do not interact with each other either inter- or intramolecularly. *(1)* was prepared from tris(trimethylsilyl)amine and sulfur oxytetrafluoride according to the following equation:

$$[(CH_3)_3Si]_3N + SOF_4 \rightarrow (CH_3)_3Si-N=S(F)=O + 2\,(CH_3)_3SiF$$

(1)

The reaction was carried out in an autoclave; the starting materials react above room temperature with moderate liberation of heat to give *(1)* in 85% yield.

Compound *(1)* can also be obtained by reaction of sulfur oxydifluoride with *N*-halogenobis(trimethylsilyl)amines, the most favorable synthesis (87% yield) being that from *N*-iodobis(trimethylsilyl)amine [2]:

$$6\,[(CH_3)_3Si]_2NI + SOF_4 \rightarrow 4\,(1) + 8\,(CH_3)_3SiF + 3\,I_2 + N_2$$

The reaction equation was confirmed by quantitative determination and by identification of by-products.

(1) is a water-clear liquid and only slightly sensitive to hydrolysis: m.p. —92 °C, b.p. 85.5 °C. It was purified by preparative gas chromatography and identified by elemental analysis and mass spectrometry [3] [*m/e* = 173 ($R_3SiNSOF_2$ 1.8%), 158 ($R_2SiNSOF_2$ 80%), 128 ($SiNSOF_2$ 2.7%), 81 (NSOF or $RSiF_2$ 90%), and 77 (R_2SiF) 100%) along with other typical fragments; 75 eV]. Both the most important absorptions in the IR spectrum [gaseous: 1495 (vs, νSO), 1275 (s, νNS), 852 (vs, ν_{as} SF), and 819 cm^{-1} (vs, ν_s SF)] and the corresponding Raman lines [3] (liquid: 1480, 1275, 853, and 810 cm^{-1}) as well as the ^{19}F-NMR spectrum (δ = —55.9 ppm against $CFCl_3$ as internal standard at 20 °C) give supporting evidence for structure *(1)* rather than for that of the isomeric compound $(CH_3)_3Si-O-SF_2\equiv N$, which was previously considered the more probable on the grounds of stability. In a heated autoclave, compound *(1)* starts to decompose at 250 °C; at 400 °C decomposition to $(CH_3)_3SiF$, SOF_2, N_2, SO_2, and S is complete.

Further evidence for the given structure is afforded by the reaction of *(1)* with mercury(II) fluoride in methylene chloride; this reaction leads to quantitative formation of mercury bis(imidosulfur oxydifluoride) *(2)*.

$$2\,(CH_3)_3Si-NSOF_2 + HgF_2 \rightarrow Hg(NSOF_2)_2 + 2\,(CH_3)_3SiF$$

(2)

This reaction parallels the synthesis of $Hg(NSO)_2$ [4]. The colorless crystals of *(2)* (m.p. 108 °C; sublimable in high vacuum at 130 °C) are only slightly sensitive to hydrolysis [5]. In air, *(2)* starts to decompose at 170 °C; the sole gaseous products formed on pyrolysis in high vacuum at 400—600 °C are SO_2, NSF and a little SiF_4 (from the glass) alongside Hg, HgF_2, S, and SN-polymers. Compound *(2)* is very soluble in ether, moderately soluble in methylene chloride, sparingly soluble in chloroform, and insoluble in petroleum ether. Its identification followed from elemental analysis and mass spectrometry [3] [*m/e* = 398—404 ($Hg(NSOF_2)_2$ 4.2%), 298—304 ($HgNSOF_2$ 6.1%), and 198—204 (Hg 100%) along with weaker signals; 75 eV]. The IR and Raman spectroscopic data [IR, Nujol: 1397 (vs, ν_{as}SO), 1362 (s, ν_sSO), 1231 (s, ν_{as}SN), and 1198 cm^{-1} (s, ν_sSN); Raman, solid: 1396 s, 1365 s, 1235 vs, and 1191 cm^{-1} m], as well as the ^{19}F-NMR spectrum [3] (δ = —58.7 ppm in methylene chloride, against $CFCl_3$ as external standard) are consistent with the structure given.

The imidosulfur oxydifluorides *(1)* and *(2)* react with halogens and halogen compounds in the manner described by us in a previous communication [6].

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Crystal and Molecular Structure of $Zn_7O_8(CH_3)_{14}$ — a Dicubane [**]

By *Manfred L. Ziegler* and *Johannes Weiss* [*]

Coates and *Ridley* [1] obtained from the reaction of dimethylzinc and methanol the compound $Zn_4O_4(CH_3)_8$, which, according to X-ray investigations by *Shearer* and *Spencer* [2], has a cubane structure.

As *Eisenhuth* and *van Wazer* [3] were able to show, this methanolysis also leads to the formation of a product having the composition $Zn_7O_8(CH_3)_{14}$. According to NMR spectroscopic measurements this latter substance has a dicubane structure.

The triclinic unit cell (a = 10.08, b = 8.76, c = 10.61 Å; α = 115.4, β = 117.3, γ = 92.1 °; space group C_i^1—$P\bar{1}$) contains one formula unit $Zn_7O_8(CH_3)_{14}$. Since this substance is extremely sensitive to hydrolysis the crystals used for measurements must be sealed in a Mark tube.

The intensities of 1225 independent reflections obtained from Weissenberg photographs ("multiple film" method) about the a-axis were estimated visually and corrected in the usual manner. No corrections were carried out for absorption and extinction.

Since only one formula unit is found in the unit cell for a two-fold general equivalent position the molecule itself must be centrosymmetric, one of the zinc atoms being situated at the center of symmetry. The positions of the zinc atoms were determined by a three-dimensional Patterson synthesis; Fourier syntheses afforded the positions of the remaining atoms. Final refinement of the structural

Table 1. Atomic coordinates.

	x	y	z
Zn^1	0	0	0
Zn^2	0.2594 (4)	0.3167 (3)	0.1221 (3)
Zn^3	—0.0103 (4)	0.1282 (3)	—0.2375 (3)
Zn^4	0.2328 (4)	—0.0558 (3)	—0.1274 (3)
O^1	0.0198 (17)	0.2338 (15)	—0.0033 (14)
O^2	0.2409 (12)	0.0733 (9)	0.1009 (8)
O^3	0.2320 (19)	0.1838 (17)	—0.1134 (14)
O^4	—0.0032 (18)	—0.0972 (16)	—0.2274 (14)
C^1	—0.0636 (31)	0.3535 (26)	0.0477 (25)
C^2	0.3460 (36)	0.0440 (32)	0.2305 (23)
C^3	0.3154 (33)	0.2777 (28)	—0.1562 (27)
C^4	—0.1027 (32)	—0.2658 (27)	—0.3720 (24)
C^5	0.4085 (36)	0.5488 (30)	0.3016 (31)
C^6	—0.1441 (38)	0.1579 (34)	—0.4255 (25)
C^7	0.3233 (33)	—0.2438 (29)	—0.2021 (25)

parameters was carried out by the method of least squares with anisotropic temperature factors. After the final cycle including all observed F(*hkl*) the factor *R* had a value 0.10.

X-ray crystallographic investigation showed, that the previously unobserved structure of a dicubane is in fact present.

The cubes are distorted. All the Zn—O—Zn angles are smaller than 90° (81°—86°) and all the O—Zn—O angles are greater than 90° (93°—98°). The four atoms centered on the cube faces lie in one plane.

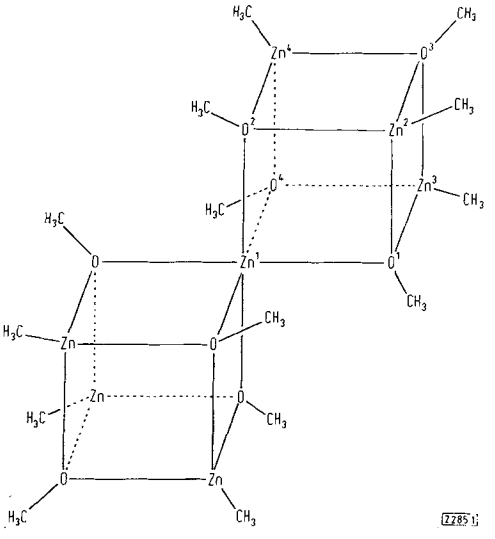


Table 2. Zn—Zn and Zn—O distances in Å.

Zn^1—Zn^2	3.068 (3)	Zn^2—Zn^3	3.033 (3)
Zn^1—Zn^3	3.134 (4)	Zn^2—Zn^4	3.095 (4)
Zn^1—Zn^4	3.173 (4)	Zn^3—Zn^4	3.033 (5)
Zn^1—O^1	2.068 (15)	Zn^3—O^1	2.103 (16)
Zn^1—O^2	2.077 (11)	Zn^3—O^3	2.069 (17)
Zn^1—O^4	2.170 (17)	Zn^3—O^4	2.026 (16)
Zn^2—O^1	2.039 (15)	Zn^4—O^2	2.147 (16)
Zn^2—O^2	2.038 (9)	Zn^4—O^3	2.041 (16)
Zn^2—O^3	2.122 (16)	Zn^4—O^4	2.039 (17)

One of the three bonds from a Zn atom to an O atom is always noticably longer than the other two (cf. Table 2) *i.e.* the cubes are elongated in one direction. The Zn—O distances at Zn^1 with CN 6 (in the center of symmetry of the molecule and in the symmetry center of the unit cell) are greater than the comparable distances at the other Zn atoms with CN 4.

The C atoms of the CH_3 groups are located in the direction of the space diagonals. The Zn—C distances have an average value of 1.953 Å, and the O—C distances between 1.42 and 1.49 Å.

The calculations were carried out (Siemens 2002) at the Astronomisches Recheninstitut der Universität Heidelberg; the refinements were carried out with the ORFLS program[4] at the Deutsches Rechenzentrum, Darmstadt.

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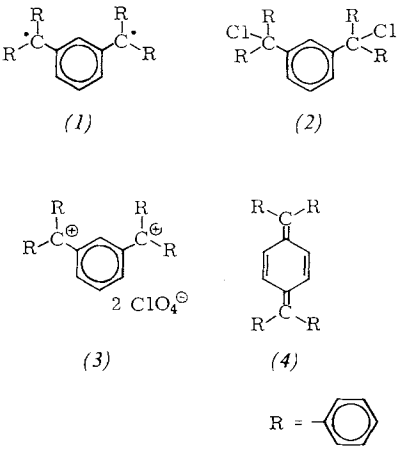
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Schlenk's Biradical. — A Molecule in the Triplet Ground State

By *Gerd Kothe*, *Karl-Heinz Denkel*, and *Wolfgang Sümmermann*[*]

Molecules that by the MO approximation have two degenerate, singly occupied, highest one-electron orbitals in the energetically lowest state usually have a triplet ground state that is more stable by the Fermi correlation energy than the corresponding singlet. The HMO model provides criteria for the degeneracy of the one-electron levels. A distinction is made between degeneracy caused by symmetry and that caused by topology[1]. Molecules of the former type must possess a three-fold or higher symmetry axis which provides the possibility of transition by geometrical rearrangement into an energetically more stable singlet state of lower symmetry (Jahn-Teller effect). A triplet ground state has been confirmed experimentally for some symmetry-degenerate molecules[2–4].

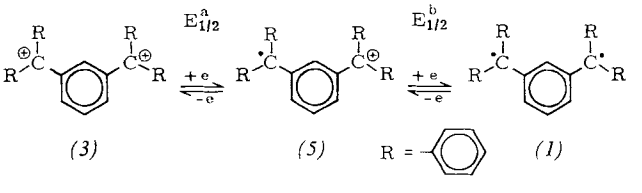
Topologically degenerate molecules may have lower symmetry. For alternant aromatic hydrocarbons the HMO approximation provides a simple relation for determining the topological degeneracy[5]: according to this, the hydrocarbon *(1)* has two non-bonding HMOs which are occupied



by only two electrons in the ground state. Thus a triplet ground state is to be expected for *(1)* from predictions of the HMO theory.

On dehalogenating the dichloride *(2)* *Schlenk* and *Brauns* obtained a colorless product whose elemental analysis accorded with the molecular formula of *(1)*. Investigation showed *(1)* to be associated to a polymer[6]. ESR studies by *Reitz* and *Weissman* also indicated association of *(1)*[7].

We attempted to produce the monomeric compound *(1)* by polarographic reduction of *(3)* at a rotating platinum electrode.



The polarogram showed only a single broad reduction wave[8]. The limiting current of this wave corresponds to a two-electron transition. Coulombmetric measurements lead to the same result. By varying the rate of rotation of the disk electrode it was proved that the limiting current is diffusion-controlled. Thus pre-established equilibria do not influence the electrode reaction. The cyclic voltammogram at a stationary electrode shows cathodic and anodic peak currents of equal strength, proving that subsequent associ-

ation of *(1)* is slow and does not interfere with the electrode reaction. Logarithmic analysis of the broad reduction wave, by computer[9], demonstrated two one-electron transitions with similar half-wave potentials and equal limiting currents. The difference between the half-wave potentials $E^a_{1/2}$ and $E^b_{1/2}$ is 70 mV; this is a measure of the electrostatic repulsion energy of the two electrons in the highest occupied MO of *(1)*[10]. For the hydrocarbon *(4)*, the potential difference is 200 mV[8]. It becomes intelligible why these potential differences should not be identical if one assumes that *(1)* has a triplet ground state; *i.e.*, the electron correlation for the triplet state leads to a repulsion energy that is lower than that for the singlet.

ESR spectroscopic measurements were carried out with the object of detecting the triplet ground state of *(1)*. To avoid complete association of *(1)*, we dehalogenated a toluene solution of *(1)* for a short time with Ag powder, then filtered the solution, warmed it to 80 °C, and thereafter immediately cooled it to −180 °C. The ESR spectrum of the resulting glassy toluene solution showed, as well as an intense monoradical transition at 3250 G, several lines with $\Delta m = 1$ which are characteristic of a triplet molecule (Fig. 1). We assign the triplet spectrum to the monomeric hydrocarbon *(1)*. The zero-field splitting parameters determined from the lines with $\Delta m - 1$[11] have the following values: $|D| = 0.0079\ cm^{-1}$, $|E| \leqslant 0.0005\ cm^{-1}$. The resonance field strength of the extremely weak transition with $\Delta m = 2$ could not be measured.

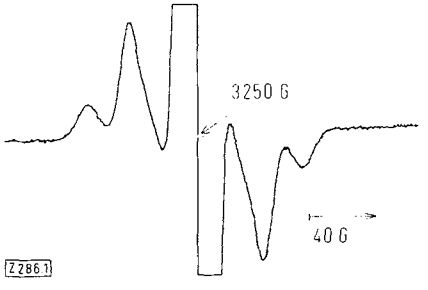


Fig. 1. ESR-Spectrum of *m*-phenylenebis(diphenylmethyl) *(1)* in glassy toluene at *ca.* −180 °C. Resonance field strength of the free electron $H_0 = 3251$ G.

We have determined the relation between the amplitudes of the transitions with $\Delta m = 1$ and temperature in the region 100–150 °K. If the effect of temperature T on signal amplitude I is interpreted as a result of a singlet-triplet equilibrium, the following relation applies[3]:

$$I = \frac{C}{T}\left(\frac{3e^{-\Delta E/RT}}{1 + 3e^{-\Delta E/RT}}\right)$$

where $\Delta E = E_{triplet} - E_{singlet}$ and C is a constant.

When $\Delta E = 0$, the relation simplifies to the Curie law, which is approximately followed for our measurements. We were unable to determine ΔE exactly from the divergences from the Curie law. Since the divergence from the equation of the simple Curie law must be appreciably smaller when $\Delta E < 0$ than when $\Delta E > 0$, our experimental findings indicate a triplet ground state for *(1)*.

To verify our results theoretically we have carried out SCF–CI calculations for *(1)* by the Pariser-Parr-Pople procedure[12–13]. The parameters used were gauged from the electron spectra of carbonium ions of the triphenylmethane series[14]. 41 singly excited configurations were introduced into the configuration interaction. The calculations were effected for a planar and for a twisted conformation of *(1)*, whose structure is related to that of the triphenylmethane carbonium ions. In each case the calculations gave a triplet ground state T_1 which is more stable than the singlet state S_0 by, respectively, 1.07 and 1.19 eV. The calculations thus confirm that *(1)* has a triplet ground state.

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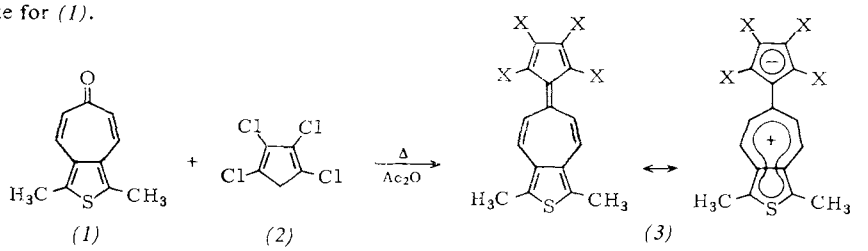
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Condensation Reactions of 1,3-Dimethyl-6*H*-cyclohepta[*c*]thiophen-6-one[1,2]

By *Gunther Seitz* and *Heinrich Mönnighoff*[*]

By using the anhydride method[3] we have effected the first condensation reactions of compounds containing reactive methylene groups with 1,3-dimethyl-6*H*-cyclohepta[*c*]-thiophen-6-one *(1)*[4].

Heating *(1)* with 1,2,3,4-tetrachlorocyclopentadiene *(2)* in acetic anhydride gives the potentially dipolar 6π–10π system *(3a)*, m.p. >340 °C, in 35% yield as brownish-red crystals, and a similar reaction with pentamethyl 1,2,3,4,5-cyclopentadienepentacarboxylate[5] gives *(3)*,

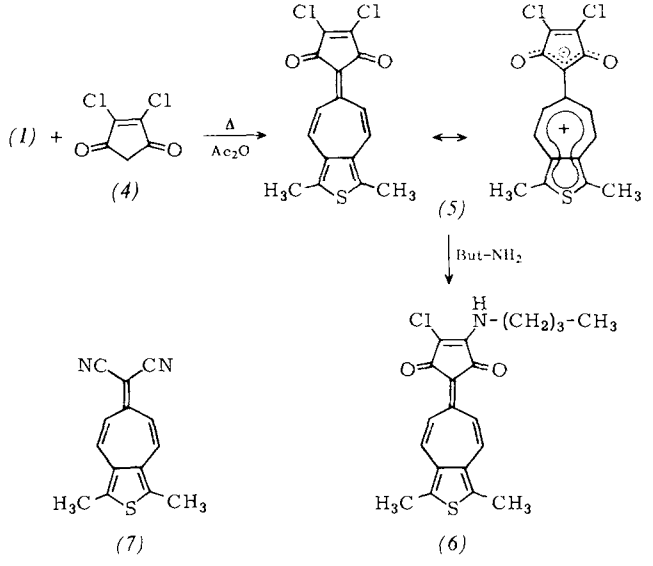


(1) *(2)* *(3)*

(a), X = Cl
(b), X = CO_2CH_3

m.p. >340 °C, in 48% yield as permanganate-colored needles with a metallic sheen.

By the same method 4,5-dichlorocyclopentene-1,3-dione *(4)*[6] afforded the ocher-colored heterosesquifulvalene-quinone *(5)*, m.p. >305 °C (dec.) (43% yield), which we characterized by conversion by butylamine into the more soluble derivative *(6)*, m.p. 232 °C (dec.) (yield 76%).



Treating *(1)* with malonodinitrile led to the orange-yellow condensation product *(7)*, m.p. >330 °C (dec.), in 24% yield.

The new compounds were characterized by elemental analysis and spectroscopic properties. However, their low solubility prevented us from obtaining usable NMR spectra for *(3a)* and *(5)* even by the Cat procedure[7]. The NMR spectra of *(3a)* and *(7)* are characterized by an AB quartet (J = 12.5 Hz) for the four seven-membered ring protons, whose resonance positions were largely influenced by the anisotropic effects of the substituents, so that they yield no information on the polarity of the ground state. In *(6)* H-5 and H-7 are magnetically non-equivalent; they were recorded as a multiplet centered at 8.12 and 8.45 ppm, whereas the multiplet for H-4 and H-8 appeared at 7.03 ppm.

The IR spectra are characterized by an intense band in the region around 1610 cm^{-1} which is ascribed to a $\nu_{C=C}$ vibration.

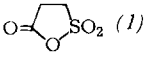
The electron spectrum of *(3a)* is of the same shape as that of the iso-π-electronic 7-(tetrachlorocyclopentadienylidene)-7*H*-benzocycloheptene[8], whose longest-wave maximum is, however, shifted bathochromically by 20 nm. The positive solvatochromism established for all the compounds from the electron spectra indicates high occupancy of the apolar limiting formula in the ground state. This is confirmed by the position of the nitrile band in the IR spectrum of *(7)* at 2217 cm^{-1}, which is at 12 cm^{-1} shorter wavelength than it is for 8,8-dicyanoheptafulvene[9].

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Separation of Compounds with Failure Sequences in the Solid-Phase Synthesis of Peptides by Means of the Anhydride of 3-Sulfopropionic Acid

By *Hans Wissmann* and *Rolf Geiger*[*]

The synthetic steps in the Merrifield solid-phase synthesis of peptides do not always afford homogeneous peptides in desirably high yields[1-3]. This leads to impurities and compounds with failure sequences that are often so similar to the desired end products that they cannot be separated from them by the available methods of purification. One way of overcoming this difficulty is to use an acylating agent to block the amino groups that escape reaction, a method that also facilitates removal of by-products. For this purpose *Wieland* and his co-workers[4] used 3-nitrophthalic anhydride. We use the cyclic anhydride of 3-sulfopropionic acid *(1)*[5], which reacts with the by-products to give N^{α}-(3-sulfopropionyl) derivatives that, owing to their high acidity, can be separated by simple filtration through a weakly basic ion-exchanger (acetate form). This treatment



(1)

with an ion-exchanger has usually to be undertaken in any case so as to afford the acetates from the peptides liberated from the carrier by HBr/trifluoroacetic acid; thus our purification does not require any additional experimental step.

If peptide bonds are also attacked under the conditions of acylation with *(1)*, the diacylamides can be cleaved by cautious aminolysis before the peptide is separated from the polymer. This would either regenerate the original peptide bond or, in the case of cleavage of the peptide chain, afford fragments that can be washed out or separated by means of the incorporated sulfo groups.

Experimental:

H-Cys(Bzl)-Tyr(Etoc)-Phe-Gln-Asn-Cys(Bzl)-Pro-Arg-(NO_2)-Gly-NH_2[6]: Boc-Gly polymer ester (10 g), prepared as described in ref.[1] with 0.36 mmole of Gly per g of resin, is deacylated and acylated with Boc-Arg(NO_2)-OH. The resin is then extracted with dimethylformamide (50-ml portions) by shaking four times, each for 3 min. During this period, *(1)* (4 g) is dissolved, with cooling, in anhydrous tetrahydrofuran (20 ml), and the cooled solution is added to the Boc-Arg(NO_2)-Gly polymer. *N*-Ethylmorpholine (7.5 ml) in dimethylformamide (15 ml) is then at once added and the whole is shaken for 1 hour at room temperature. The solvent is then filtered off and the solid is washed four times with ethanol (50-ml portions) and four times with glacial acetic acid (40-ml portions), after which the Boc group is removed by 1 N HCl in glacial acetic acid. The further amino acids are added by analogous procedures, the following derivatives being used: Boc-Pro-OH[7], Boc-Cys(Bzl)-OH[7], Nps-Asn(Mbh)-OH[8], Nps-Gln-(Mbh)-OH[8], Boc-Phe-OH[7], Boc-Tyr(Etoc)-OH[9]. — Yield: 14.9 g of peptide-polymer compound.

This compound (3.0 g) was treated with HBr/trifluoroacetic acid as described in ref.[1]. The crude peptide mixture was reprecipitated from ethanol by ether and then heated in trifluoroacetic acid/anisole (9:1) for 5 min for complete removal of the Mbh groups, and was finally precipitated by

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Amino acid analysis [a]	Cys	Tyr	Phe	Glu	Asp	Cys	Pro	Arg	Gly
Before removal from carrier	–	–	0.98	0.97	1.00	–	1.12 [b]	1.09 [b]	1.42
After removal and filtration through ion-exchanger	–	0.90 [b]	0.92	0.96	1.00	–	0.97	0.97 [b]	1.00

[a] A dash denotes that the amino acid was not determined quantitatively.
[b] Corrected value.

The peptide Boc-Glu(Mbh)-Asn(Mbh)-Cys(Bzl)-Pro-Leu-Gly-NH_2 was prepared similarly.

Amino acid analysis [a]	Glu	Asp	Cys	Pro	Leu	Gly
Before removal from carrier	0.88	1.00	–	1.32	1.47	1.17
After removal and filtration through ion-exchanger	1.02	0.99	–	1.00	1.03	1.00

ether, dissolved in 90% methanol, and filtered through a column (15 × 1 cm) of Amberlite IR-45 (acetate form). The resin was then washed with 90% methanol (150 ml), the eluates were evaporated in a vacuum, and the residue was dissolved in ether. Yield: 300 mg.

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[1] *R. B. Merrifield*, J. Amer. Chem. Soc. *85*, 2419 (1963).

[2] *E. Bayer, H. Eckstein, K. Hägele, W. König, W. Brüning, H. Hagenmaier*, and *W. Parr*, J. Amer. Chem. Soc. *69*, 1735 (1970).

[3] *H. Hagenmaier*, Tetrahedron Lett. *1970*, 283.

[4] *Th. Wieland, Chr. Birr*, and *H. Wissenbach*, Angew. Chem. *81*, 782 (1969); Angew. Chem. internat. Edit. *8*, 764 (1969).

[5] *M. S. Kharasch, T. H. Chao*, and *H. C. Brown*, J. Amer. Chem. Soc. *62*, 2393 (1940). Obtainable from Ega-Chemie, 7924 Steinheim (Germany)

[6] Abbreviations according to the IUPAC-IUB Commission on Biochemical Nomenclature, Hoppe-Seyler Z. physiol. Chem. *348*, 256, 262 (1967). Also: Bzl = benzoyl; Etoc = ethoxycarbonyl: Nps = 2-nitrophenylsulfenyl; Mbh = 4,4'-dimethoxybenzhydryl. Amino acid analysis: hydrolysis for 72 h in 6 N HCl at 110 °C.

[7] *E. Schnabel*, Liebigs Ann. Chem. *702*, 188 (1967).

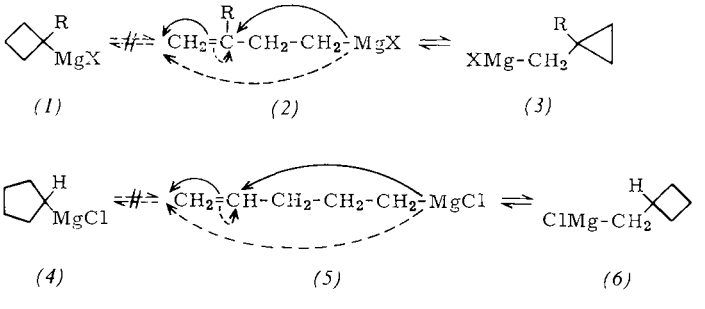
[8] *W. König* and *R. Geiger*, Chem. Ber. *103*, 2041 (1970).

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Ring Contraction on Rearrangement of 3-Cyclohexenyl Grignard Compounds [**]

By *Adalbert Maercker* and *Reinhart Geuss* [*]

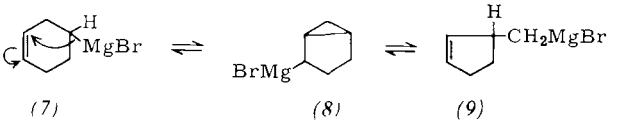
Presence of cyclobutane derivatives has never been observed in the equilibrium mixtures resulting from rearrangement of homoallylic anions in contrast to rearrangements that occur by way of carbonium ions [1]. Even when a phenyl group was present in the 3-position relative to the metal, as in *(2)*, R = C_6H_5, the presence of *(1)* at equilibrium could be excluded [2]. Also, higher homologs of the 3-butenyl Grignard compound *(2)*, R = H, are in equilibrium only with the smaller of the possible cyclic compounds, *e.g.*, *(5)* only with *(6)* [3], although a reduction of about 20 kcal/mole in ring strain would be expected for *(4)*.



(1) *(2)* *(3)*

(4) *(5)* *(6)*

If a double bond is present in a six-membered ring *(7)*, the smaller and the larger ring must be formed simultaneously, while *(8)* arises during a rearrangement.



(7) *(8)* *(9)*

A solution of 3-cyclohexenylmagnesium bromide *(7)* in diethyl ether or tetrahydrofuran is stable for days at room temperature. If the solution is heated for some hours at 80 °C, 2-cyclopentenylmethylmagnesium bromide *(9)* is formed (its presence being proved by an α-proton doublet in the NMR spectrum on the far side of the TMS signal) and this must have been formed by way of the bicyclo[3.1.0]-hexane intermediate *(8)* although this could not be detected in the equilibrium mixture by NMR spectroscopy. An attempt to synthesize *(8)* by an independent route in diethyl ether led to a mixture of *(9)* and *(7)* in the proportion 5:1.

The equilibrium constant for the equilibrium *(7)*⇌*(9)* was determined by NMR spectroscopy and by carboxylation of the products. It is dependent on the concentration and on the solvent, being, *e.g.*, 8.08 ± 0.12 and 9.26 ± 0.11 for 1.3 M and 0.7 M solutions, respectively, in ether. Thence the energy difference ΔG between the two Grignard compounds can be calculated, showing that *(9)* is more stable than *(7)* by 1.46 or 1.55 kcal/mole, respectively, in spite of the greater ring strain in the former [4]. The driving force for ring contraction can be sought in the energy gain on conversion of the secondary into the primary carbanion.

This equilibrium *(7)*⇌*(9)* [5] thus enables the difference in stability between primary and secondary Grignard compounds to be estimated. Since the equilibrium constants between 80 and 120 °C were found to be independent of temperature, this difference in stability ought to be of the same order of magnitude as the difference in ring strain so that ΔH for the reaction becomes zero.

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] *M. E. H. Howden, A. Maercker, J. Burdon*, and *J. D. Roberts*, J. Amer. Chem. Soc. *88*, 1732 (1966); for a review see *D. J. Cram*: Fundamentals of Carbanion Chemistry. Academic Press, New York 1965, Chapter 6.

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[3] a) *E. A. Hill, H. G. Richey jr.*, and *T. C. Rees*, J. Org. Chem. *28*, 2161 (1963); b) *H. G. Richey jr.* and *T. C. Rees*, Tetrahedron Lett. *1966*, 4297.

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[5] Because of the relatively large energy differences, equilibria between primary and secondary carbanions are normally so extreme towards one side that it is difficult to determine the equilibrium constants [3a]; cf. *D. E. Applequist* and *D. F. O'Brien*, J. Amer. Chem. Soc. *85*, 743 (1963); *R. E. Dessy, W. Kitching, T. Psarras, R. Salinger, A. Chen*, and *T. Chivers*, *ibid.* *88*, 460 (1966).

Binuclear Organometallic Compounds

By *Michael F. Lappert* [*]

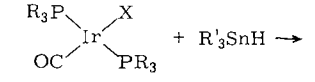
Binuclear organometallic compounds having bonds between a transition metal (M) and a Main Group metal (M') are conveniently synthesized by the amine elimination reaction. A better known synthesis is the salt elimination route.

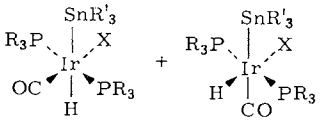
$$LM\text{-}H + L'M'\text{-}N(CH_3)_2 \rightarrow LM\text{-}M'L' + (CH_3)_2NH$$

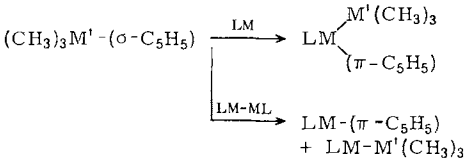
The transition metals considered were, in the main, chromium, molybdenum, and tungsten; titanium, zirconium, hafnium; and, to a lesser extent, cobalt, rhodium, and platinum. The Main Group metals considered were silicon, germanium, and tin.

In some cases complications arise; an example of this is the situation wherein the hydride contains chlorine ligands, in which case dehydrochlorination can occur.

Examples of oxidative addition reactions for formation of M—M' bonds are provided by the following equations:

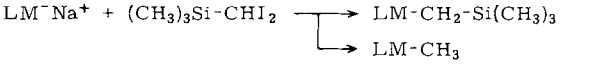






Physical properties of these complexes were examined, especially from the standpoint of the strength of the M'—M bond. In the compounds π-$C_5H_5M(CO)_3$—M'-$(CH_3)_3$, bond dissociation (mass spectral) energies increase along the series Cr < Mo < W and Si < Ge < Sn. Vibrational spectral (IR and Raman) data allowed identification of ν(M—M'). Regarding M—Si bonds, the uniquely long distance for Zr—Si in the compound $(\pi\text{-}C_5H_5)_2Zr(SiPh_3)Cl$ of 2.81 Å, which is at least 0.3 Å longer than other M—Si lengths, warrants particular attention. A possible interpretation is that in a d^0 complex π-bonding is not possible.

The compounds $LMCH_2Si(CH_3)_3$ are representatives of a novel series in which M and M' are not directly linked, but are bridged through a carbon atom. A particularly unexpected feature is that described by the reaction:



A deuterium labeling experiment using $(CH_3)_3SiCHDI$ led to the postulate that a transition metal carbene complex of the form $[LM{=}CH_2]^-$ occurs as an intermediate.

Lecture at Mülheim/Ruhr on March 19, 1970 [VB 252 IE]
German version: Angew. Chem. *82*, 940 (1970)

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Catalyzed Reactions in Analytical Chemistry

By *Dieter Klockow* [*]

Kinetic methods of analysis employing catalyzed reactions can be said to be of great importance in modern trace analysis. Catalytically active substances can be detected in concentrations from a few ppm down to fractions of ppb, in some cases with marked selectivity (particularly in enzymatic reactions).

The methods used for determining catalyst concentrations from kinetic data can be divided into two main groups, *i.e.* into differential methods (differential form of the rate equation) and integral methods (integrated form of the rate equation). The former methods are limited to a relatively short period of a reaction in which the concentrations of the reactants, and thus also the reaction rate, remain practically constant.

A recently described determination of traces of molybdenum (0.01—0.2 ppm) may be regarded as a variant of these differential methods; the method involves use of a potentiostat [1] to follow quantitatively the course of the reaction

$$H_2O_2 + 2\,I^- + 2\,H^+ \rightarrow I_2 + 2\,H_2O$$

which is catalyzed by molybdenum. One of the reactants (hydrogen peroxide) is present in excess, and the other one (iodide) is added from an automatic burette to the reaction mixture at a rate sufficient to maintain a certain, defined electrochemical potential. The rate of addition from the burette is a measure of the reaction rate and thus also of the catalyst concentration.

The same technique has also been used to study the zirconium-catalyzed reaction between perborate and iodide. Under suitable conditions, fluoride has a strong inhibiting effect on this system and can consequently be determined in very low concentrations (0.4—4 ppb) [2].

Catalytic reactions have found an interesting new application as end-point indicators in volumetric analysis. If a catalyst K which accelerates the reaction between two substances A and B is stoichiometrically blocked by an inhibitor R, the end point of a titration of R with a solution of K in the presence of A and B as an indicator mixture can be recognized by the start of the reaction between A and B. As an example may be mentioned the titration of Ag^+ ions (R) with a standard solution of iodide (K) making use of the iodide-catalyzed reaction between Ce^{IV} and As^{III} (A and B).

Such titrations, in which a catalyst initiates a reaction at the end point, have been applied to precipitation titrations [3] and chelatometric determinations [3,4]. The start of the catalyzed reaction at the end point can be detected visually or instrumentally, *e.g.* potentiometrically [5] or thermo-

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[1] *H. Weisz, D. Klockow*, and *H. Ludwig*, Talanta *16*, 921 (1969).

[2] *D. Klockow, H. Ludwig*, and *M. A. Giraudo*, Anal. Chem., in press.

[3] *H. Weisz* and *U. Muschelknautz*, Z. Anal. Chem. *215*, 17 (1966).

[4] *H. Weisz* and *T. Janjič*, Z. Anal. Chem. *227*, 1 (1967).

[5] *H. Weisz* and *D. Klockow*, Z. Anal. Chem. *232*, 321 (1967).

[6] *H. Weisz, T. Kiss*, and *D. Klockow*, Z. Anal. Chem. *247*, 244 (1969).

[7] *H. Weisz* and *T. Kiss*, *ibid. 249*, 302 (1970).

[8] *D. Klockow* and *L. García Beltrán*, Z. Anal. Chem. *249*, 304 (1970).

metrically[6,7]. Moreover, the substitution principle used in chelatometry can also be applied to these titrations[8]: The catalyst is added in an inactivated form as KR, together with A and B, to the sample solution to be titrated and is demasked by a titrant T when the end point is exceeded.

$$KR + T \rightarrow TR + K$$

The indicator reaction is thus initiated.

Lecture at Freiburg on May 15, 1970 [VB 253 IE]
German version: Angew. Chem. *82*, 886 (1970)

All-Electron Calculations on Lithium Cyanide and Formamide

By *Børge Bak*[*]

All-electron calculations have been performed on lithium cyanide (LiCN), lithium isocyanide (LiNC), and formamide ($HCONH_2$). Linear combinations were carried out using atomic orbitals (LCAO) of the Gaussian-type. In referring to these, (*l*, *m*, *n*,) (*q*) means: *l* Gaussian functions (G.F.) of s-type symmetry (spherical), *m* G.F. of p-type ($\equiv m$ of p_x-, *m* of p_y-, and *m* of p_z-type), *n* G.F. of d-type symmetry for each "heavy" atom, and *q* G.F. of s-type for each hydrogen.

For LiCN and LiNC (7,3,0) and (11,7,0) basis sets were successively used. Since there are no vapor-phase data available for these species the calculated properties are true predictions of experimental results to be obtained.

Independent of the basis set the predicted dipole moments of LiCN and LiNC are, respectively, 3.7 "atomic units" (a.u.) (~9 D) and 3.4 a.u. For both species the predicted C≡N distance is 2.19 a.u. (1.15 Å). The predicted Li—C distance (in LiCN) is 3.63 a.u. (1.91 Å), the predicted Li—N distance (in LiNC) is 3.33 a.u. (1.75 Å). Gaseous LiNC is predicted to be 0.014 a.u. (10 kcal/mole) more stable than LiCN in the hypothetical vibrationless state. The vibrational zero-point energy difference is of the order 0.3 kcal/mole in favor of LiCN. The predicted normal vibration frequencies ν_3 (C≡N stretch), ν_2 (bending mode), and ν_1 are (for Li = ^{6}Li): 2375, 2367; not calculated, 250; 670, 785 cm^{-1} for LiCN and LiNC[1].

(11,7,0)(5) and (11,7,6)(5) basis sets were successively used for formamide[2] to reproduce experimentally the established properties (a)—(d):

(a) The amide hydrogens are slightly out-of-plane with coplanar HCON.

(b) The measured dipole moment is 3.6 Debye.

(c) The barrier to internal rotation about the C···N bond is 20 kcal/mole.

(d) The measured nitrogen quadrupole coupling constants χ_a,χ_b, and χ_c are 1.9, 1.7, and −3.6 MHz.

From qualitative valence theory we would expect that:

(e) the C···N bond must lose its "double bond character" when the NH_2 group is twisted 90° from its ground state position, showing up as a lengthening of the twisted bond. The (11,7,0)(5) set, reproduced (b)—(e) satisfactorily, but not (a). With the (11,7,6)(5) set, non-planar formamide was correctly found as being more stable than the planar by about 0.1 kcal/mole. The experimental value is 1 kcal/mole. The calculated dipole moment was 4.07 Debye, the calculated barrier to internal rotation 20.1 kcal/mole. The calculated χ_a, χ_b, and χ_c (assuming a nitrogen nuclear quadrupole moment of 1.60×10^{-26} cm^2) were 1.98, 1.94, and −3.92 MHz. The lengthening of the C···N bond upon 90° twist was 0.05 Å.

Lecture at Kiel on May 5, 1970 [VB 257 IE]
German version: Angew. Chem. *82*, 939 (1970)

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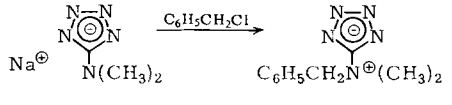
[1] *B. Bak*, J. Chem. Phys., in press.

[2] *B. Bak, D. Christensen*, and *R. Kortzebom*, J. Chem. Phys., in press.

SELECTED ABSTRACTS

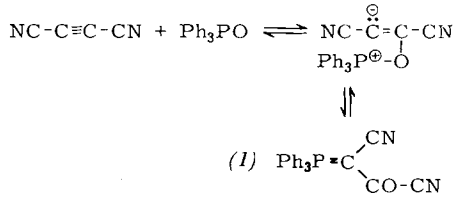
The synthesis of selenaheptathiocene, S_7Se, has been accomplished by *R. Cooper* and *J. V. Culka* by condensation of S_7Cl_2 with H_2Se. Separate solutions of both reactants were added very slowly to an anhydrous solution of diethyl ether cooled to 15 °C. After removal of part of the solvent by evaporation and subsequent cooling of the reaction mixture, yellow needles of S_7Se crystallized out. At higher temperatures this compound disproportionates to selenium-rich octatomic molecules, which could be readily detected by mass spectrometry; the mass spectrum shows very strong mass lines of S_8 and S_2. / J. Inorg. Nucl. Chem. *32*, 1857 (1970) / —Kr. [Rd 242 IE]

5-Tetrazolyl ylides have been investigated by *L. Huff, D. M. Forkey, D. W. Moore*, and *R. A. Henry*. Reaction of 5-dimethylaminotetrazole with benzyl chloride in aqueous ethanolic caustic soda leads to formation of the water-soluble ylide *(1)* (m.p. 205 °C, 29% yield) in addition to the expected 1- and 2-benzyl derivatives. The ethyl derivative can be obtained analogously. The structure was confirmed by NMR spectroscopy. A suspension of *(1)* in anhydrous ethanol can be kept for a period of weeks at room temperature; addition of methyl iodide leads to isomerization to the 2-benzyl derivative and to cleavage of the benzyl group. / J. Org. Chem. *35*, 2074 (1970) / —Kr. [Rd 245 IE]



(1)

Reverse Wittig reactions have been investigated by *E. Ciganek*. In the Wittig reaction a P—O bond is formed whereas in the reverse Wittig reaction it is cleaved. Thus, dicyanoacetylene and triphenylphosphine oxide react in

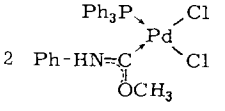


benzene at 160 °C to give the phosphorane *(1)* in 78% yield. On heating to 300 °C, compound *(1)* decomposes to the starting materials. Other acetylenes do not undergo

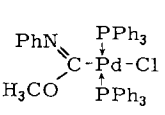
this reaction. Triphenylarsine oxide, however, also reacts *inter alia* with methyl propiolate, dimethyl acetylenedicarboxylate, and hexafluoro-2-butyne to give analogous compounds. / J. Org. Chem. *35*, 1725 (1970) / —Kr.

[Rd 246 IE]

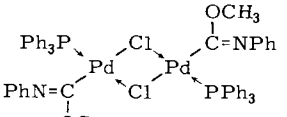
New compounds with palladium(II)-carbon σ-bonds can be obtained from carbene derivatives according to a report by *B. Crociani* and *T. Boschi*. Thus, the carbene derivative *(1)* reacts rapidly and almost quantitatively at room temperature with stoichiometric amounts of ethanolic potassium hydroxide; from the resulting red solution the brick-red compound *(2)* can be isolated in 92% yield. *(2)* dissolves



(1)



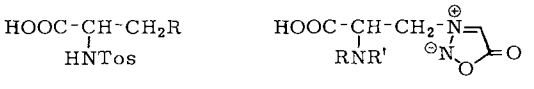
(3)



(2)

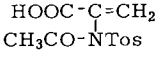
in 1,2-dichloroethane with partial dissociation and reacts with a stoichiometric amount of triphenylphosphine to give the complex *(3)* in quantitative yield. The reaction *(1)* →*(2)* is reversed on heating the reaction mixture under reflux with methanolic hydrochloric acid. / J. Organomet. Chem. *24*, C 1 (1970) / —Kr. [Rd 247 IE]

Fragmentation of a sydnone by elimination has been observed by *L. J. Fliedner jr.* and *I. Moyer Hunsberger*. Attempted preparation of the sydnone-substituted *(2a)* from *(1a)*, which was first converted in several steps into the *N*-nitroso-compound *(1b)*, yielded the acetyltosyl compound and/or



(1a), R = NH_2 *(2a)*, R = R' = H

(1b), R = $N(NO)CH_2$-COOH *(2b)*, R = CH_3CO, R' = Tos

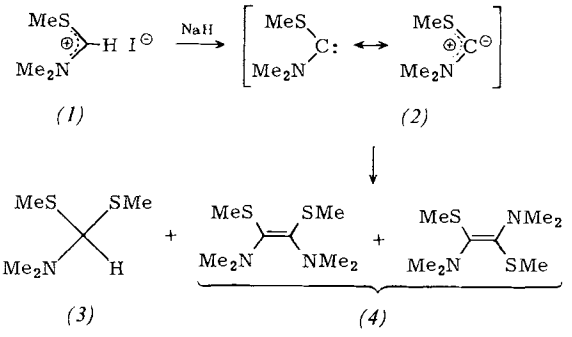


(3)

the fragmentation product *(3)*, depending upon the reaction conditions, instead of the expected *(2a)* during the final cyclodehydrogenation step with acetic anhydride. Compound *(3)* could also be prepared from *(2b)* by heating with acetic anhydride. The fate of the leaving group is still unknown. / J. Org. Chem. *35*, 2447 (1970) / —Ee.

[Rd 249 IE]

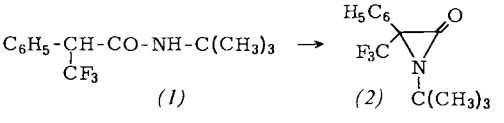
α-Dimethylamino-α-methylthiocarbene *(2)* is formed, according to *T. Nakai* and *M. Okawara*, on deprotonation of *N,N*-dimethyl-*S*-methylthioformimidoyl iodide *(1)* with sodium hydride at 0—5 °C in THF and can be detected by the formation of the thioacetal *(3)* and the two isomeric olefins *(4)*. The isomerization of dimethyl maleate to di-



(1) *(2)* *(3)* *(4)*

methyl fumarate by a mixture of *(1)* and NaH is remarkable since neither component of the mixture is able to bring about such a reaction on its own. It was found that it was not the carbene but the product *(4)* that effects the isomerization. / Chem. Commun. *1970*, 907 / —Ee. [Rd 250 IE]

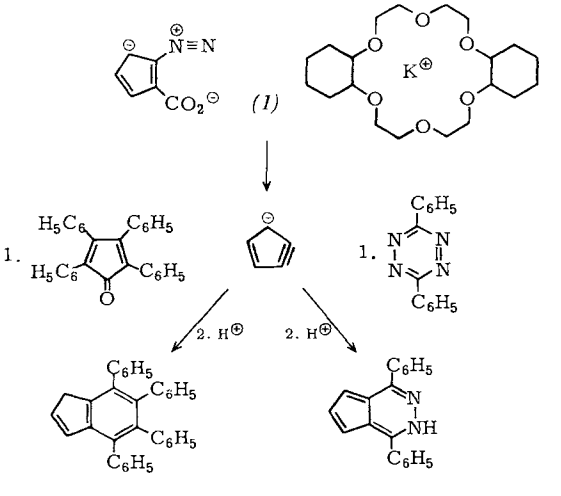
1-*tert*-Butyl-3-phenyl-3-[trifluoromethyl]aziridin-2-one *(2)*, an unusually stable trisubstituted α-lactam, has been investigated by *E. R. Talaty* and *C. M. Utermoehlen*. 3,3,3-Trifluoro-2-phenylpropionic acid was first converted into the amide *(1)*, which was subsequently transformed, by ring closure, to *(2)* by treatment with *tert*-butyl hypochlorite



(1) *(2)*

and potassium *tert*-butoxide. Compound *(2)* is sufficiently stable to survive purification procedures such as heating in high vacuum (<0.05 torr) at bath temperatures of 105 to 120 °C. Small amounts of *(2)* remain undecomposed even after 24 hours' refluxing in anhydrous methanol; decomposition at 90 °C is complete within 3.5 hours. / Tetrahedron Lett. *1970*, 3321 / —Kr. [Rd 253 IE]

The dehydrocyclopentadienyl anion, a new aryne, has been prepared by *J. C. Martin* and *D. R. Block* by pyrolysis of the complex *(1)*. Capture of such an anion is best achieved



by compounds which undergo a Diels-Alder reaction (1,4-cycloaddition) with the expected anion. Almost equivalent amounts of N_2 and CO_2 were transformed in the pyrolysis. / 160th Nat. Meeting of the Amer. Chem. Soc. 1970, Abstracts ORGN 26 / —Ma. [Rd 257 IE]

Cyclopentadienyl[trifluoromethyl]stannane has been used by *E. W. Abel, S. A. Keppie, M. F. Lappert,* and *S. Moorhouse* for the oxidative cleavage of the metal-metal bond in bi- or multinuclear carbonylmetal complexes. Such a cleavage is accomplished by heating the components under reflux in the absence of air, *i.e.* under nitrogen. Reaction proceeds almost quantitatively, but decomposition of the products sometimes takes place during attempts at their isolation. For example:

$$Mn_2(CO)_{10} + (CH_3)_3SnC_5H_5 \rightarrow \pi\text{-}C_5H_5Mn(CO)_3\ (54\%) + (CH_3)_3Sn\text{–}Mn(CO)_5\ (58\%)$$

$$[\pi\text{-}C_5H_5(CO)_2Fe]_2 + (CH_3)_3SnC_5H_5 \rightarrow (\pi\text{-}C_5H_5)_2Fe\ (33\%) + \pi\text{-}C_5H_5(CO)_2Fe\text{–}Sn(CH_3)_3\ (38\%)$$

/ J. Organomet. Chem. *22*, C 31 (1970) / —Kr.

[Rd 256 IE]

BOOK REVIEWS

Gmelins Handbuch der anorganischen Chemie (Gmelin's Handbook of Inorganic Chemistry), 8th fully revised edition. Published by the Gmelin-Institut für anorganische Chemie und Grenzgebiete in der Max-Planck-Gesellschaft zur Förderung der Wissenschaften under the direction of *Margot Becke-Goehring*. Verlag Chemie GmbH., Weinheim/Bergstr. [*].

System No. 6: Chlorine. Supplementary Volume. Part B, 2. Conclusion of the Compounds. Detection and Determination. Principal editor: *Hans Karl Kugler*. 1969. iv, xix, 308 pp., 40 figures, linen DM 376.

The present supplementary volume describes the compounds of chlorine with oxygen, nitrogen, and fluorine. The literature has been fully evaluated up to the end of 1966 and largely taken into account up to 1968. This volume concludes the monograph on the element chlorine. However, it can also be used independently of the earlier parts where the material of interest falls within the field covered. A completely updated collective work on the subject is of great value, since intensive investigations have been focused on the compounds of chlorine with oxygen, nitrogen, and fluorine over the past ten years in the search for strong oxidizing agents for rocket fuels.

Of the chlorine-oxygen compounds, which have only recently become known, we shall mention only Cl_2O_3. Advanced techniques are now allowing increasingly detailed studies on unstable radicals, such as ClClO, ClO, ClOO, and ClO_4. 106 pages are devoted to the oxo acids of chlorine, though there is nothing fundamentally new to be mentioned in this field. The same is true of a series of long-known chlorine-nitrogen compounds such as NCl_3 or nitrosyl and nitryl chlorides. On the other hand, there have been many new observations in connection with the corresponding perchlorates and with dichlorofluoramine NCl_2F and chlorodifluoramine $NClF_2$ (p. 588: printing error in the heading).

Among the brand-new compounds in the chapter on chlorine and fluorine, mention should be made of ClF_5, which can be obtained from the elements by heating if a large excess of fluorine is used, and of the difluorochlorates(I) and tetrafluorochlorates(III).

A number of new members have also been added to the class of chlorine-oxygen-fluorine compounds. The compounds ClOF, ClO_2F, $(ClO_2F_3)_n$, ClO_3F, and ClO_4F are now known.

A final chapter presents a survey of the methods for the detection and determination of chlorine and its compounds as well as of the isotopes of chlorine.

System No. 47: Lead. Part C, 1: Technical Production of Lead, Compounds of Lead (Lead and Inert Gases, Hydrogen, Oxygen, Nitrogen, Fluorine, Chlorine). Principal editor: *G. Hantke*. 1969, iv, xxii, 346 pp., 69 figures, linen DM 421.—.

Part C, 1 first describes the metallurgy of lead in 46 pages. A brief survey of the raw materials is followed by the description of the dry and wet metallurgical processes for the treatment of lead ores. The section on roast-reduction, which is the method most widely used today, is particularly thorough and detailed. Access to monographs and articles in collective works on the metallurgy of lead is provided by a bibliography at the beginning of the chapter.

Most of the volume (300 pages) is devoted to the compounds of lead with the elements mentioned above. While the lead-inert gas and lead-hydrogen systems cover only a few pages, the lead-oxygen system takes up more than 150 pages. The compounds of lead with oxygen include a series of products that are widely used in industry, such as litharge PbO, red lead Pb_3O_4, and PbO_2. Just as for all other compounds, their chemical and physical behavior is discussed in detail. However, practical examples of the preparation processes, standards, and purity tests are also given. Among the lead-nitrogen compounds, the greatest space is devoted to the chemistry of the nitrite and nitrate compounds, which form many basic salts. The basic salts (though often not well characterized) also help, together with the complex compounds, to increase the number of substances in the case of the chlorine compounds.

System No. 47: Lead. Part C, 2: Lead and Bromine, Iodine, Sulfur, Selenium, Tellurium, Polonium, Boron, Carbon. Principal editor: *G. Hantke*. 1969. iv, xxii, 460 pp., 115 figures, linen DM 555.—.

Part C, 2 continues the description of the lead halides with the bromine and iodine compounds. The mere size of this section (65 pp.) shows the multiplicity of the compounds, as well as the importance that is now assigned to this class of compounds. Many of the works cited originated in the last two decades, and the considerable proportion of Russian references is particularly striking. The careful search of the Russian literature, which is only inadequately represented in most libraries either in the original or in translations, deserves special praise, since this allows access to the articles of interest.

The next 194 pages are devoted to the lead-sulfur system, and within this system to the compound PbS. The lead-selenium and lead-tellurium systems are also discussed in surprising detail; as in the case of the lead-sulfur system, it is the electrical properties in particular that are dealt with thoroughly in the literature and that are of great importance in the electrical industry. The chemist will probably be more interested in the remainder of the volume, apart from the lead-polonium and lead-boron systems. The former covers only half a page, while the latter is dominated by the chemistry of boric acid rather than by that of lead. However, the section on the lead-carbon system is very interesting, and deals not only with lead carbonate but also with the many lead salts of organic acids such as hydrocyanic, cyanic, thiocyanic, formic, acetic, oxalic, and citric acids. Finally, it should be mentioned that measurement data that are of little importance to the result could have been omitted in many places (*e.g.* the measuring frequency for NMR spectra, p. 691).

System No. 63: Ruthenium. Supplementary volume. Principal editor: *E. Schleitze-Steinkopf*. 1970. vi, xviii, 586 pp., 86 figures, linen DM 689.—.

The present volume supplements the first volume on the ruthenium system, which was first published in 1938. In this

[*] Cf. Angew. Chem. internat. Edit. *6*, 100 (1967).

volume one finds many differences from the earlier conception of Gmelin's Handbook. The most important, in the reviewer's opinion, appears to be the successful abandonment of the historical but long outdated division into an inorganic and an organic section. A considerable part of the book is devoted to the organoruthenium compounds. If the same procedure is followed in future volumes, the value of "Gmelin" to the chemist will be greatly enhanced. Even a quick glance through the present volume gives the impression that it is a *chemical* reference book, and not merely a collection of physical constants, as many of the earlier volumes seemed to be.

Another innovation is the abandonment of the earlier, often excessively rigid arrangement in favor of a chemically more logical classification. Salts of complex acids of ruthenium are now dealt with under the various nonmetals. $LiRuF_6$, for example, is to be found in the section on "Ruthenium and Fluorine".

Finally, a very welcome change is that the present volume almost attains the currency of progress reports. The literature is completely evaluated up to the end of 1968, and many important publications from 1969 are also taken into account.

The first two main sections of the volume deal with the properties of the element and its alloys. Ruthenium, which was of no special importance in industry a relatively short time ago, has rapidly grown in importance during the past few years. It is an efficient catalyst in many hydrogenation reactions, and the nuclear chemist is concerned with its isotopes as fission products of uranium and plutonium, while some of its alloys have superconducting properties.

The third main section describes the compounds of ruthenium. Considerable space is devoted to the discussion of the very numerous nitrosyl compounds. This is followed by a description of the compounds with neutral and inner complex forming ligands, the carbonyl compounds, and the organometallic compounds of ruthenium.

A further innovation is found at the end of the volume in the form of an alphabetic subject index and a formula index for the ligands, which make it much easier to find groups of compounds and individual compounds.

Ekkehard Fluck [NB 894 IE]

Zahlentafeln zur Massenspektrometrie und Elementaranalyse (Numerical Tables for Mass Spectrometry and Elemental Analysis). By *G. Ege*. Verlag Chemie, Weinheim/Bergstr. 1970. 1st Edit., xxvi, 352 pp., 356 tables.

The determination of empirical formulas from elemental analyses is made much easier with *Ege*'s "Zahlentafeln zur Elementaranalyse" (Numerical Tables for Elemental Analysis). However, if an analysis is not exact, several possible formulas have to be considered; for example, the C and H analytical values of homologs are often situated so close together that it is impossible to decide in favor of one or the other compound. In such cases it is possible to reach a decision on the basis of the molecular weight, which can be determined mass-spectrometrically.

Acknowledging this fact, *Ege* has now expanded his original Tables into their present form.

To keep the volume of the material within reasonable limits the tables are restricted to carbon compounds with not more than 40 carbon, 6 nitrogen, 12 oxygen, and an appropriate number of hydrogen atoms. On the whole this should prove adequate. The numerical tables encompass compounds with molecular weights from 16 to 845 arranged according to increasing mass.

The idea of grouping the theoretical analytical values into groups of ten is commendable, since it greatly facilitates rapid location of the empirical formulas.

In addition, one column gives the exact molecular weight of each compound, so that the tables can also be used to determine empirical formulas with the aid of high-resolution mass spectra. In such cases elemental analysis becomes superfluous. Data on double bond equivalents constitute another welcome feature.

In contrast, the data on the intensity ratio of M^+ and $(M + 1)^+$ peaks could well have been omitted, since in practice the intensity ratios of M^+ and $(M + 1)^+$ ions obtainable from spectra are too inaccurate, at any rate in the case of compounds of higher molecular weight, to enable useful conclusions to be drawn.

Nevertheless, this point in no way detracts from the value of the tables, which can be warmly recommended to all laboratories engaged on the investigation of organic compounds.

Gerhard Spiteller [NB 910 IE]

Rechenseminar in physikalischer Chemie. (Problems in Physical Chemistry). By *K. Torkar*. Friedr. Vieweg u. Sohn, Braunschweig 1968. 1st Edit., xii, 172 pp., 48 figures, 38 tables, bound DM 9.80.

There are a considerable number of books dealing with physicochemical calculations. These generally list the laws of physical chemistry in a logical order and make use of them as a basis for examples of simple calculations. *K. Torkar* follows an entirely different plan. He confines his book to four problems:

1. Calculation of the pressure relations in an autoclave. 2. Calculation of a chemical equilibrium. 3. Boiling diagrams. 4. Chemical reaction kinetics.

Under these headings he deals with 1) the formation of boehmite in an autoclave or an automobile CO_2 fire extinguisher, 2) the reduction of chromium oxide by graphite or the conversion of carbon monoxide with steam, 3) the benzene-toluene system or the A-B system in general, and 4) reactions of the types $A \rightarrow$ products, $aA + bB \rightarrow$ products, or $H_2 + Br_2 \rightarrow 2\,HBr$.

The author thus starts with concrete problems from practice and explains the calculation procedure for the examples named in the smallest detail. He compares the various calculation methods, indicates where the necessary numerical values are to be found, and compares the data from different tabulated values. The clarity of presentation is improved by tables and graphs.

This book offers the student a bridge between formula and application, and should encourage the teacher to hold similar problem seminars.

Gerd Wedler [NB 898 IE]

Practical Manual of Gas Chromatography. Ed. by *J. Tranchant*. Elsevier Publishing Company, Amsterdam-London-New York 1969. 1st Edit., xix, 387 pp., numerous illustrations, bound, Dfl. 85.—. English translation of the second French edition.

When a book on chromatography is translated from the French into English and joins the long ranks of works already published in English in this field, it is only natural to wonder whether the translation was simply motivated by the existence of the wider readership, or whether this readership may itself derive some benefit. The far-reaching and most welcome exclusion of theoretical ballast — an intention already proclaimed by the title — as well as the typically Gallic conciseness and precision of the presentation add up to a positive reply to the latter question. The content of the book and its points of emphasis can be conveniently indicated by enumerating the titles and numbers of pages of the nine chapters contributed by six authors: 1. Principles and retention values (11 pp.); 2. Isothermal-isobaric chromatography (15 pp.); 3. Programmed chromatography (18 pp.); 4. Apparatus (37 pp.); 5. Columns (73 pp.); 6. Detectors (40 pp.); 7. Qualitative analysis; separation and identification (39

pp.); 8. Quantitative analysis (32 pp.); 9. Applications and techniques (92 pp.). The emphasis of the book is quite clearly on practical aspects. Nevertheless, all the important equations derived from theory are included in the most concise possible form. It would be wrong to regard this merely as a dutiful exercise in theory, since important practical conclusions are almost invariably derived from the relationships. The two chapters on columns and applications merit special mention. Containing 263 and 809 literature references respectively, they not only provide an excellent survey but represent well-balanced and self-contained treatises containing all the essential details.

Happily, there is none of the overlapping all too often observed in multi-author volumes. All the authors use the same symbols which are collected together in a single list. It is unfortunate that out-of-date statements, now recognized as incorrect, are made in the discussion of the van Deemter equation on p. 23, in connection with mass transport in the mobile and the stationary phase. This is evidently due to the fact that the author of this chapter has relied on a (cited) paper whose experimental conditions were inappropriate to the theoretical conclusions based upon them. In its nine chapters the book presents all the essential points of gas chromatography. It is particularly suitable for all those who are daily confronted by analytical and experimental problems of gas chromatography, and can be recommended as a really excellent work.

G. Deininger [NB 909 IE]

Methods in Free-Radical Chemistry. Edited by *E. S. Huyser*. Marcel Dekker Inc., New York 1969, 1st Edit., Vol. 1: 208 pp., numerous illustrations, bound $11.75. Vol. 2: xi, 242 pp., numerous illustrations, bound $12.75.

Since the publication of *C. Walling*'s book "Free Radicals in Solution" in 1957, such extensive progress has been made in this branch of chemistry that it would no longer be possible for a single author to present a comprehensive treatment. As in other fields, therefore, monographs in free-radical chemistry are being replaced by progress reports covering a limited area. The present new series can consequently claim a place of special importance alongside "Advances in Free-Radical Chemistry" [1]. A wide selection of the results of work carried out in free-radical chemistry over the past twelve years is discussed in a total of five sections by young authors working in this field.

The first two chapters (Free Radical Study by Electron Paramagnetic Resonance by *L. Kevan*, 35 pp.; Free Radical and Photochemical Reactions by *D. C. Neckers*, 44 pp.) are dominated by the discussion of the methods and their theoretical principles on the basis of selected results. Their value lies in the concise and lucid survey and in the references to the original literature. The sections "Free-Radical Chlorinations" (*M. L. Poutsma*, 114 pp.), "Free Radical Brominations" (*W. A. Thaler*, 106 pp.), and "Thiyl Radicals" (*R. M. Kellog*, 120 pp.), on the other hand, deal systematically from the preparative and mechanistic standpoints with free-radical substitutions and additions of free radicals. The important relations between structure and reactivity are clearly recognizable from the numerous tables and diagrams. These chapters undoubtedly constitute the more valuable part of the present work, since the literature, which would now be very difficult to scan, is reviewed critically and comprehensively up to the latest position.

In presentation and quality, the two volumes may be regarded as supplements to *Walling*'s classic work. They should therefore find a place in every library and are especially recommended to all those who are interested in free-radical chemistry.

Ch. Rüchardt [NB 902 IE]

[1] Cf. Angew. Chem. internat. Edit. *6*, 475 (1967).

Laser Raman Spectroscopy. By *T. R. Gilson* and *P. J. Hendra*. Wiley-Interscience, Division of J. Wiley and Sons, New York 1970. 1st Edit., ix, 266 pp., numerous illustrations, bound, 90s.

Although laser light sources have considerably simplified the techniques of Raman spectroscopy, the term "laser Raman spectroscopy" is no more appropriate than "Nernst-lamp infrared spectroscopy". This is one of the faults of the present book, which is meant to be "an introduction to Raman spectroscopy with particular emphasis on the developments resulting from the use of laser sources". It is divided into the following sections: 1. Introduction (20 pp.), 2. Experimental (40 pp.), 3. Raman Intensity and Depolarization Ratios (23 pp.), 4. Single-crystal Raman Spectroscopy (58 pp.), 5. Raman Spectra of Gases (11 pp.), 6. Powders, Liquids and Solutions (13 pp.), 7. Polymers (17 pp.), 8. Miscellaneous Raman Experiments (15 pp.), 9. Sources of Information (3 pp.). There are two appendices, one devoted to lasers (I, 6 pp.) and the other to "Results from Group Theory" (II, 47 pp.).

The first four chapters are instructive and useful. The beginner, however, would profit more from Chapter 4 and Appendix II if examples had been treated in detail and knowledge of the original work had not been presupposed, as is the case on pp. 109—123. The later chapters show evidence of unquelled enthusiasm over laser light sources ("Laser has revolutionized the study" (of polymers) p. 166). One learns a great deal about the successful recording of individual spectra but not enough about how useful this is. An unexperienced reader would doubtless get the impression that Raman spectroscopy was a very new method and that a large store of experience in the field of "mercury-lamp Raman spectroscopy", as collated for example in the books of *Kohlrausch*, *Herzberg*, and *Siebert*, did not exist. The book is also disappointing for the organic chemist. Only one page (155) is given to structural determination and there are only nine lines (p. 165), without references, on his main concern, the detection of compounds whose vibrations in the infrared are too weak. The reader is told nothing of the important problem of appropriate sample preparation and the dependence of intensity on the grain size in powders. Chapter 9 makes no mention either of the very useful DMS Reference Service "IR Raman Microwaves" which has been operating since 1963, or of the spectra collections of the API and in Landolt-Börnstein. Printing errors are rare. The book would be more useful for beginners and for specialists if the last chapters in particular were thoroughly revised.

Bernhard Schrader [NB 913 IE]

The Halides of the Lanthanides and Actinides. By *D. Brown*. John Wiley and Sons Ltd., London-New York-Sydney-Tokyo-Mexico City. 1968. 1st Edit., x, 280 pp., numerous illustrations, bound, *ca.* DM 43.—.

Until recently only two review papers have been available on the halides of the f transition elements, namely one on the lanthanoid halides [1][*] and one on the actinoid halides [2][*]. *D. Brown*, who is himself an authority in the field of the actinoid and lanthanoid halides, has now attempted to present a comparative description of the halides of all the f transition elements. This attempt may be regarded as highly successful. One's only regret is that the halides of the transcurium elements were discovered too recently to be included in this book.

[1] *R. E. Thoma*, ORNL-3804 (May 1965); Progr. Sci. Technol. Rare Earths 2, 90 (1966).

[2] *J. J. Katz* and *I. Sheft*, Advan. Inorg. Chem. Radiochem. *2*, 195 (1960).

[*] According to the IUPAC Commission on the Nomenclature of Inorganic Chemistry the names lanthanoids and actinoids should be used for elements 57–71 and 89–103 respectively; cf. C.R. XXIII IUPAC Conference, Paris 1965, p. 183.

The author begins with an introduction, in which he deals first with general properties such as electronic structure of the elements and oxidation states; the known halides and oxide-halides of the lanthanoids and actinoids are grouped together in four synoptic tables. A survey of ionic radii is followed by a brief summary of the most important nuclear properties of the actinoid nuclides suitable for preparative work, and a section — unfortunately rather short — on the micropreparative methods, particularly important with regard to the actinoid halides. The four chapters that follow are concerned with the compounds of the f elements with fluorine, chlorine, bromine, and iodine. Each of these chapters is subdivided strictly according to oxidation states in the sequence M^{6+}, M^{5+}, M^{4+}, M^{3+}, and M^{2+}. Each section dealing with an oxidation state is in turn further divided into subsections on "halides", "complex halides", "oxide halides", and "complex oxide halides", as the case may be. This very clear arrangement of the subject matter makes it possible to locate any given compound very rapidly.

The text is kept as brief as possible by confining it to chemical properties and methods of preparation. Numerical data, such as lattice constants, IR frequencies, vapor pressure parameters, and other physical data are conveniently offered in tabulated form. Data that would have been difficult to fit into the selected framework are collected separately at the back, so that we have thermodynamic data in Appendix A, certain IR data in Appendix B, and data on mixed halides of uranium and protactinium in Appendix C. The frequently highly complicated crystal structures of the halides and oxide-halides are explained with the aid of readily understandable illustrations.

A comprehensive list of references (numbered consecutively) is given at the end of each chapter, the total amounting to almost 1300. However, it is a pity that one finds so many printing errors in this material. Despite this shortcoming, which can in any event be eliminated in the next edition, the work can be highly recommended. It provides a veritable gold mine both for those working in the field of lanthanoid and actinoid halide chemistry, and for students with more general interests. The wealth of information stored in this book is such that it will enable practically any query relating to the halides of the f elements to be swiftly and reliably answered. This invaluable book is recommended without reservation, and no chemical library should be without it.

Fritz Weigel [NB 907 IE]

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Volatile Flavoring Substances in Foodstuffs

By Hans Gerhard Maier [*]

The odor of most foods is produced by mixtures of many volatile flavoring substances. Over the past century, numerous food flavors have been analyzed in sufficient detail to allow a survey of the classes of substances responsible, the formation of individual flavoring substances, and their fixation in the foods. In addition to special biosynthetic pathways, the breakdown of fats and the Maillard reaction have been found to be particularly important to the formation of flavoring substances.

1. Introduction

Flavoring substances are important components of most foodstuffs. Without them, the foods are rejected even by hungry subjects, or if they are eaten, they are not digested so well [1]. The term "flavoring substances" refers here to the chemically definite compounds that cause the flavor of foodstuffs. "Flavor" is used in two senses, one of which is an overall impression left behind in the nose and tongue by odor-producing and taste-producing substances; the second meaning is a mixture or preparation of flavoring substances. The expression "essential oil", which is occasionally used instead of "flavor", should be reserved for the flavors from spices and expressly odoriferous plants [2]. The oils from the flavedo of citrus fruits occupy an intermediate position in this connection. The essential oils will not be considered in this article (but cf. [3]). The flavor of tobacco smoke is also largely disregarded (but cf. [4]).

It is difficult to distinguish between volatile flavoring substances and other volatile components of foodstuffs. Only a few volatile substances (*e.g.* N_2, O_2, inert gases) evoke no sensation of smell at all; the rest differ widely in the intensity of their odor. Some examples are shown in Table 1. The "threshold value" (limiting concentration) given in the table is the lowest concentration of the substance at which its presence is recognized in comparison with a blank test. It is not normally possible at this concentration to determine the nature of the odor. The values vary with the medium, as is shown in Table 2 by the results of the taste tests, in which the flavoring substances are also sensed by the nose. The threshold values are influenced by other flavoring substances [7,8]; for example, the odors of two flavoring substances may cancel each other out in suitable

Table 1. Odor threshold values of some volatile flavoring substances from foodstuffs in air (averages for several test subjects) [5, 6].

Flavoring substance	Threshold value (mg/l)
Methanol	8×10^{0}
Methyl salicylate	1×10^{-1}
Amyl acetate	4×10^{-2}
Safrole	5×10^{-3}
Hydrogen sulfide	2×10^{-4}
Coumarin	2×10^{-5}
Citral	3×10^{-6}
Ethanethiol	7×10^{-7}

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[1] *H. Glatzel*, Dtsch. Lebensm.-Rdsch. *64*, 1 (1968).

[2] *K. Gierschner* and *G. Baumann* in *J. Solms* and *H. Neukom*: Aroma- und Geschmacksstoffe in Lebensmitteln. Forster-Verlag, Zürich 1967, p. 49.

[3] *E. Gildemeister* and *F. Hoffmann*: Die ätherischen Öle. Akademie-Verlag, Berlin 1956–1966.

[4] *R. L. Stedman*, Chem. Rev. *68*, 153 (1968).

[5] *J. May*, Staub *26*, 385 (1966).

[6] *M. A. Amerine*, *R. M. Pangborn*, and *E. B. Roessler*: Principles of Sensory Evaluation of Food. Academic Press, New York 1965, p. 184.

[7] *G. Bennett*, *B. J. Liska*, and *W. L. Hempenius*, J. Food Sci. *30*, 35 (1965).

[8] *A. M. Burger*: Die natürlichen und künstlichen Aromen. Hüthig, Heidelberg 1968, p. 15.

Table 2. Taste threshold values of some volatile flavoring substances in various media [11].

Flavoring substance	Water (mg/kg)	Oil (mg/kg)	Milk (mg/kg)	Butter (mg/kg)
n-Hexanal	0.016	0.19	0.05	0.80
n-Heptanal	0.031	0.75	0.12	0.90
Biacetyl	0.0054	0.055	0.014	0.032
Ethyl acetate	6.6	22.0	4.7	—
Ethyl butyrate	0.015	0.60	0.016	—
Dimethyl sulfide	—	0.009	0.919	0.17

mixing ratios[9], or the odor of stronger-smelling components may be altered by components having only a very weak odor or none at all.

For these reasons, the classification of volatile substances as scented or odorless is more or less arbitrary[10]. All volatile substances, with the exception of the odorless "permanent gases" and water, should therefore be regarded as flavoring substances. However, flavoring substances that are either present in the foodstuffs in relatively high concentrations or have a very strong odor so that they can be effective even in low concentrations are particularly interesting.

Most foodstuff flavors consist of many flavoring substances, none of which is alone typical of the aroma in question – spices, of course, are an exception. The total content of flavoring substances in foods is roughly between 1 and about 1000 mg/kg (*e.g.* 10–100 mg/kg in fruit[12]). We know relatively little at present about the contents of individual flavoring substances; they may be assumed to range from <0.001 to 100 mg/kg. This is not so of spices, in which the quantities are greater (*e.g.* up to 29 g of vanillin per kg in vanilla pods).

Since flavoring substances are normally present only in small quantities, it is only during the last two decades that it has become possible to determine the complicated compositions of most flavors by the use of chromatographic methods, and particularly by combination of gas chromatography with mass spectrometry, IR spectroscopy, and thin layer chromatography. It was formerly thought in many cases that only a few flavoring substances were typical of a given foodstuff. The development of research on flavoring substances is illustrated in Figure 1, which shows a plot of the number of flavoring substances identified in roasted coffee since the 1920's. The total is now 370 substances, and approximately as many more have been isolated but have not yet been identified, so that it is estimated that 600–700 components must be present in all. Though the components that have not yet been identified are present in lower concentrations than the others, it may be assumed that these trace components also contribute to the flavor,

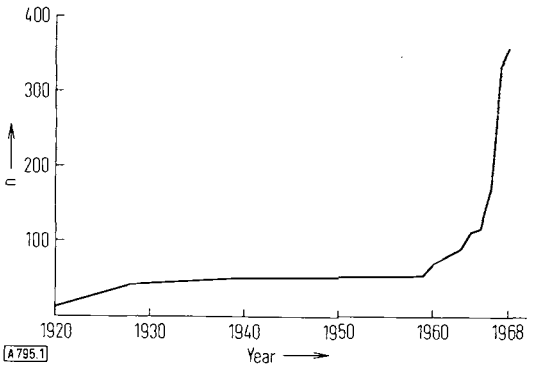


Fig. 1. Number *n* of flavoring substances identified in roasted coffee during the last few decades.

since no satisfactory coffee flavor has yet been produced by mixing the flavoring components that are already known.

Examples of the classes of substances from which some foodstuff flavors are built up are shown in Table 3. The qualitative composition tells us nothing about the importance of individual flavoring substances in determining the odor. This importance can only be roughly estimated if the threshold values of the various flavoring substances are known. Table 4 shows the percentage contributions of some steam-volatile components of carrots to the odor, as calculated from the contents and the threshold values of the substances[13]. According to these calculations the terpenes, which are present in relatively large

[9] *R. H. Wright*, Chem. Can. *10*, 37 (1958); Chem. Zbl. *130*, 5647 (1959).

[10] *T. Bassiri*, Soap, Perfumery Cosmetics *36*, 877 (1963).

[11] *Th. J. Siek, I. A. Albin, L. A. Sather*, and *R. C. Lindsay*, J. Food Sci. *34*, 265 (1969).

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[14] *W. Walter* and *H.-L. Weidemann*, Z. Ernährungswiss. *9*, 123 (1969).

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[16] *G. P. Rizzi*, J. Agr. Food Chem. *15*, 549 (1967).

[17] *B. van der Wal, G. Simpa, D. K. Kettens*, and *A. Th. J. Semper*, Recl. Trav. Chim. Pays-Bas *87*, 238 (1968).

[18] *E. L. Wick, T. Yamanishi, A. Kobayashi, S. Valenzuela*, and *P. Issenberg*, J. Agr. Food Chem. *17*, 751 (1969).

[19] *R. Tressl, F. Drawert, W. Heimann*, and *R. Emberger*, Z. Naturforsch. *24b*, 781 (1969).

[20] *F. Drawert* and *R. Tressl*, Brauwissenschaft *22*, 169 (1969).

[21] *R. Tressl, F. Drawert*, and *W. Heimann*, Z. Naturforsch. *24b*, 1201 (1969).

[22] *W. H. McFadden, R. Teranishi, J. Corse, D. R. Black*, and *T. R. Mon*, J. Chromatography *18*, 10 (1965).

[23] *B. Willhalm, E. Palluy*, and *M. Winter*, Helv. Chim. Acta *49*, 65 (1966).

[24] *F. Müggler-Chavan, R. Viani, J. Bricout, D. Reymond*, and *R. H. Egli*, Helv. Chim. Acta *49*, 1763 (1966).

[25] *H. A. Bondarovich, A. S. Giammarino, J. A. Renner, F. W. Shephard, A. J. Shingler*, and *M. A. Gianturco*, J. Agr. Food Chem. *15*, 36 (1967).

[26] *J. Bricout, R. Viani, F. Müggler-Chavan, J. P. Marion, D. Reymond*, and *R. H. Egli*, Helv. Chim. Acta *50*, 1517 (1967).

[27] *K. Ina, Y. Sakato*, and *H. Fukami*, Tetrahedron Lett. *1968*, 2777.

[28] *T. Yamanishi, A. Kobayashi, W. Nakamura, A. Uchida, S. Mori, K. Ohsawa*, and *S. Sasakura*, Agr. Biol. Chem. (Tokyo) *32*, 379 (1968).

[29] *J. Schormüller* and *H.-J. Kochmann*, Z. Lebensm.-Untersuch.-Forsch. *141*, 1 (1969).

[30] *R. Viani, J. Bricout, J. P. Marion, F. Müggler-Chavan, D. Reymond*, and *R. H. Egli*, Helv. Chim. Acta *52*, 887 (1969).

[31] *E. v. Sydow* and *K. Anjou*, Lebensm.-Wiss. Technol. *2*, 15 (1969).

Table 3. Compositions of some foodstuff flavors. (Position at the end of 1969; compounds containing several functional groups are counted several times, and compounds with uncommon functional groups were not take into account.)

	Roast coffee [14]	Straw-berry [21–23]	Cocoa [15–17]	Banana [18, 19]	Beer [20]	Black tea [24–28]	Tomatoes [29, 30]	Rye crispbread [31]
Total number of flavoring substances	370	251	201	194	183	106	98	92
Aliphatic hydrocarbons	21	18	—	—	3	1	4	—
Alicyclic hydrocarbons	3	5	4	—	3	1	3	—
Aromatic hydrocarbons	19	8	18	—	—	—	6	2
Heterocycles without functional groups	67	—	17	—	2	2	3	14
Alcohols	26	40	27	49	42	28	16	9
Phenols	28	—	17	1	2	4	9	7
Ethers	12	1	6	4	—	—	3	1
Thiols	4	1	—	—	3	—	—	—
Sulfides	8	1	4	—	1	1	—	1
Di- and trisulfides	5	—	4	—	—	—	1	1
Other aliphatic and inorg. S compounds	4	1	—	—	5	—	—	—
Amines	2	—	9	—	13	—	—	—
Nitriles	3	—	2	—	—	3	2	—
Aldehydes	34	13	29	9	10	21	22	16
Acetals	—	22	—	—	1	1	3	—
Ketones	102	12	30	13	9	18	15	13
Carboxylic acids	15	30	18	40	29	14	5	7
Carboxylic acid esters	33	94	37	81	61	12	7	12
Lactones	7	6	5	—	1	3	5	5
Anhydrides and Imides	4	—	—	—	—	—	—	—
Of which there are:								
aromatic compounds	59	21	58	6	11	12	21	17
alicyclic compounds	27	7	18	—	5	14	11	6
heterocyclic compounds	151	3	36	—	2	7	3	34

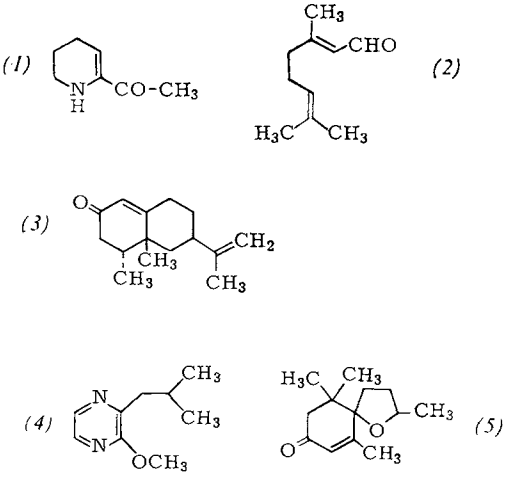
Table 4. Contributions of some flavoring substances from the steam-volatile fraction of carrots to the odor (after [13]).

Flavoring substance	Content (%)	Threshold value (μg/l)	Contribution to odor (%)
Terpinolene	38	200	1
Sabinene	4.0	75	0.5
Myrcene	0.8	13	0.4
Terpinenol-(4)	0.7	340	0.01
α-Terpineol	0.7	350	0.01
Bornyl acetate	0.6	75	0.05
Myristicine	0.4	25	0.1
2-Nonenal	0.3	0.08	22
Octanal	0.2	0.7	2
Carotol	0.2	8	0.1
Heptanal	0.05	3	0.1
2-Decenal	0.04	0.3	0.8

quantities, contribute little, whereas the aldehydes, which are present in small quantities, make a very large contribution to the flavor. These results must be regarded with caution, since synergism or antagonism may occur. This is also true of the results in Table 5, in which some foods are listed together with characteristic flavoring substances. The list is intended only as an indication; examples are known in which a flavoring substance that smells similar to the entire aroma is present, but does not determine the

Table 5. Particularly characteristic flavoring substances in some foodstuffs.

Foodstuff	Flavoring substance	Ref.
Bread crust (fresh)	1,4,5,6-Tetrahydro-2-acetylpyridine *(1)*	[36]
Lemons	Citral *(2)*	[37]
	2-Nonanone	[12]
Grapefruit	Nootkatone *(3)*	[38]
Hamlin oranges (undamaged)	Butyl acetate	[39]
Paprika (green)	2-Methoxy-3-isobutylpyrazine *(4)*	[40]
Soybeans (raw)	Ethyl vinyl ketone	[41]
Sweet-corn conserve	Dimethyl sulfide	[42]
Tea (black)	Theaspirone *(5)*	[27]



[32] *F. Drawert, A. Rapp,* and *H. Ullemeyer,* Vitis *6,* 177 (1967).

[33] *F. Drawert, W. Heimann, R. Emberger,* and *R. Tressl,* Z. Lebensm.-Untersuch.-Forsch. *140,* 65 (1969).

[34] *W. G. Jennings,* Lebensm.-Wiss. Technol. *2,* 75 (1969).

[35] *E. v. Sydow* and *K. Anjou,* Lebensm.-Wiss. Technol. *2,* 78 (1969).

[36] *I. R. Hunter, M. K. Walden, J. R. Scherer,* and *R. E. Lundin,* Cereal Chem. *46,* 189 (1969).

[37] *H. Drews* in *J. Schormüller:* Handbuch der Lebensmittelchemie. Springer, Berlin 1968, Vol. V/2, p. 33.

[38] *W. D. MacLeod,* Tetrahedron Lett. *1965,* 4779.

[39] *J. A. Attaway* and *M. F. Oberbacher,* J. Food Sci. *33,* 287 (1968).

[40] *R. G. Buttery, R. M. Seifert, R. E. Lundin, D. G. Guadagni,* and *L. Ling,* Chem. and Ind. (London) *1969,* 490.

[41] *L. R. Mattick* and *D. B. Hand,* J. Agr. Food Chem. *17,* 15 (1969).

[42] *D. D. Bills* and *T. W. Keenan,* J. Agr. Food Chem. *16,* 643 (1968).

aroma, since its concentration is too low; the mixture of all the other flavoring substances just happens to have a smell similar to that of the one flavoring substance in question. This is true *e.g.* of α-furylmethanethiol in coffee. Characteristic flavoring substances of this type may, however, be suitable for artificial flavoring.

2. General Formation Pathways

The groups of flavoring substances found in foodstuffs are discussed in Section 3, where they are arranged according to the class of substance, and where their formation is also described when possible. First, however, we shall outline some pathways by which various types of flavoring substances may be formed. Botanically closely related species often contain similar flavoring substances [34,35].

The flavoring substances present in living material are biosynthesized by widely differing routes [2,32,33]. Microbial, enzymatic, oxidative, and thermal changes occur on injury or death, as well as during the storage and processing of the plants. The degradation of *fats* plays a special part in these changes. In particular, the autoxidation of unsaturated fatty acids by a free-radical reaction mechanism leads *via* hydroperoxides to saturated and unsaturated aldehydes, alcohols, ketones, and lower fatty acids, which act as flavoring substances [41,43]. Lipoxygenases and alcohol dehydrogenases cause the formation of aldehydes and alcohols from unsaturated fatty acids [44–46]. Heating also results in the formation (favored by metal catalysis) of aldehydes, ketones, lactones, and lower fatty acids from saturated fatty acids [47,48].

Carbohydrates are important precursors of flavoring substances in heated foodstuffs. Pyrolysis of carbohydrates alone (known as caramelization in the case of sugars) results in the formation of many flavoring substances above 300 °C, among which furan derivatives, ketones, and aromatic hydrocarbons are particularly prominent [49,50]. Carbohydrates react with *amino acids* even at much lower temperatures, and occasionally even at room temperature. This complex of reactions, which is known as the Maillard reaction, leads to the formation of brown pigments and of flavoring substances that are characteristic of heated (and frequently also of stored) foodstuffs, and particularly of cooking and roasting flavors. The principal pathways by which flavoring substances can be formed in the Maillard reaction are summarized in Figure 2 [51–58].

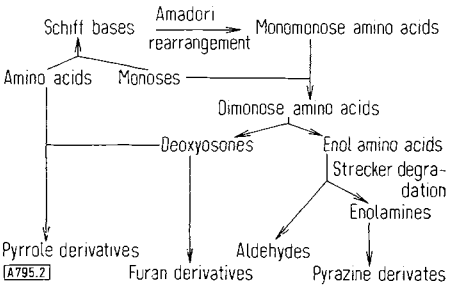


Figure 2. Principal pathways proposed for the formation of flavoring substances in the course of the Maillard reaction.

3. The Principal Flavoring Substances

3.1. Aliphatic and Alicyclic Compounds

Aliphatic hydrocarbons normally have very weak odors, and are therefore of practically no importance to the flavors of foodstuffs. They are present in small quantities in fruits [2] (*e.g.* ethylene and ethane in apples [59]). They are formed in rather greater quantities on heating of fats [60,61] and on storage of dehydrated potatoes [62]. The most important compounds in this class are probably the terpene hydrocarbons; these are the principal constituents of the essential oils of citrus fruits, where they are partly formed from linalool [63]. They are also present in large numbers in black currants [2]. The terpene hydrocarbons in roasted coffee are presumably formed by pyrolysis of the lipids (cafestol, kahweol, squalene) [64]. The terpene hydrocarbons present in hops (mainly myrcene, caryophyllene, and humulene) are not carried over into beer [65]. Nor do the terpenes

[43] *H. v. Pezold* in *J. Schormüller*: Handbuch der Lebensmittelchemie. Springer, Berlin 1969, Vol. IV, p. 289.

[44] *F. Drawert, W. Heimann, R. Emberger*, and *R. Tressl*, Liebigs Ann. Chem. *694*, 200 (1966).

[45] *W. Grosch*, Nahrung *13*, 393 (1969).

[46] *W. Grosch* and *D. Schwencke*, Lebensm.-Wiss. Technol. *2*, 109 (1969).

[47] *H. Thaler* and *H.-J. Kleinau*, Fette, Seifen, Anstrichmittel *70*, 465 (1968); *71*, 92, 261 (1969).

[48] *M. H. Brodnitz*, J. Agr. Food Chem. *16*, 994 (1968).

[49] *K. Heyns* and *M. Klier*, Carbohydr. Res. *6*, 436 (1968).

[50] *I. S. Fagerson*, J. Agr. Food Chem. *17*, 747 (1969).

[51] *H. Streuli* in *J. Solms* and *H. Neukom*: Aroma- und Geschmacksstoffe in Lebensmitteln. Forster, Zürich 1967, p. 119.

[52] *R. H. Egli* in *J. Solms* and *H. Neukom*: Aroma- und Geschmacksstoffe in Lebensmitteln. Forster, Zürich 1967, p. 253.

[53] *J. A. Newell, M. E. Mason*, and *R. S. Matlock*, J. Agr. Food Chem. *15*, 767 (1967).

[54] *S. J. Cole*, J. Food Sci. *32*, 245 (1967).

[55] *K. Heyns, G. Müller*, and *H. Paulsen*, Liebigs Ann. Chem. *703*, 202 (1967).

[56] *H. Kato* and *M. Fujimaki*, J. Food Sci. *33*, 445 (1968).

[57] *A. A. Spark*, J. Sci. Food Agr. *20*, 308 (1969).

[58] *P. E. Koehler, M. E. Mason*, and *J. A. Newell*, J. Agr. Food Chem. *17*, 393 (1969).

[59] *F. Drawert, W. Heimann, R. Emberger*, and *R. Tressl*, Phytochemistry *7*, 881 (1968).

[60] *S. Ota, N. Iwata, A. Mukai*, and *H. Enei*, Yukagaku *12*, 403 (1963); Chem. Abstr. *59*, 15863 (1963).

[61] *W. W. Nawar*, J. Agr. Food Chem. *17*, 18 (1969).

[62] *R. G. Buttery* and *R. Teranishi*, J. Agr. Food Chem. *9*, 245 (1961).

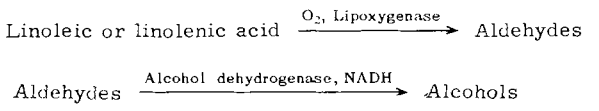
[63] *J. A. Attaway* and *B. S. Buslig*, Phytochemistry *8*, 1671 (1969).

[64] *F. Gautschi, M. Winter, Y. Flament, B. Willhalm*, and *M. Stoll*, J. Agr. Food Chem. *15*, 15 (1967).

[65] *R. G. Buttery, D. R. Black, M. J. Lewis*, and *L. Ling*, J. Food Sci. *32*, 414 (1967).

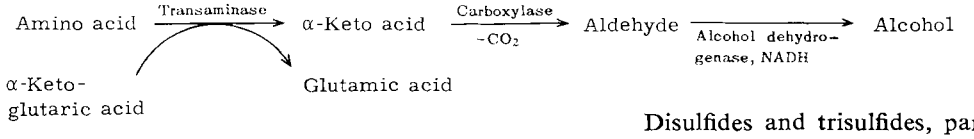
determine odor; they may, however, lead to a bad smell on storage of foodstuffs, as when the γ-terpinene in oil of lemon changes into *p*-cymene [12].

Alcohols are present in nearly all foodstuff flavors, but usually do not determine the odor, though they constitute the principal component from the point of view of quantity in many cases, *e.g.* in black tea [28] and in honey [66]. Exceptions are some unsaturated alcohols such as 1-octen-3-ol, whose mushroom-like odor occurs in oxidized lipids. It is also formed on swelling of raw soybeans in water [67]. Isoamyl alcohol is characteristic of the odor of over-ripe bananas [12]. Saturated and unsaturated alcohols are responsible for the odor of stored green peas (off-flavor). They are largely formed in accordance with Scheme 1 [45].



Scheme 1.

The higher alcohols known as "fusel oils" also determine the odor of alcoholic drinks. They are formed in various ways during the alcoholic fermentation [32], the Ehrlich mechanism predominating in the case of the branched-chain alcohols (Scheme 2).

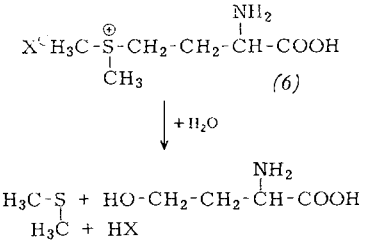


Scheme 2.

Since alcoholic fermentation occurs during the preparation of yeast dough or leaven, alcohols of this type also occur in bread. Straight-chain alcohols are probably largely formed in plants by the acyl metabolism [33].

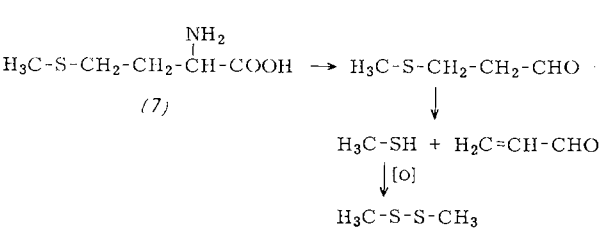
Aliphatic *ethers* occur only very rarely in foodstuff flavors, *e.g.* in apples and citrus fruits [2]. Compounds containing *epoxide* groups are occasionally found, mainly in citrus fruits [2] and in dehydrated carrots [68]. Acetals have been detected in the flavor concentrates of several fruits [2], in wine [69], and in Bourbon whisky [70]. It is possible that these were formed only on storage.

Sulfur compounds often have particularly low threshold values, and so make a considerable contribution to the flavor even in low concentrations. Hydrogen sulfide, methanethiol, dimethyl sulfide, and dimethyl disulfide are widely found in quantities of about 1 to 100 μg/kg. They are formed, often together with higher homologs, particularly on heating *e.g.* of meat, eggs, milk [52], tomatoes [71], potatoes [72], and strawberries [73]. Whereas the hydrogen sulfide is thought to be formed mainly from SH groups of (free or protein-bound) amino acids [74], methionine is a precursor of dimethyl sulfide. This compound is formed when methionine and pectin [42] are heated, but mostly from the *S*-methylsulfonium salt *(6)* of methionine, even in the cold, in milk, tea, tomatoes, sweet corn, cabbage, and asparagus [42, 74].



Too much dimethyl sulfide is responsible for the "feed flavor" of butter. Methanethiol and dimethyl disulfide can also be formed from methionine *(7)* by the action of light in the presence of riboflavin or by Strecker degradation [74].

Disulfides and trisulfides, particularly the propenyl derivatives, are characteristic of the aroma of cooked onions [75, 76]. The sulfenic and sulfinic acids and the isothiocyanates (mustard oils) that determine the flavor of raw onions, garlic, leeks, some varieties of



cabbage, radishes, mustard, and cress will merely be mentioned in passing, since numerous publications dealing with these flavoring substances have already appeared (cf. [77, 78]). Less common sulfur compounds

[66] *E. Cremer* and *M. Riedmann*, Z. Naturforsch. *19b*, 76 (1964).

[67] *A. F. Badenhop* and *W. F. Wilkens*, J. Amer. Oil Chemists' Soc. *46*, 179 (1969).

[68] *J. E. Ayers, M. J. Fishwick, D. G. Land*, and *T. Swain*, Nature *203*, 81 (1964).

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[70] *J. H. Kahn, E. G. La Roe*, and *H. A. Conner*, J. Food Sci. *33*, 395 (1968).

[71] *P. E. Nelson* and *J. E. Hoff*, J. Food Sci. *34*, 53 (1969).

[72] *M. R. Gumbmann* and *H. K. Burr*, J. Agr. Food Chem. *12*, 404 (1964).

[73] *J. L. Sloan, D. D. Bills*, and *L. M. Libbey*, J. Agr. Food Chem. *17*, 1370 (1969).

[74] *H. van Duin* in *J. Solms* and *H. Neukom*: Aroma- und Geschmacksstoffe in Lebensmitteln. Forster, Zürich 1967, p. 91.

[75] *R. A. Bernhard*, J. Food Sci. *33*, 298 (1968).

[76] *M. H. Brodnitz, C. L. Pollock*, and *P. P. Vallon*, J. Agr. Food Chem. *17*, 760 (1969).

[77] *A. Klemer* in *J. Schormüller*: Handbuch der Lebensmittelchemie. Springer, Berlin 1965, Vol. I, p. 542.

[78] *A. I. Virtanen*, Angew. Chem. *74*, 374 (1962); Angew. Chem. internat. Edit. *1*, 299 (1962).

that deserve mention are 2-mercaptoethanol in butter, the methyl and ethyl esters of β-methylthiopropionic acid in pineapple, and lenthionine *(8)*, the odorous principle of the eastern Asian edible mushroom *Lentinus edodes* [79].



(8)

Volatile *amines* do not occur very widely in foodstuff flavors, but they usually have a very strong smell. Trimethylamine is found, together with numerous other amines, as a typical odorous substance in fish, in which it is formed enzymatically from trimethylamine oxide. It is also responsible for the fishy taste of condensed milk, where it is probably formed from lecithin. Nine volatile amines were detected in wine [80], nine in cocoa [15], five in raw potatoes [81], and three in apples, where they are probably formed from the aldehydes by transamination [82]. Ammonia is present in small quantities *e.g.* in cooked meat [52]. It is formed in fish from amino acids by the Stickland reaction.

Aldehydes are present in practically all foodstuff flavors, and often determine the flavor because of their strong smell, as *e.g.* in cucumbers [83] and in black tea together with theaspirone and dihydroactinidiolide *(9)* [27,28]. The most widespread as far as quantity is concerned is acetaldehyde [34], which is the principal flavoring substance of yoghurt [84], and is formed (in other milk products too) from pyruvate [85], but has a relatively weak odor. The *n*-alkanals, *n*-2-alkenals, and *n*-2,4-alkadienals containing more than two carbon atoms are more important. They are produced by breakdown of fats or amino acids, Maillard reaction, caramelization, or photosensitized decomposition ("sunlight flavor" [86]) of foodstuff components. They are formed in fruits and leaves only after the cells have been damaged [33], and can act as phytoncides (substances that protect higher plants against microorganisms) [87]. An exception is found in the citrus fruits, in which they are probably of native occurrence. The aldehydes in this case are higher members (octanal and decanal) than in other fruits [2], in which 2-methylbutanal and 2-hexenal are particularly common. The oily smell of fish is due to *n*-alkanals and *n*-alkenals containing 6 and 7 C atoms, and the rancid tallowy smell to those containing 8–10 C atoms.

Ketones also occur very widely (particularly acetone), but they are mostly present in smaller quantities than the aldehydes. They are also less important than the latter in determining odor. Exceptions are biacetyl (in butter and many other foodstuffs), 1-octen-3-one, which is responsible for the metallic taste of butter, and some methyl ketones, which make a substantial contribution to the flavor of blue cheese [88] and coconut [89], and to the taste of boiled milk [90]. These methyl ketones are formed in cheese by the action of molds on fatty acids containing one C atom more [91]. Biacetyl is formed in milk products and in beer from acetyllactic acid, which may be formed from lactose or citric acid *via* pyruvic acid [74,92]. Biacetyl is also formed on pyrolysis of sugars [51]. The formation of ketones is observed on oxidation of fats, in the Maillard reaction, and on caramelization [50]. Interesting ketones occurring in special cases include 2-hydroxy-2,6,6-trimethylcyclohexan-1-one (in tea and tomatoes [24,30]), α- and β-ionones (in tea and raspberries [2,24]), and several hydroxycyclopentenones, which occur in roasted coffee and are also formed in alkaline fructose solutions on heating [93].

Carboxylic acids are present in most foodstuff flavors. They determine the odor in many cheeses and in browned butter, and are responsible in particular for the rancid odor of foodstuffs [94]. They are mainly *n*-aliphatic acids formed by biosynthesis [95] or fat breakdown. β-Methylbutyric acid constitutes 50% of the flavor of cranberries [96].

A few *nitriles* occur in black tea as well as in coffee and cocoa. *Hydrogen cyanide* contributes to the flavor of some foodstuffs (bitter almonds, kirsch). It is formed on enzymatic hydrolysis of the cyanogenic glycosides and also occurs in the flesh of cherries and peaches [2], and in particular in quantities of up to 100 mg/kg in apricots, cherries, and plums canned with the stones [12].

Esters of carboxylic acids are present in particularly large quantities in fruit flavors, in which, together with alcohols and aldehydes, they determine the odor [12,23]. They are probably formed in the acyl

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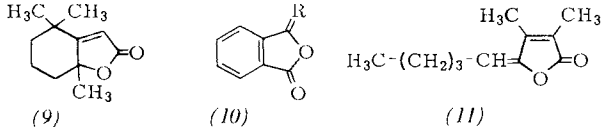
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metabolism of the plants. Particularly common representatives are acetates and butyrates of alcohols that also occur free in the fruits. Several esters of carboxylic acids also occur in milk, coffee, bread, beer, and whisky [34,70,97]. Cherries, raspberries, grapefruit, and pineapple are relatively poor in esters [2].

Like the esters, the *lactones* also play an important part in foodstuff flavors, though they probably do not occur so widely. Simple γ- and δ-lactones are found in several fruits [98–100], in coconuts, in roasted peanuts [101], and in heated fats [102,103]. They are largely responsible for the flavor of dried milk, and they also contribute to the flavor of butter. They are formed in fats from γ- and δ-hydroxy fatty acids, which probably result *in vivo* from the oxidation of saturated fatty acids. The hydroxy fatty acids are liberated from the fats on heating, and change spontaneously into lactones [61,103]. The possibility of formation from ascorbic acid has been discussed [104]. Special lactones, apart from coumarin, include dihydroactinidiolide *(9)*, which is found in tobacco [105], black tea [27], tomatoes [30], and crispbread [31], and the phthalides, which, together with dihydrophthalides, determine the flavor of celery [106]. Bovolide *(11)*, which is present in butter, and probably comes from the green feed, also has a celery-like odor [74].



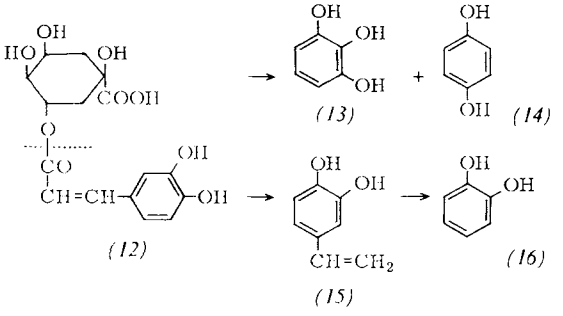
(9) *(10)* *(11)*

R = =CH-CH(CH$_3$)$_2$

R = =CH-CH$_2$-CH(CH$_3$)$_2$

3.2. Aromatic and Heterocyclic Compounds

Aromatic compounds occur in many foodstuff flavors. The aromatic hydrocarbons occur widely, but never in large quantities [29,107,108]. They could be formed from ethylene by biosynthesis [95], as well as from carotenoids, and possibly also from fats, on heating [107]. Among the alcohols, benzyl alcohol and 2-phenylethanol are worth mentioning. The latter is formed in alcoholic fermentation from phenylalanine. Phenols play a decisive part in many flavors, *e.g.* those of coffee [109] and of tobacco smoke. They are also abundant in the flavor of crispbread [31]. Pyrogallol *(13)*, hydroquinone *(14)*, *p*-vinylpyrocatechol *(15)*, and pyrocatechol *(16)* are formed when coffee is roasted, probably from chlorogenic acid *(12)* [51], while guaiacol and similar compounds are formed from esters of ferulic acid [110].



(13) *(14)* *(12)* *(15)* *(16)*

Among the aldehydes, benzaldehyde occurs particularly widely, mainly in fruits [98]. Vanillin is found in coffee, in alcoholic distillates that have been stored in wooden containers [111], and in heated milk, which also contains acetophenone [90]. The methyl and ethyl esters of anthranilic acid and *n*-butyl phthalate occur in many types of grapes [2], and the first of these esters is also present in citrus oils and citrus honeys [112]. Nitriles include benzonitrile in cocoa [17] and UHT milk (sterilized by injection of steam at 150 °C) [90], as well as phenylacetonitrile in tomatoes [30] and black tea [26]. Coumarin and its derivatives occur in raspberries and citrus fruits [2]. Particularly large numbers of aromatic compounds, mainly benzoic acid and its esters, are present in the flavors of cranberries and bilberries [35,96,113]. Aromatic alcohols and esters are essential to the type odor of natural honeys.

Furan derivatives are formed in the Maillard reaction and from carbohydrates or ascorbic acid on caramelization [104], and are therefore very often present in heated foods, *e.g.* in crispbread [31] and dried grapes [100]. The furan derivatives in roasted coffee could also be formed in part from the terpenes resulting from the breakdown of the lipids [64]. Furfural, hydroxymethylfurfural, and furfuryl alcohol are particularly common, though these usually

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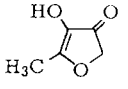
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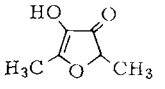
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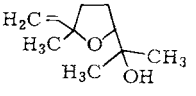
contribute little to the flavor. They are occasionally regarded as responsible for "cooked flavor" [114]. The furanone derivatives *(17)* and *(18)* are essential



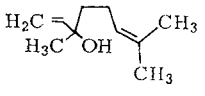
(17)



(18)



(19)



(20)

to the odor of beef broth [115]. 2-Pentylfuran is responsible for the reversion flavor of fats [116]. Pineapple contains 2,5-dimethyl-4-hydroxy-3(2*H*)-furanone *(18)* [2] and *trans*-tetrahydro-α,α,5-trimethyl-5-vinylfurfuryl alcohol *(19)* [99]. *(19)* at least is probably formed from linalool *(20)*.

Thiophene, pyrrole, and *pyridine derivatives* are only occasionally found in foodstuffs, mostly in roasted coffee. It seems possible that these are formed in the Maillard reaction [100] and that thiophene derivatives are also formed from thiamine [117]. *N*-Methylpyrrole and pyridine are formed from trigonelline on roasting of coffee [51]. Pyridine plays an important part in the flavor of over-roasted coffee. However, the *pyrazine derivatives*, which occur in roasting flavors (coffee, cocoa, peanuts, potato chips [118], crispbread [31]) are generally more important. These are mostly made up from several compounds containing alkyl groups. They are formed in the Maillard reaction. The C atoms of these compounds are derived from the sugars, and the N atoms from the amino acids [58]. Derivatives of dioxolane [29], oxolanone [31], thiazole [30], oxazoline and trithiolane [119], and indole occur only very occasionally. Mention should be made of the γ-pyrone derivative maltol, which is found in malt coffee, pure coffee, and other foodstuffs [51], and is also used in concentrations of 0.005–0.025% as an artificial flavor reinforcer in sweet foods.

4. Fixation of the Flavoring Substances

Flavoring substances can be lost from the foodstuffs by oxidation, polymerization, reactions with other components of the food, and evaporation. Loss by evaporation at least can be retarded or prevented by suitable fixation of the flavoring substances. The term "fixation" is used here to denote a state in which the volatility of the flavoring substance is reduced, as well as a process by which the volatility is reduced. Only reversible fixation is of interest to the technologist, since the flavoring substance is lost in any case if the fixation is irreversible even during consumption. Good fixation of flavoring substances in foodstuffs is important during storage and prolonged transportation. This affects dehydrated products in particular, since flavoring substances, which can often no longer be fixed to a sufficient degree in the dried product, escape during production. This is so *e.g.* in the case of coffee extracts, whereas fixation of the flavor is very good in roasted coffee [120].

The fixation of the flavoring substances depends on the structure of the foodstuffs and on the substances present. Intact cells bind flavoring substances better than homogenized materials. The permeability to flavoring substances can be reduced by intercalation of suberin (a fatty substance found in cork cell walls) or by deposition of cutin (a polymerization product of hydroxylated fatty acids found on the surface of plant epidermis cells). Living cells have a lower permeability than dead cells for many substances, *e.g.* methanol [121].

The fixation of flavoring substances in cell systems has not been so thoroughly investigated as the semipermeable membrane that is formed on the surface of drying droplets of coffee extract or maltodextrin solution, which allows water to pass through it, but not flavoring substances [122]. It probably consists of macromolecular carbohydrates, and binds the flavoring substance after the manner of nonstoichiometric inclusion compounds. Inclusion compounds of this type are formed on drying of polysaccharides containing water and flavoring substances. They were first investigated for cellulose [123] and starch [124], but are also formed with dextrin, pectin, agar, and methylcellulose, and with foodstuffs that contain these substances [125]. Only very small molecules of flavoring substances, which can form particularly strong hydrogen bonds to the solids, such as methanol, ethanol, formic acid, and aliphatic amines, cannot be bound in this way. Since the other flavoring substances are bound indiscriminately, and since the fixation is due only to steric "imprisonment" in the ideal case, and not to principal valences or molecular forces (though the latter are involved to some extent in practice), the flavors are thus fixed gently and sub-

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stantially completely. They can readily be liberated again by addition of water.

If no inclusion occurs, the greater part of the flavoring substances is bound to the foodstuff components by physical sorption (dissolution or adsorption). Liquid phases (water, fat) have greater sorption capacities than solid phases. Fats in particular are very good binders for food flavors [126, 127], since most flavoring substances are lipophilic. In emulsions, therefore, most of the flavoring matter should be situated in the lipid phase. Model experiments have been carried out with liquid paraffin/aqueous sodium sulfate solution [128].

The fixation of flavoring substances in foodstuffs containing water and having low fat contents is not only determined by the partition coefficients of the flavoring substances between air and water. Dissolved sugars and salts normally increase the vapor pressures of the flavoring substances, while casein decreases them [129, 130]. Table 6 shows the changes in the concentrations of flavoring substances in the vapor space over aqueous solutions on addition of 1 % of solid (dissolved or suspended).

Table 6. Changes in the concentrations of flavoring substances in the vapor space over their aqueous solutions (concentration given) on addition of 1 % of solid. Values as percentage of the initial value; negative values indicate a decrease in concentration, and positive values an increase. The values were determined by gas chromatography (those for the last four flavoring substances being determined alongside each other).

Additive	Flavoring substance				
	Acetone 0.01 mole/l	Ethanol 0.1 mole/l	Acetaldehyde 9×10^{-3} mole/l	Ethyl acetate 2.5×10^{-3} mole/l	Diethyl ether 0.9×10^{-3} mole/l
Casein	− 7.9	− 4.6	− 2.1	+ 4.0	−1.9
Dextrin	− 4.0	− 4.4	− 8.4	0	0
Fructose	− 0.5	+ 5.3	− 3.1	+ 4.9	+4.1
Gelatin	− 5.5	− 3.6	− 9.5	− 1.0	0
Methyl-cellulose	−10.0	−19.1	− 8.4	− 0.5	0
Ovalbumin	− 5.0	+ 5.3	−14.6	+ 1.0	+2.0
Pectin	−10.0	−23.6	−11.6	−10.0	−1.4
Saccharose	− 2.1	0	− 6.3	+ 1.5	+2.0
Sorbitol	− 6.2	− 5.3	−12.5	+ 1.0	−2.0
Starch	− 2.1	0	−11.5	− 1.5	+2.0

The sorption capacity of the solid components of the foodstuff, which depends on the available surface area, is usually small for crystalline low molecular weight substances and greater for macromolecular substances. Amines are particularly well sorbed on carbohydrates (Maillard reaction occasionally occurs), and alcohols, ketones, and aldehydes are also bound. Proteins bind alcohols particularly well, and then amines, aldehydes, and ketones. Carboxylic acids (except formic acid and acetic acid) and their esters are much less readily sorbed by both groups of substances, and thiols, ethers, and hydrocarbons less readily still [125]. If individual flavoring substances are allowed to act on dry foodstuff components, heats of sorption of the same order of magnitude as the heats of vaporization of the flavoring substances are normally found [131], while the IR absorption bands are only slightly displaced in relation to those in the vapor state. Both of these facts point to physical fixation. Chlorophyll can form chelates with flavoring substances [132, 133].

In special cases, the flavoring substances are bound by principal valence forces. This bonding naturally occurs during their formation; one then speaks of flavor precursors. However, the final flavoring substances may also form reversible principal valence bonds with nonvolatile food components. Thus salt formation has been detected between nonvolatile acids and volatile amines and ammonia, as well as between nonvolatile basic food components (*e.g.* proteins) and volatile acids. Acids and alcohols may be bound as esters, but this is only rarely observed in enzyme-free, solid foodstuffs [125].

The most reactive of the important flavoring substances are the aldehydes. These are particularly readily bound to NH_2 and SH groups. These bonds, particularly in the case of the higher homologs, are often reversible, at least partly on heating in water. Schiff bases are probably formed with proteins and amino acids, dialkylideneureas with urea, and 2-alkylthiazolidine-4-carboxylic acids with cysteine or cysteinium salts [134, 135]. The formation of hemiacetals, acetals, and ketals, which occurs readily with the pure substances, has not yet been observed under conditions approximating to those in foodstuffs. Dithiohemiacetals and monothiohemiacetals have so far been detected only in coffee flavor [136].

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5. Outlook

Research in the field of foodstuff flavoring substances is proceeding in three directions.

Most of the articles being published at present deal with the *analysis of flavors*. The main emphasis is on the qualitative composition, and increasing interest is being shown in the trace components. Quantitative analyses of the individual flavoring substances are also being carried out with ever-increasing frequency. These are essential to the application of the results *e.g.* in the artificial preparation of flavors. The determination of the odor contributions of the various flavoring substances and the study of synergistic interactions will probably gain increasing importance in the future.

A growing number of articles deal with the *formation of the flavoring substances*. The process of inactivation of enzymes (*e.g.* by methanol [33]) in living systems during the analysis has led to important progress in recent years. Further progress is to be expected from the elucidation of the complicated processes involved in the oxidation of fats and in the Maillard reaction. Detailed knowledge about the formation of flavoring substances should enable us to develop these, when necessary, from nonvolatile precursors in dried foodstuffs that lack flavor. This is possible (by the action of enzymes) only in isolated cases at present [88].

The study of the *fixation and alteration of flavoring substances* has a direct bearing on technology. There are two main objects. Firstly, the flavoring substances of fresh foodstuffs should be retained during processing and storage, and secondly, attempts are being made to flavor an "artificial" foodstuff so that it smells and tastes like a known food. This is essential if it is to be consumed in large quantities, particularly in developing countries. The protein concentrates obtained from fish and from petroleum, and the foodstuffs from algae in particular, present a problem of worldwide importance in this respect.

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Principles and Latest Developments in the Field of Metallic and Nonmetallic Hard Materials[**]

By Richard Kieffer and Peter Ettmayer [*]

A survey of some fundamental aspects of the theory of hardness is followed by a discussion of recent developments in the field of sintered hard metal alloys. For example, good results have been obtained by the addition of hafnium carbide to hard metals. Niobium carbide can sometimes replace the more expensive tantalum carbide; vanadium carbide can be used to inhibit grain growth, especially in the case of ultrafine carbides. A brief outline is given of the results of investigations on ternary and quaternary systems with the components TiC, HfC, NbC, TaC, and WC. The utilization of sintered nitride and carbonitride hard metals in the field of machining appears feasible. Recently developed high-pressure/high-temperature autoclaves permit work on nitride systems under a high nitrogen pressure. The authors comment on the latest work in the field of nonmetallic hard materials and on diamond synthesis.

1. Theory of Hardness

Even today the physical definition of hardness and its precise and reproducible measurement continue to pose serious problems since, being a mechanical quantity, it is to a certain extent dependent on the method of measurement. Nevertheless, numerous attempts have been made to relate hardness to physically measurable quantities, and above all to improve its predictability. Indubitably, hardness is a function of interatomic forces which it is at present impossible to measure directly. The type of structure and bonding must, of course, play an important part; more densely packed structures are harder for the same atomic distance than less highly coordinated lattices. For the same bonding energy, covalent bonding would give a substance greater hardness than predominantly metallic or ionic bonding. For these reasons hardness can be related to macroscopic physical data only in the case of isotypically crystallizing materials with the same type of bonding.

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Starting from the premise that hardness is above all characterized by the resistance offered by structural components to mutual displacement, *Nowotny*[1] found the following relation for the hardness H:

$$H = C\nu = K\sqrt{(T_s - T)}V^{2/3}$$

where ν represents the oscillation frequency from the Lindemann formula, C and K are proportionality factors, T_s is the absolute melting temperature (°K), T the test temperature (°K), M the molecular weight, and V the molar volume. This formula, which provides excellent hardness indices especially in the case of pure metals, also gives good parallelism with the hardness series for isotypic, identically bonded monocarbides (Table 1). The tendency for the hardness to decrease in the direction TiC → HfC and VC → TaC is quite striking.

Table 1. Melting point, hardness, and frequency factors of carbides.

Carbide	Melting point (°K)	Microhardness (kg/mm²)	Frequency factor (according to *H. Nowotny* [1])
TiC	3400	3200	5.6
ZrC	3800	2600	4.2
HfC	4300	2200 [a]	3.4
VC	3100	2800	5.3
NbC	3730	2400	3.8
TaC	4150	1800 [b]	3.4

[a] The values vary between 1800 and 2700 kg/mm², and according to recent measurements between 2000 and 2400 kg/mm².
[b] 2000 to 2200 kg/mm² for slightly substoichiometric TaC.

Samsonov[2] postulates that hardness is essentially dependent on the statistical weight of the stable electron configuration of the metal and nonmetal atoms and on the number of electrons that contribute to the bond. Since the exact measurement of electron states in solids still involves considerable experimental problems, *Samsonov*'s theory at best indicates the direction of the hardness curve in structurally similar materials; the predictability of the hardness of new hard materials remains very poor.

It would be most interesting to develop already existing and highly promising formulas for the calculation of hardness, and to investigate whether relationships may not be found between hardness and free energy of formation, the melting points and the heats of fusion of the individual components, the modulus of elasticity, and so on.

2. Auxiliary Metal Bath Technique

From the point of view of the usefulness of hard materials in industry, hardness is for many applications, and especially the machining of metals, a necessary but by no means sufficient property. It must be accompanied by certain strength characteristics which enable a tool to absorb bending and torsional forces so as to enable it to withstand impact stresses. The art of making cemented carbides thus consists in combining the greatest possible hardness with optimal toughness. To some extent these properties are in mutual opposition, although there are effects which cause both properties to improve or to deteriorate simultaneously. The detrimental effects include the porosity of the cemented carbides, which may be due, for example, to nonoptimal sintering conditions and which can therefore be prevented by improving the sintering operation. The second cause of porosity is the content of oxygen and nitrogen in the sintered particles themselves. At the high sintering temperatures these impurities are liberated as elemental nitrogen or as carbon monoxide and give rise to microporosity. A typical example of microporosity in a cemented carbide is illustrated in Fig. 1; the

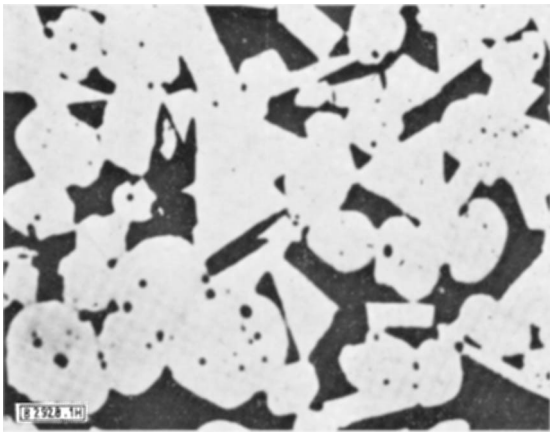


Fig. 1. Polished section of a cemented carbide of the type WC/TiC/Co sintered for a prolonged period. Micropores in the WC/TiC solid solution × 1000.

microcavities are located inside the carbide crystallites. To manufacture high-grade cemented carbides possessing good strength properties it is therefore important to use materials having low nitrogen and oxygen contents. The content of these undesirable impurities can best be determined by hot extraction analysis[3]. To improve degasification it is possible to select an auxiliary metal bath, generally iron, cobalt, nickel, or an alloy of these metals, which possess a certain dissolving capacity for the transition metal carbides and accelerate the liberation of gases. On cooling the carbides crystallize out of the metal melt and are highly pure as regards the oxygen, nitrogen, and hydrogen contents. We have developed this analytical technique into a preparative one, with the aid of which we have been able to prepare for investigation a series of carbides in high vacuum[4–6].

[1] *H. Nowotny* in *R. Kieffer* and *F. Benesovsky*: Hartstoffe. Springer-Verlag, Wien 1963, p. 13.

[2] *G. V. Samsonov* and *V. V. Stasovskaya*, Poroškovaja Metallurg. *12*, No. 12, p. 95/99 (1966); Soviet Powder Metallurgy and Metal Ceramics *12*, No. 12, p. 48 (1966).

[3] *E. Lassner*, 5th Plansee Seminar 1964, in *F. Benesovsky*: Metalle für die Raumfahrt. Springer-Verlag, Wien 1965.

[4] *R. Kieffer*, *H. Rassaerts*, and *O. Schob*, Mh. Chem. *96*, 686 (1965).

[5] *R. Kieffer* and *H. Rassaerts*, Int. J. Powder Metallurgy *2*, No. 2, p. 15/21 (1966).

[6] *R. Kieffer*, J. Inst. Metals *97*, 164 (1969).

Table 2. Comparative analyses of some carbides.

a) Technical carbides produced by reacting the components in the solid state.

Carbide	C_{total} (%)	C_{free} (%)	O_2 (ppm)	N_2 (ppm)	Remarks
WC	6.12	0.04	800	—	
TiC	19.70	0.40	2000	800	
TaC	6.17	0.04	250	80	Nb < 500 ppm
NbC	11.10	0.056	800	400	Ta < 500 ppm

b) Carbides produced with an auxiliary metal bath.

Carbide	C_{total} (%)	C_{free} (%)	O_2 (ppm)	N_2 (ppm)	Remarks
WC	6.13	0.03	50	—	
TiC	20.0	0.3–0.50	300–500	80–120	
TaC	6.19	0.05	40	<10	Nb < 500 ppm
NbC	11.60	0.30	100	<10	Ta < 500 ppm

Table 2 shows the oxygen and nitrogen contents of conventional carbides produced by reaction in the solid state in comparison with those obtained by the auxiliary metal bath method. The use of a vacuum with the auxiliary metal bath purification is desirable although not absolutely essential, providing care is taken to ensure a reasonably clean, oxygen- and nitrogen-free protective gas atmosphere. In the U.S.A. this auxiliary metal bath technique at normal pressure is known as the "McKenna Menstruum process". The carbides of the transition metals can be isolated by acid treatment of the auxiliary metal. Coprecipitated graphite particles can be removed by decantation or floated away from the carbides. The carbides frequently occur in the form of beautiful crystals

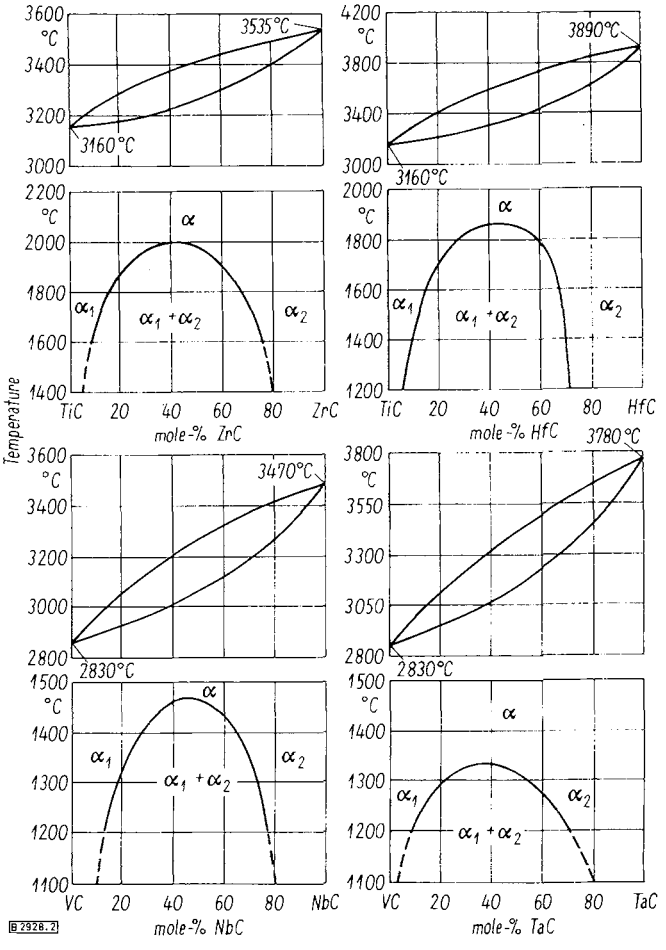


Fig. 2. Miscibility gaps in the TiC/ZrC, TiC/HfC, VC_{1-x}/NbC, and VC_{1-x}/TaC systems.

Table 3. Analyses of carbides from the auxiliary metal baths.

Auxiliary metal	Weight ratio transition metal: auxiliary metal	Temperature (°C)	Heating duration (h)	C content (wt-%) total	free	bound	Phases and lattice parameters	Remarks
Co	Ti 1:5	1800	3	20.6	1.1	19.5	TiC 4.32_7 [c]	
	Ti 1:1	2000 [b]	1	19.9	0.9	19.6	TiC 4.32_3	
	Zr 1:4	1800	3	9.3	0.7	8.6	Zr(C,N,O) 4.70_1 4.68_7	2 cubic phases
	Zr 1:6	2000 [b]	0.5	11.2	—	11.2	ZrC 4.70_1 [d]	
	Hf 1:3 [a]	2000 [b]	0.5	6.60	0.05	6.55	HfC 4.63_1 [e]	
	V 1:2	2000 [b]	0.5	18.1	0.4	17.7	VC_{1-x} 4.16_8 [f]	
	Ta 1:2	1800	3	6.25	0.12	6.13	TaC 4.45_5	
	Nb 1:2	1800	3	11.6	0.30	11.3	NbC 4.47_1	
	Cr 1:1	1800	3	9.4	0.75	8.65	Cr_7C_3 [g]	11.5% Co
	Mo 2:3	1800	3	6.17	0.32	5.85	Mo_2C [g]	
	W 2:3	1800	3	6.15	0.05	6.10	WC [g]	
Fe	Ti 1:4	1800	2	20.0	0.80	19.2	TiC (4.32_6)	
	Zr 1:3	2000	0.5	11.5	0.30	11.2	ZrC (4.70_1)	
	V 1:2	2000	0.5	18.1	0.45	17.65	VC (4.16_8)	
	Ta 2:3	1800	2	6.3	0.25	6.05	TaC (4.45_5)	
	Cr 2:3	1800	2	8.6	0.45	8.15	$(Cr, Fe)_7C_3$ [g]	
	W 2:3	1800	2	6.15	0.08	6.07	WC [g]	
70% Fe 30% Ni	Ti 1:3	2000	0.5	19.8	0.06	19.2	TiC (4.32_5)	
	Zr 1:3	2000	0.5	11.8	0.7	11.1	ZrC (4.70_1)	
	V 1:3	2000	0.5	18.4	0.60	17.8	VC (4.16_9)	
	Nb 1:1	1800	2	11.3	0.10	11.2	NbC (4.47_1)	
	Ta 1:1	1800	2	6.16	0.08	6.08	TaC (4.45_5)	
	W 1:1	1800	2	6.2	0.10	6.10	WC [g]	
Ni	Ti 1:3	1800	2	20.4	1.1	19.3	TiC (4.32_5)	
	W 1:1	1800	2	6.15	0.05	6.10	WC [g]	

[a] Contains 2.2% Zr. [b] Heating curve: 5 min to 1500 °C, 15 min to 2000 °C.
[c] Lit. value for a (edge length of the cubic crystal) = 4.3316 Å, theoretical C content 20.05 wt-%.
[d] Lit value for a = 4.69764 Å, theoretical C content 11.64 wt-%.
[e] Lit. value for a = 4.628 Å, theoretical C content 6.30 wt-%.
[f] Lit. value for a = 4.182 Å, theoretical C content 19.08 wt-%. [g] Not determined.

(*e.g.* TaC as golden yellow cubes or NbC as violet cubes), they have a high content of bound carbon, and with the exception of the chromium carbides they have a low content of the metal used for extraction (cf. Table 3).

The principle of producing carbides by the metal bath process can also be extended to carbide solid solutions [7]. The metallic solvent permits the minimum preparation temperature to be reduced to about 1400 °C. It was unexpectedly found that in the pseudobinary systems TiC/ZrC, TiC/HfC, VC_{1-x}/NbC, and VC_{1-x}/TaC miscibility gaps occur, the one in the TiC/HfC system being of particular interest from the point of view of cemented carbide technology. The form of the miscibility gaps is shown in Fig. 2.

It will be seen that the miscibility gaps are disposed somewhat asymetrically and are displaced toward the lower melting components (with the smaller molar volumes) [8].

3. Carbide Systems

The modern tendency to use multicomponent materials, a tendency that has spread to the cemented carbide sector, prompted us to undertake a more detailed investigation of some ternary and quaternary systems comprising carbides. The purpose of the investigation of the TiC/TaC/NbC/WC system (Fig. 3) was to study the solubility relationships of

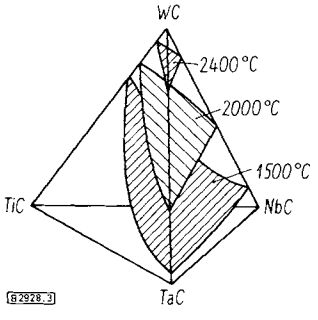


Fig. 3. The TiC/TaC/NbC/WC system (coordinates in wt-%).

the isotypic carbides TiC/NbC and TaC as well as their ability to dissolve WC [9]. TiC is known to be a good solvent for WC, whereas TaC possesses only a poor dissolving capacity for this carbide and also reduces its solubility in a solid solution of TiC/TaC. A partial replacement of TaC by NbC in TiC/TaC/WC compositions would be economically attractive, although the addition of NbC is said to make the material more brittle. The authors' investigations have shown, however, that in materials of the type TiC/TaC/WC with 10% Co one-third, and in many cases as much as one-half, of the TaC component can be replaced by NbC without any significant deterioration of the strength properties in comparison with materials containing no NbC [9] (cf. Fig. 4).

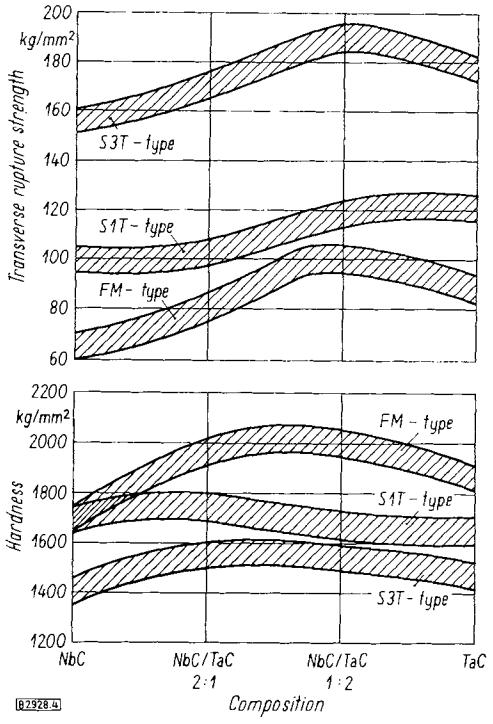


Fig. 4. Transverse rupture strength and hardness of cemented carbides of the type WC/TiC/TaC/Co with partial replacement of TaC by NbC. See Table 4 for type designations.

Hafnium carbide (HfC) is most promising as regards application in the cemented carbide industry. Obviously, like TaC [10], it is capable of bringing about a decisive improvement in the properties of the cemented carbides. Moreover, the initially high cost of HfC has ceased to be an obstacle now that HfC/NbC and

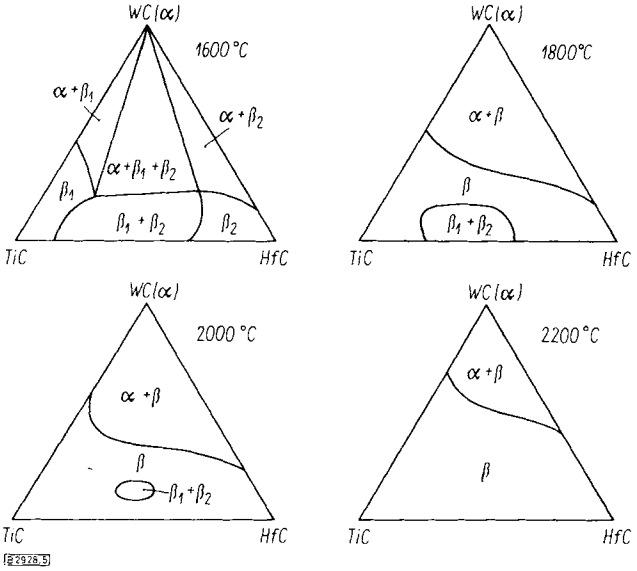


Fig. 5. Sections through the TiC/HfC/WC system at 1600, 1800, 2000, and 2200 °C (coordinates in mole-%).

[7] *G. Jangg, R. Kieffer*, and *L. Usner*, J. Less-Common Metals [Amsterdam] *14*, 269 (1968).

[8] *R. Kieffer, H. Novotny, A. Neckel, P. Ettmayer*, and *L. Usner*, Mh. Chem. *99*, 1020 (1968).

[9] *R. Kieffer, G. Trabesinger*, and *N. Reiter*, Planseeber. Pulvermetallurgie *17*, 25 (1969).

[10] *R. Kieffer* and *F. Benesovsky*: Hartmetalle. Springer-Verlag, Wien 1965.

HfC/TaC solid solutions are available at the same price as TaC. It appears that the addition of HfC to TiC/TaC/WC can impart to the material not only an appreciable increase in hardness but also a notable abrasion and cratering resistance.

Studies on a series of systems with HfC as one of the components were carried out as a fundamental step in the development of cemented carbides. These investigations concerned the ternary systems TiC/HfC/WC (Fig. 5), HfC/NbC/WC (Fig. 6), and TiC/HfC/NbC (Fig. 7), as well as the quaternary system TiC/HfC/NbC/WC (Fig. 8)[9,11]. The TiC/HfC/WC system (Fig. 5) shows the interesting phenomenon that the miscibility gap existing in the TiC/HfC boundary system moves away from the boundary at about 2000 °C and occurs as an island of immiscibility surrounded on all sides by the single-phase region. At the normal sintering temperatures for cemented carbides of 1450 to 1550 °C one observes a three-phase region which contains HfC-rich ternary solid solution and WC in addition to TiC-rich ternary solid solution. It may be expected that cemented carbides with this carbide compositions will exhibit particularly interesting properties to which it would be well worthwhile devoting further attention. In the quaternary system TiC/HfC/NbC/WC (Fig. 8) the picture is not substantially changed. Once again in the case of this system a three-phase region with a TiC-rich solid solution, a HfC-rich solid solution, and WC is found at not too high NbC contents[11].

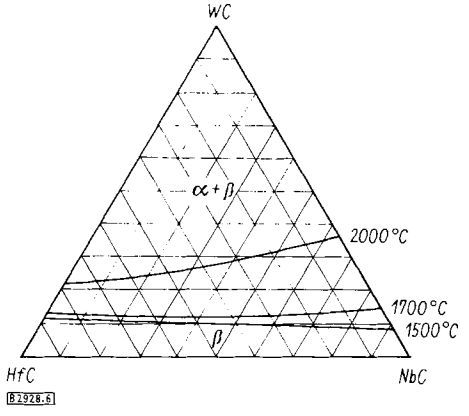


Fig. 6. The HfC/NbC/WC system (coordinates in wt-%).

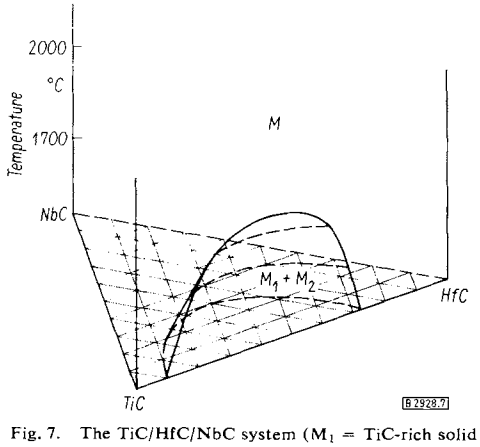


Fig. 7. The TiC/HfC/NbC system (M_1 = TiC-rich solid solution M_2 = HfC-rich solid solution).

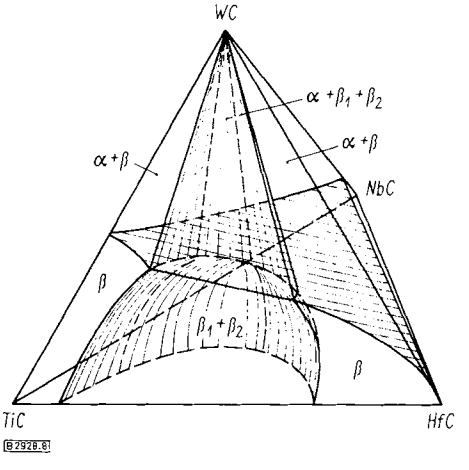


Fig. 8. Section through the TiC/HfC/NbC/WC system at 1450 °C (coordinates in mole-%).

[11] *N. Reiter*, Dissertation, TH Wien 1969.

Table 4. Properties of some cemented carbides containing NbC and HfC.

a) Transverse rupture strength (kg/mm²) of cemented carbides containing NbC/HfC of the type S3T, S1T, and FM.

Proportions of added carbides NbC : TaC : HfC	Type S3T	S1T	FM
6 : 0 : 2	180	120	95
4 : 2 : 2	190	125	105
4 : 0 : 4	190	145	105
0 : 8 : 0 [a]	185	120	100

[a] Reference alloy.

b) Hardness (kg/mm²) of hard metals containing NbC/HfC.

Proportions of added carbides NbC : TaC : HfC	Type S3T	S1T	FM
6 : 0 : 2	1550	1750	1950
4 : 2 : 2	1550	1700	2000
4 : 0 : 4	1600	1750	2050
0 : 8 : 0 [a]	1500	1700	1900

[a] Reference alloy.

c) Composition (wt-%) of the investigated cemented carbides.

Designation of types	TiC	NbC/TaC/HfC	Co	WC
S3T	7	8	10	75
S1T	16	8	7	69
FM	40	8	7	45

Application experiments too have shown HfC to be a suitable additive. Table 4 shows the transverse rupture strengths and hardness values of conventional cemented carbides in which TaC was replaced either by NbC/HfC or by TaC/HfC solid solutions. The hardness values and transverse rupture strengths resulting from the substitution are invariably as good as, or even better than those of the original hard metals. If TaC in WC/TiC/TaC/Co compositions is replaced by a 1:1 solid solution of TaC/HfC or quantitatively by HfC, then in some cases the transverse rupture strength passes through a maximum[9] (cf. Fig. 9).

Excellent cutting results are obtained with HfC-containing cemented carbides. The wear on HfC-containing tools in the machining of steel is for the

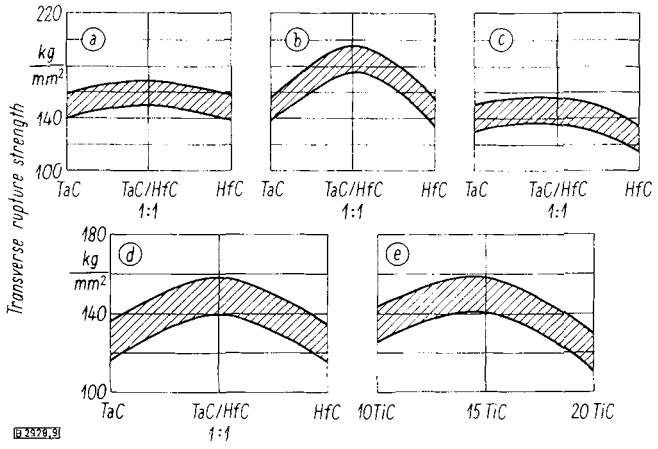


Fig. 9. Transverse rupture strength of cemented carbides of the type TiC/TaC/WC/Co with partial replacement of TaC by HfC.

a) 10 TiC, 5 TaC/HfC), 8 Co, remainder WC; b) 15 TiC, 5 TaC (HfC), 8 Co, remainder WC; c) 20 TiC, 5 TaC(HfC), 8 Co, remainder WC; d) 15 TiC, 5 TaC (HfC), 6.5 ± 0.5 Co, remainder WC; e) 5 TaC/HfC 1:1, 6.5 ± 0.5 Co, remainder WC. (The figures quoted in front of the element symbols indicate the content in wt-%.)

most part lower than in the case of corresponding, hafnium-free alloys. This observation may be explained by the resistance to friction welding of HfC, which must be responsible for the smaller erosion and cratering by the departing chip.

HfC has also proved its worth as an additive to WC-free cemented carbides based on TiC/Mo_2C/Ni. This type of hard alloy has recently regained some popularity in the U.S.A. although the discovery of these materials goes back almost 40 years [10]. Unfortunately, the toughness of the cemented carbides produced at that time was so inadequate that they were unable to compete against the WC–TiC-containing compositions. A systematic investigation of this type of hard alloy yielded an unexpected result: in marked contrast to WC-containing cemented carbides, in

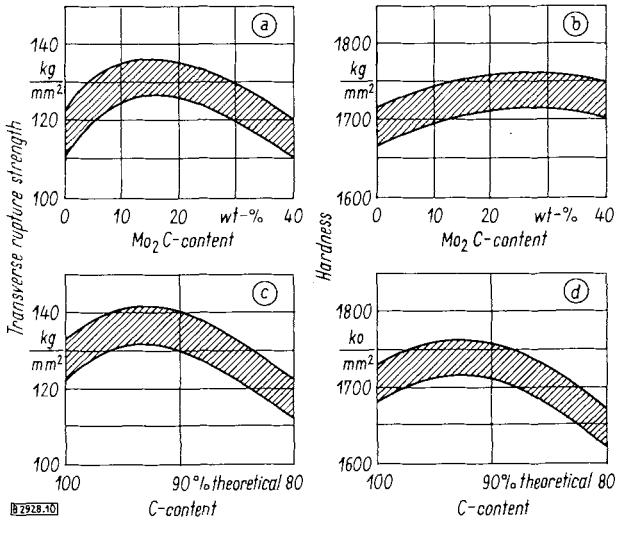


Fig. 10. Transverse rupture strength and hardness of WC-free cemented carbides based on Mo_2C/TiC/Ni with 14% Ni.

a) Transverse rupture strength as a function of the Mo_2C content in the solid solution; b) hardness as a function of the Mo_2C content in the solid solution; c) transverse rupture strength of a cemented carbide with a TiC/Mo_2C(80/20) solid solution (14% Ni binder) as a function of the carbon deficiency; d) hardness of a TiC/Mo_2C (80/20) cemented carbide as a function of the carbon deficiency.

TiC/Mo_2C/Ni alloys a certain carbon deficiency can produce a significant increase in both strength and hardness [12] (cf. Fig. 10).

Similar effects can be obtained by using classical Ni–Mo alloys containing a maximum of 25 wt-% of Mo in place of the pure nickel binder [10]. This observation also supports the postulate that the carbon deficiency causes part of the molybdenum to diffuse out of the (low carbon) solid solution into the nickel binder during sintering, thus producing a certain rise in the amount of the binder (increased toughness) as well as improving the hardness and strength of the binder by the formation of an alloy similar to Hastalloy. At a binder content of 10 to 14% Ni one obtains transverse rupture strengths of 125 to 140 kg/mm², almost double the values obtained in 1930 for alloys of the same composition. By hot pressing it is even possible to attain transverse rupture strengths of 150 to 170 kg/mm².

Further attempts to improve the classical cemented carbides were based on the known fact that it would be possible to increase the already outstanding properties of the hard alloys if a way could be found to reduce the size of the carbide particles in the hard alloy below the presently usual 2–4 μm (cf. the development of Widia H from Widia N). It is scarcely possible to bring the particle size down much below 1 μm by grinding, even with the most powerful grinders; in fact, pyrophoric properties are often observed in the case of such finely ground hard metals. Ciba of Basel and, independently, DuPont de Nemours in the U.S.A. have developed processes that permit the production of submicroscopically fine carbides [13]. In the Ciba technique, a mixture of metal halide vapor, methane, and hydrogen is heated in a plasma

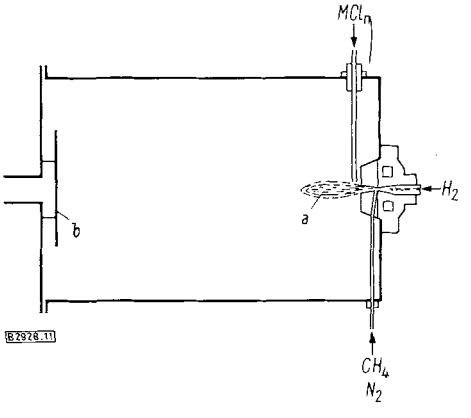


Fig. 11. Schematic representation of the Ciba apparatus for preparing ultrafine carbides and nitrides in a plasma jet:

a) plasma jet; b) baffle.

jet (Fig. 11) and the fine carbide particles are quenched on a baffle and removed. These ultrafine carbides (0.01 to 0.1 μm) of necessity have a higher oxygen content, which must be reduced in the usual way by

[12] *R. Kieffer, N. Reiter,* and *D. Fister,* BISRA-ISI-Conference on Materials for Metal Cutting, Scarborough 1970.

[13] *E. Neuenschwandter,* J. Less-Common Metals [Amsterdam] *11,* 365 (1966).

the formation of solid solutions with WC. In addition, these carbides display a strong tendency to grain growth on sintering which completely nullifies the initial advantage. Experiments undertaken jointly with *Krepler* [14] showed that grain growth can be inhibited by the addition of as little as a few tenths of one percent of VC_{1-x}, and to a lesser extent also by NbC or TaC, so that it is possible to obtain particle sizes $<1\ \mu m$ in the final cemented carbide.

The classical cemented carbides contain almost exclusively monocarbides as the hard constituents. In highly alloyed special steels, however, one is unlikely to find monocarbides but, instead, a variety of complex carbides which apparently play an important role in the hardening mechanism of such steels. The precise composition of these phases has generally been determined by residue analysis [15], preference being given recently to the use of the electron-beam microprobe analyzer. We have attempted to prepare some of these carbides synthetically and to investigate their suitability for special alloys [16, 17]. It should not, of course, be expected that these complex carbides will prove superior to the monocarbides as regards strength, but they could be of considerable interest for particular applications, as for example chromium carbides for non-scaling hard alloys. If these carbides are bound with less than 20% of auxiliary metals then alloys of the cemented carbide type are obtained; the use of about 30–50% of auxiliary metal matrix yields novel sintered steels that close the existing gap between high-speed steels (carbide content $\approx$20%) and cemented carbides (carbide content $\approx$70–90%). It is also possible to produce high-speed steels from synthesized special carbides and alloyed steel powder using powder metallurgical techniques and to modify their properties by suitable alloying additions.

In contrast to the monocarbides, the complex carbides are always in equilibrium with the binder metal; they sometimes display considerable solubility in the binder, and sometimes the binder dissolves in the complex carbide. Due attention must be given to this fact in the powder-metallurgical manufacture of sintered components from complex carbides and binder metal. The auxiliary metal bath technique can be used to determine the equilibrium composition of the complex carbide and the metal melt [4, 5]. The complex carbide isolated from the regulus has been in equilibrium with the melt. It is advantageous to use for the binder metal an alloy whose composition corresponds to the auxiliary metal phase [16].

With the aid of the auxiliary metal bath technique it is of course also possible to obtain other hard material phases, for example silicides and borides. Here again the composition of the auxiliary metal melt determines the composition of the hard material phases separated out. Depending on the silicon content of the copper melt, it is possible, for example, to obtain WSi_2 or W_5Si_3 crystals from the solidified regulus on the addition of tungsten [18].

4. Carbidothermic Reactions

A new field of application for the refractory carbides of the transition metals is the production of high-melting metals and alloys. One example of this is the reduction of niobium pentoxide by niobium carbide according to the equations

$$Nb_2O_5 + 7\,C \xrightarrow{H_2} 2\,NbC + 5\,CO$$

$$Nb_2O_5 + 5\,NbC \xrightarrow{\text{vacuum}} 7\,Nb + 5\,CO$$

which was used up to a few years ago by the Wah Chang Corporation of Albany, Oregon, U.S.A., for the production of pure niobium [19]. For this purpose mixtures of NbC and Nb_2O_5 were compressed in large isostatic presses and were reacted in high-frequency vacuum furnaces. With a careful choice of the amount of oxide and carbide one obtains technically pure niobium which is hydrided, comminuted, dehydrided, and remelted in an electron beam furnace. This principle has also been used to produce ductile vanadium [20], although in this case the experimental problems are much greater owing to the formation of low-melting oxide/carbide eutectics. In contrast to the metals of Groups VB and VIB of the periodic system, metals of Group IVB can only be prepared by carbidothermic reactions under extreme conditions and with high evaporation losses, if at all (cf. Table 5). Fig. 12 shows the relationship between the CO pressure, temperature, and phase composition predicted for the Ti/C/O and Zr/C/O systems by thermodynamic calculations. In agreement with the calculations, it was found possible to prepare detectable (by X-ray diffraction and analytical techniques) amounts of titanium with a purity of 96% at tem-

Table 5. Minimum temperatures (°K) as a function of CO pressures for carbidothermic preparation of metals.

Metal	p_{CO} (at)			
	10^{-4}	10^{-6}	10^{-8}	10^{-10}
Ti	—	—	2030	1830
Zr	—	—	2300	2000
Hf	—	—	2300	2000
V	—	1760	1530	—
Nb	—	1690	1490	—
Ta	—	1700	1500	—
Cr	1530	1320	—	—
Mo	930	800	—	—
W	820	710	—	—

[14] *A. E. Krepler*, Dissertation, TH Wien 1967.

[15] *W. Koch*: Metallkundliche Analyse. Verlag Stahleisen, Düsseldorf 1965.

[16] *W. Pernegger*, Dissertation, TH Wien 1968.

[17] *H. Krünes*, Dissertation, TH Wien 1969.

[18] *G. Jangg, R. Kieffer*, and *H. Kögler*, Z. Metallkunde *59*, 546 (1968).

[19] *R. Kieffer* and *H. Braun*: Vanadin, Niob, Tantal. Springer-Verlag, Berlin-Göttingen-Heidelberg 1963.

[20] *R. Kieffer, H. Bach*, and *H. Lutz*, Metall *21*, 19 (1967).

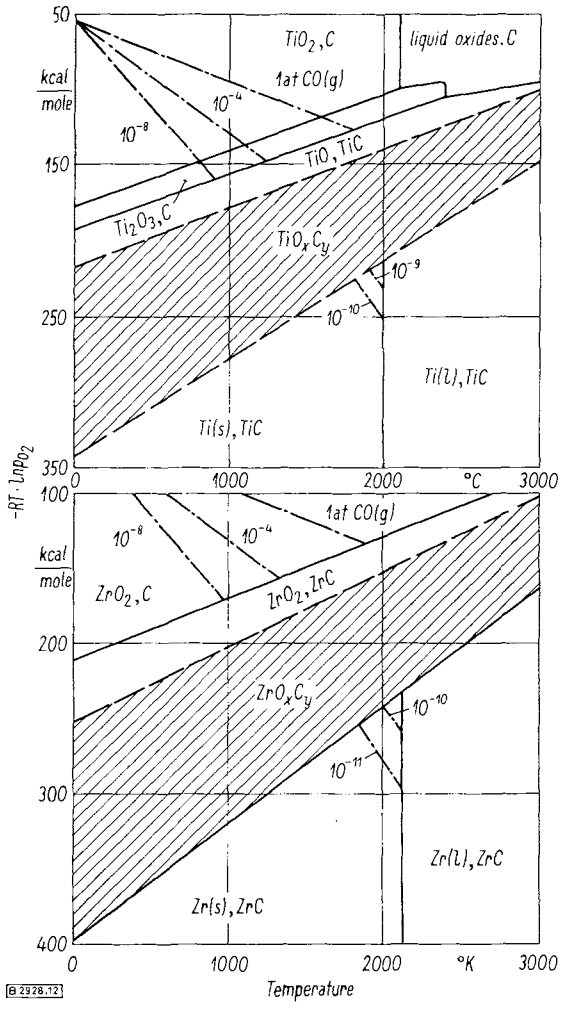


Fig. 12. Pourbaix-Ellingham diagrams of the systems Ti/C/O (top) and Zr/C/O (bottom).

peratures of the order of 1700 °C and pressures $<10^{-5}$ torr [21]. In practice, however, it is impossible to prepare metals of Group IVB in the pure state by this technique. On the other hand, alloys of these metals with metals of Groups VB and VIB of the periodic system can be obtained carbidothermically by using a carbide of another metal for the reduction. An example of this is the reduction of MoO_2 with TiC and C. Titanium, which has a strong affinity for oxygen, is diluted by alloy formation with molybdenum, in which β-titanium is completely soluble at high temperatures, and its activity is thereby reduced. Figure 13 shows a plot of the CO equilibrium pressures based on thermodynamic calculations against the composition of the Ti/Mo alloy. It was shown experimentally that Ti/Mo alloys could be produced up to a composition of about 40 wt-% Ti and 60 wt-% Mo, the difficulties increasing with increasing Ti content. The results of an experiment carried out to produce a 40 Ti/60 Mo alloy are shown in Table 6. Starting with a TiO_2/Mo_2C mixture the metal content can be raised to 99.75 % [22]. It was likewise possible to produce alloys based on V/Nb, V/Ta, V/Cr, Nb/Zr, Ta/Hf/W, *etc.* [21,22].

[21] *R. Kieffer, F. Lihl,* and *E. Effenberger,* Z. Metallkunde 60, 94 (1969).

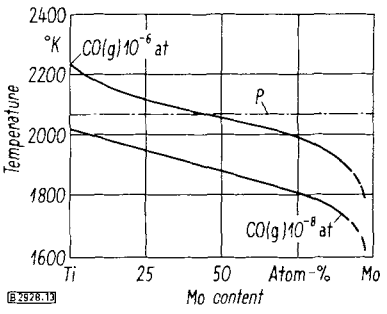


Fig. 13. Equilibrium pressure of CO over TiC/MoO_2 mixtures as a function of the Mo content. P = peritectic temperature in the system Ti—Mo—CO.

Table 6. Reduction of MoO_2 with TiC and C to an alloy containing 40 % Ti and 60 % Mo.

Material and treatment	Reaction time (h)	T_{max} (°C)	Chemical analysis (wt-%) C	O_2	Ti, Mo
Initial mixture	—	—	11.2	14.8	74
1) Indirect sintering	10	1600	7.8	3.8	88.4
2) Indirect sintering	10	1750	2.8	2.3	95.1
3) Presintering of rod	1	1700	—	—	—
4) Direct sintering	4	1900	0.32	0.147	99.6
5) Presintering of rod	1	1700	—	—	—
6) Direct sintering [a]	3	2000	0.14	0.11	99.75

[a] Hardness HV (20) in the as sintered condition = 320 kg/mm²; hardness in the remelted condition. HV(20) = 410 kg/mm².

5. Nitrides

Despite pronounced similarities to the hard and high-melting carbides, nitrides have gained relatively little popularity. The nitrides of the transition metals are hard, like the carbides, and many of them are also high-melting. They are electrically conducting and exhibit a metallic luster, and are completely miscible with the corresponding isotypic carbides [23]. Nitrides are somewhat less hard than carbides, they decompose under vacuum and at high temperatures, and their preparation is less straightforward than that of the carbides. Nevertheless, it seems desirable to undertake a systematic investigation of the nitrides and to study their properties in greater detail.

Titanium nitride and carbonitrides are distinguished, for example, by their characteristic color, which changes with rising carbon content from golden yellow in the case of titanium nitride through red-gold and bronze to violet-gray. With suitable binder metals, nitrides and carbonitrides can be processed to sintered hard alloys which, despite a considerable hardness, ranging from 1550 to 1700 kg/mm², still display transverse rupture strengths of 100–140 kg/mm². Nitrides and carbonitrides would therefore seem to be fundamentally suitable for application in the machining sector, in particular because nitrides

[22] *R. Kieffer, F. Lihl,* and *E. Effenberger,* 5. Internat. Leichtmetalltagung, Leoben 1968, p. 2, Aluminium-Verlag, Düsseldorf 1968.

[23] *R. Kieffer* and *F. Benesovsky*: Hartstoffe, Springer-Verlag, Wien 1963.

appear to be somewhat less susceptible to erosion (cratering) by the departing chip [12]. This property, which according to the experience obtained to date is specific to nitrides, also offers advantages in coating throwaway tips with nitrides. Carbide coatings have already proved their worth in practice; 5–10 μm-thick titanium carbide coatings on throwaway tips made of standard cemented carbide reduced cratering to between 25 and 30% [24]. With nitride- and carbonitride-coated hard metals it was even possible to reduce wear to between 10 and 15% [12].

The work performed on nitrides included a detailed investigation of the resistance of refractory carbides to nitrogen. In the temperature region from 1100 to 1800 °C and at pressures up to 300 at only TaC and WC of the carbides of the transition metals of Groups IVB, VB, and VIB of the periodic system are completely stable with respect to nitrogen [25]. NbC and Mo_2C react with nitrogen only to a small extent, and all other carbides react with nitrogen to carbonitrides with liberation of carbon. Quite in accordance with thermodynamic predictions, the tendency to carbonitride formation increases with rising nitrogen pressure and decreases with rising temperature. Chromium carbide (Cr_3C_2) reacts at 1400 °C with nitrogen at a pressure of 300 at with the formation of a ternary carbonitride phase, which had already been observed in the course of the investigation of the Cr/C/N system [26, 27]. The existence of this phase is of interest in that this was the first metallic compound to be discovered in which the otherwise so similar nitrogen and carbon atoms assume crystallographically non-equivalent positions [28].

For this work and for the investigations on nitride systems it was essential to develop large high-pressure/high-temperature autoclaves. All of these autoclaves are constructed on the principle of the internally heated autoclave with cooled wall and are designed for temperatures up to 2500 °C. The medium-pressure autoclave (see Fig. 14) which was built to our specifications by the furnace construction division of Degussa, Wolfgang b. Hanau, and which was inspired by an idea of *Nowotny et al.* [29], is designed for pressures up to 30 at. High-pressure autoclaves developed by us according to the same basic principle (cf. *e.g.* Fig. 15) operate at internal pressures of 1000 and 2000 at, respectively. Further details will be found in a recently published work [30].

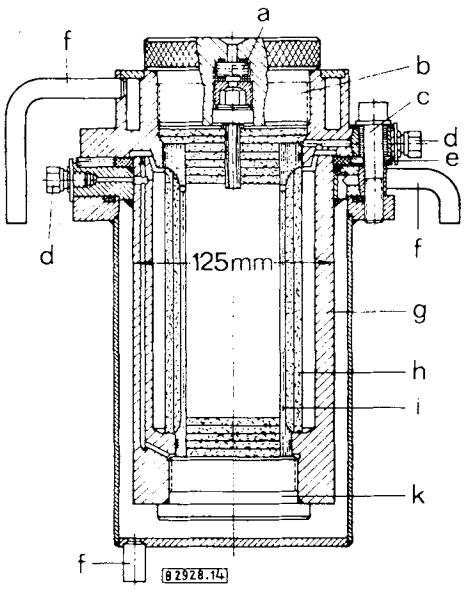


Fig. 14. Section through the medium-pressure autoclave for temperatures up to 2500 °C and pressures up to 30 at.

a) Quartz window; b) screw-on lid with quartz window; c) bolts; d) compressed gas connection; e) electrical insulation; f) cooling water connection; g) pressure vessel wall; h) graphite felt; i) carbon heating tube; k) bottom plate.

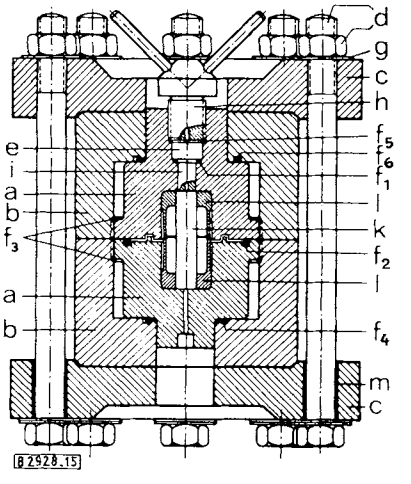


Fig. 15. Large high-pressure/high-temperature autoclave (360 mm dia., 20 ml useful capacity, 370 mm height, pressures up to 2000 at).

a) Pressure vessel; b) stressed autoclave casing; c) pressure plates; d) bolts; e) quartz window; f_1–f_6 sealing rings; g) shim plates; h) screw cover; i) screening tube; k) graphite heating tube; l) contact rings; m) electrical insulation.

A number of binary and ternary nitride systems have already been studied with the aid of these autoclaves. In addition to Cr/C/N [26, 27], they include the systems U/C/N [31], Ti/Cr/N [32], Zr/Cr/N [32], Hf/Cr/N [32], V/Cr/N [33], Mo/Cr/N [34], W/Cr/N [34], Mo/N [35], Mo/C/N [36], and Cr/Mn/N [37].

[24] *G. Schuhmacher*, Techn. Zbl. prakt. Metallbearb. *83*, 275 (1969).

[25] *R. Kieffer, H. Nowotny, P. Ettmayer*, and *M. Freudhofmeier*, Mh. Chem. *101*, 65 (1970).

[26] *R. Kieffer, P. Ettmayer*, and *Th. Dubsky*, Z. Metallkunde *58*, 560 (1967).

[27] *P. Ettmayer*, Mh. Chem. *97*, 1248 (1966).

[28] *P. Ettmayer, G. Vinek*, and *H. Rassaerts*, Mh. Chem. *97*, 1258 (1966).

[29] *H. Nowotny, E. Bauer*, and *A. Stempfl*: Alfons Leon Gedenkschrift. Verlag Allgemeine Bauzeitung, Wien 1951.

[30] *P. Ettmayer, H. Priemer*, and *R. Kieffer*, Metall *23*, 307 (1969).

[31] *R. Kieffer* and *P. Ettmayer*, Contribution to IAEA (International Atomic Energy Agency) Panel on the Thermodynamic Properties of Uranium- and Plutonium-Carbides, Wien, Sept. 9–13, 1968.

[32] *P. Ettmayer, R. Kieffer*, and *F. Petter*, in preparation.

[33] *W. Schebesta*, Diplomarbeit, TH Wien 1970.

[34] *P. Ettmayer, R. Kieffer*, and *H. Priemer*, in preparation.

[35] *P. Ettmayer*, Mh. Chem. *101*, 127 (1970).

[36] *P. Ettmayer*, Mh. Chem., in press.

[37] *P. Ettmayer, R. Kieffer*, and *E. Horvath*, in preparation.

6. Nonmetallic Hard Materials

Apart from the hard oxides, the nonmetallic hard materials are formed from boron, carbon, nitrogen, and silicon. Whereas the binary systems B/C, B/N, B/Si, C/Si, and N/Si have been extensively studied, little is known about the ternary systems and practically nothing about the quaternary system. The Si/C/N system was investigated with the aid of the high-pressure/high-temperature autoclaves. Figure 16 shows the result of this work [38], which displays

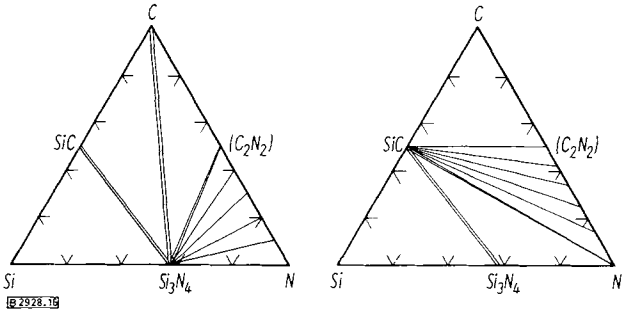


Fig. 16. Phase field divisions in the Si/C/N system at 1900 °K (left) and 2000 °K (right) and 1 at.

complete agreement with thermodynamic calculations [39]. No ternary carbonitride phase was found; the solubilities of carbon in silicon nitride and of nitrogen in silicon carbide is evidently very low. Nevertheless, hexagonal α-SiC can be transformed quantitatively into cubic β-SiC by nitrogen pressure above 2200 °C. The β-SiC obtained in this manner can be converted back into α-SiC by heating to 2500 °C *in vacuo* or in argon. Table 7 shows the experimental details of this nitrogen-induced transformation α-SiC ⇌ β-SiC [40]. This phase transformation has lent fresh strength to the old hypothesis that the polytypism observed in SiC may depend among other things on minute proportions of impurities (*e.g.* nitrogen, oxygen). Boron and aluminum are said to have similar effects on the structure of SiC.

Table 7. Experiments with SiC under nitrogen pressure at high temperatures.

No.	Heat treatment			Phases		Analyses	
	temp. (°C)	time (min)	pressure (at)	SiC starting material	SiC reaction product	N_2 (ppm)	O_2 (ppm)
1	2500	3	30 N_2	α	β	700	330
	2300	30					
2	2500	3	30 N_2	α	β	1300	250
	2200	60					
3	2500	3	30 N_2	α	β, (α)	700	290
	2000	120					
4	2500	3	30 N_2	α	β, α	700	230
	1800	240					
5	2500	3	30 N_2	α	α, (β)	14700	100
	1600	480					
6	1600	720	30 N_2	α	α	17300	270
7	2500	30	1 Ar	β from 1	α	< 100	190
8	2500	30	8 N_2	α from 7	β	< 100	270
9	2500	30	1 Ar	β from 8	α	< 100	220
10	2500	30	2 N_2	α from 9	β	< 100	190
11	2500	30	1/8 N_2	β from 10	β	300	170
12	2500	30	1/2 N_2	α	α	< 100	110
13	2400	60	40 N_2	α	β	220	210
14	2300	120	40 N_2	α	β	240	200
15	2200	60	8 N_2	α	α	100	160
16	2200	60	30 N_2	α	α	300	150

In recent times SiC has claimed the interest not only of structural chemists and semiconductor researchers, but also of materials scientists attracted by the outstanding properties of this material. Great hardness, good oxidation stability up to about 1500 °C, and low density are only some of the interesting characteristics. Unfortunately, SiC is very brittle up to extremely high temperatures, and it is impossible to compact sufficiently either by hot pressing or by other sintering techniques. Consequently, efforts to make SiC with adequate strength characteristics have so far proved of little avail. One possible way of producing compact SiC shaped parts is to infiltrate porous SiC bodies with silicon so as to give practically compact materials, which then naturally contain considerable amounts of undesirable free silicon. However, by producing bodies that in addition to SiC also contain sufficient free carbon in the pores, one obtains infiltrated bodies which, together with small amounts of residual silicon metal, also contain considerable amounts of secondary SiC. The strength characteristics of the SiC parts made in this way are already sufficiently encouraging to make them potentially interesting for many industrial applications [41,42].

In conclusion, let us briefly consider the present state of development in the domain of diamond, the hardest material of all. Thanks to the progress made in physical chemistry, it was known from about the middle of the last century that the transformation of graphite into diamond could only occur at high pressure. *Bundy*'s phase diagram of carbon [43], shown in Figure 17, shows the pressure/temperature region in which an industrial diamond synthesis is carried out. It has never been conclusively established whether *Moissan* did not, after all, succeed, in the course of his attempt at diamond synthesis at the turn of the century, in producing the necessary pressure and obtaining microscopically small diamonds from the iron melt supersaturated with carbon. At present a substantial proportion of industrial diamonds is already being produced by catalytic high-pressure/high-temperature synthesis using nickel, iron/nickel, and recently also cobalt/niobium/copper alloys [44] as catalysts. Fine bort has recently been produced by

[38] *E. Gugel, P. Ettmayer*, and *A. Schmidt*, Ber. dtsch. keram. Ges. *45*, 395 (1968).

[39] *H. Rassaerts* and *A. Schmidt*, Planseeber. Pulvermetallurgie *14*, 110/14 (1966).

[40] *R. Kieffer, E. Gugel, P. Ettmayer*, and *A. Schmidt*, Ber. dtsch. keram. Ges. *43*, 621/23 (1966).

[41] *R. Kieffer, P. Ettmayer, E. Gugel*, and *A. Schmidt*, Mater. Res. Bull. *4*, 153 (1969).

[42] *R. Kieffer, E. Eipeltauer*, and *E. Gugel*, Ber. dtsch. keram. Ges. *46*, 486 (1969).

[43] *F. P. Bundy*, Science (Washington) *137*, 1057 (1962).

[44] *Masao Wakatsuki, Toshio Aoki, Nobuyuki Wakamatsu*, and *Shinichiro Takasu*, US-Pat. 3436183, April 1, 1969 (Tokyo Shibaura Electric Co. Ltd.).

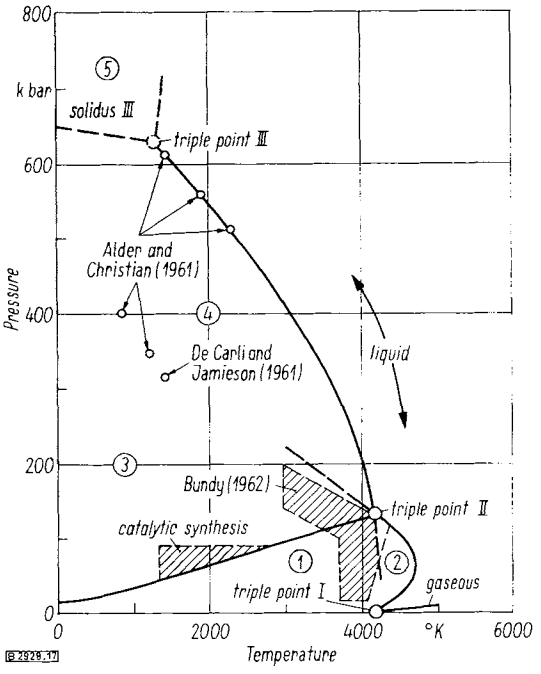


Fig. 17. The phase diagram of carbon (after *Bundy* [43]).
1) Graphite + metastable diamond; 2) graphite; 3) metastable graphite + diamond; 4) diamond; 5) metallic phase.

explosion shock waves using an iron catalyst (Du Pont), the technique being developed from *Moissan*'s experiments, and even a catalyst-free transformation seems feasible, although this could only be done at much higher pressures still, *i.e.* in the region of "metallic carbon" (see Fig. 17). The conditions so far attainable for diamond synthesis are still inadequate to produce large diamonds of gem quality. However, it is already possible to control specific properties of diamonds within certain limits, *e.g.* to vary the color by admixtures to the catalysts and to influence the habit of the diamond crystals. Nitrogen imparts semiconductor properties to diamond and gives it a yellow to brown coloration, boron is reported to make it blue. Figure 18 shows a schematic arrangement for

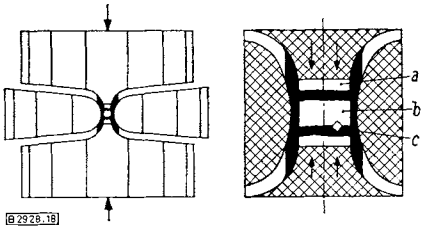


Fig. 18. Schematic arrangement for diamond synthesis.
Left: sectioned cemented carbide anvil and die; right: detail of the reaction space: a) metal; b) graphite; c) diamond crystal.

diamond synthesis. The carbon tube heating element, which is insulated with pyrophyllite, is introduced between cemented carbide anvils into annular shrunk cemented carbide dies. Cobalt-bonded tungsten carbide is used for the anvils and dies. This material continues to form the basis of the cemented carbide industry and synthetic diamonds would be inconceivable without it.

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Modern Industrial Microbiological Fermentations and Their Effects on Technical Developments[**]

By H.-J. Rehm[*]

Owing to the development of many new processes and techniques, the production of primary and secondary metabolites with the aid of microorganisms has not only expanded greatly, but has also been simplified in many details, and has therefore become more widely feasible on the industrial scale. The present article surveys the principal fermentation processes and the main types of equipment, which shows a trend toward continuous processes and increasing automation. Some recent developments observed e.g. in the cultivation of animal cells or the production of electrical energy, and particularly in the production of proteins by microorganisms, are also described.

1. Isolation of Primary Metabolites

Man has been trying for thousands of years to develop apparatus for the controlled cultivation of microorganisms by processes and special techniques best suited to the needs of the microorganisms. Following the discovery of large numbers of microorganisms and the elucidation of many of their biochemical properties, cultivation methods that have proved adequate almost to the present day were developed in the late 1800's and early 1900's. The cultures were carried out in open or closed tanks, usually without protection against extraneous organisms. As far as

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[**] Based on a lecture to the Dechema conference in Frankfurt/M. on June 26, 1969, and to the 2nd Symposium on Industrial Microbiology on April 14, 1970 in Berlin.

possible, the growth conditions were kept such that only the desired organisms could develop. The object of the process is essentially either the production of the cells themselves, as in the growth of yeast, or the production of their primary metabolites, such as ethanol, butanol, acetone, and glycerol, as well as of many simple organic acids. The first phase of industrial microbiology may be regarded, for simplicity, as the preparation of primary metabolites. This phase dates from the first attempts to obtain alcoholic drinks or organic acids up to around the middle of this century.

2. Isolation of Secondary Metabolites and Derived Processes

Penicillin was the first important secondary metabolite to be required in very large quantities. Its production led to the development of revolutionary new processes, which can be described collectively as sterile aerated submerged fermentation, and which allowed considerable simplification as compared with the extremely laborious sterile surface methods that were already known. The microorganisms are grown in aerated and stirred culture solution under constant conditions in large fermenters with effective capacities of 50000 to 250000 l, and there is no possibility of infection by extraneous organisms (for details, cf. [1–3]).

Many difficulties had to be overcome in the development of these processes:

1) The fermenter and the nutrient solution were sterilized by introducing superheated steam into the pipes and the fermenter, heating the culture solution as it flowed, and introducing the concentrated culture solution into the fermenter, the contents then being made up to the required volume with condensing steam.

2) The entire fermenter was kept sterile throughout the fermentation (which took several days) by ensuring that its internal pressure was slightly above atmospheric.

3) Sterilizable measuring equipment had to be developed.

4) For sterile foam reduction, automatic defoaming equipment was designed in which a sterile defoaming liquid was added to the substrate. The agents used are mainly fats, oils, higher fatty alcohols, and silicone oils.

5) The introduction of sterile air initially presented special difficulties. The air was first passed through wash towers containing acids, alkalis, or disinfectants, but was later forced through sterilizable glass wool-carbon filters.

The solution of these problems and the adaptation of microorganisms for submerged culture provided a fermentation method for the production of many other secondary metabolites as well as penicillin with the aid of microorganisms. The variety of products, which include most antibiotics, many enzymes, various alkaloids, polysaccharides, nucleotides, gibberellins, and various vitamins, frequently necessitated the design of new fermenters, and the result was an extremely diversified development.

The development of further microbiological processes naturally did not stop at the submerged process. Great interest was also stimulated in the production of laboratory shakers suitable for the cultivation of microorganisms under practically submerged conditions. Besides a number of variants based on the conventional principle, *e.g.* with constant temperature regulation, with special shaking speeds, *etc.*, completely new designs have also appeared. Because of the unfavorable center of gravity in conventional shakers, stabilization with several platforms (tablars) is often difficult. For this reason, *e.g.* the point of application of the drive in a new design by Infors AG (Basel/Switzerland) is situated exactly at the center of gravity of the moving upper part as well as of the counterweight.

Further work was also carried out on the surface process, which was still needed for the preparation of certain products. One example is the fermentation cup process (a method for surface culture) described by *Schröder* and *Brandl* (cf. [1]). These authors developed a sterile aerated surface process in which the

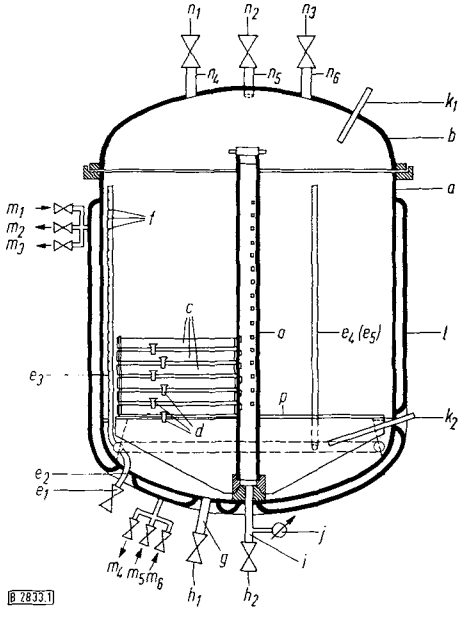


Fig. 1. Longitudinal section of a fermentation cup container (after [1] p. 158).

a, Container; b, lid; c, exchangeable fermentation cups; d, overflow devices; e_1 to e_5, aerators; f, air outlet holes; g, discharge pipe; h_1, h_2, valves; i, deaeration pipes; j, manometer; k_1k_2, thermometer glands; l, double wall; m_1 to m_6, valves for heating steam (m_1,m_4), cooling water (m_2,m_5), and recirculation water (m_3,m_6); n_1 to n_6, nutrient feed; o, perforated central bracing tube; p, perforated base.

[1] *R. Brunner* and *G. Machek*: Die Antibiotika. Vol. I, Die grossen Antibiotika. Verlag Hans Carl, Nürnberg 1962.

[2] *R. Müller* and *K. Kieslich*, Chemie-Ing.-Techn. *38*, 813 (1966).

[3] *H. J. Rehm*: Industrielle Mikrobiologie. Springer Verlag, Berlin-Heidelberg-New York 1967, and further literature cited therein.

many laborious operations are largely combined and automated, *e.g.* automatic introduction of the culture medium, automatic sterilization of the many surface-growth dishes (making good use of experience gained in the submerged process), simple inoculation of the complete solution, possibility of sterile aeration, and simple temperature control (cf. Fig. 1).

3. Kinetics of Batch Submerged Fermentations

The submerged processes with their constant conditions for the growth of microorganisms made it possible for the first time to obtain really accurate information on the kinetics of the fermentation process. Since about 1946, and particularly since 1954, many articles dealing with this problem have been published.

3.1. Patterns of Development of the Microorganisms in the Fermenter

Whereas very long incubation times must be expected in normal microorganism cultures, the exponential phase of the growth of the microorganisms can be considerably prolonged and the incubation time shortened in the fermenter (cf. Fig. 2). Microbiological fermentations are influenced and characterized in particular by substrate consumption, occurrence of the end product, and development of the biomass. Movement of the substrate, aeration, accumulation and disappearance of intermediate products, and other factors such as temperature and pH changes, which can be relatively easily kept constant, are very important.

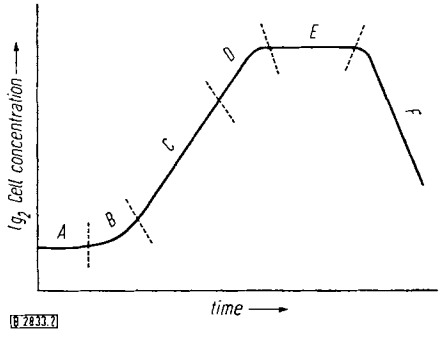


Fig. 2. Growth curve of bacteria (from [3]).
Various phases of development: A, incubation phase; B, acceleration phase; C, exponential growth phase; D, transition phase; E, stationary phase; F, lethal phase.

3.2. Patterns of Formation of the Fermentation Product

The fermentations are classified according to various rules. One classification that seems reasonable is that proposed by *E. L. Gaden* and *F. H. Deindorfer*, who distinguish three types (cf. [4]):

Type I: The main fermentation product is formed as a result of the primary energy metabolism. It is often formed on direct oxidation of the primary carbohydrate, *e.g.* in the alcoholic fermentation or the formation of lactic acid from glucose. The mass cultivation of many microorganism cells must also be regarded as fermentations of this type (Fig. 3a).

Type II: The main fermentation product is formed only indirectly from the energy metabolism. Examples are the formation of itaconic acid and of citric acid; the amino acid fermentations may also belong to this group. The reaction steps are complex, and inhibited or anomalous metabolism occurs. Figure 3b shows that the growth and the sugar consumption have two maxima. The specific yield curve

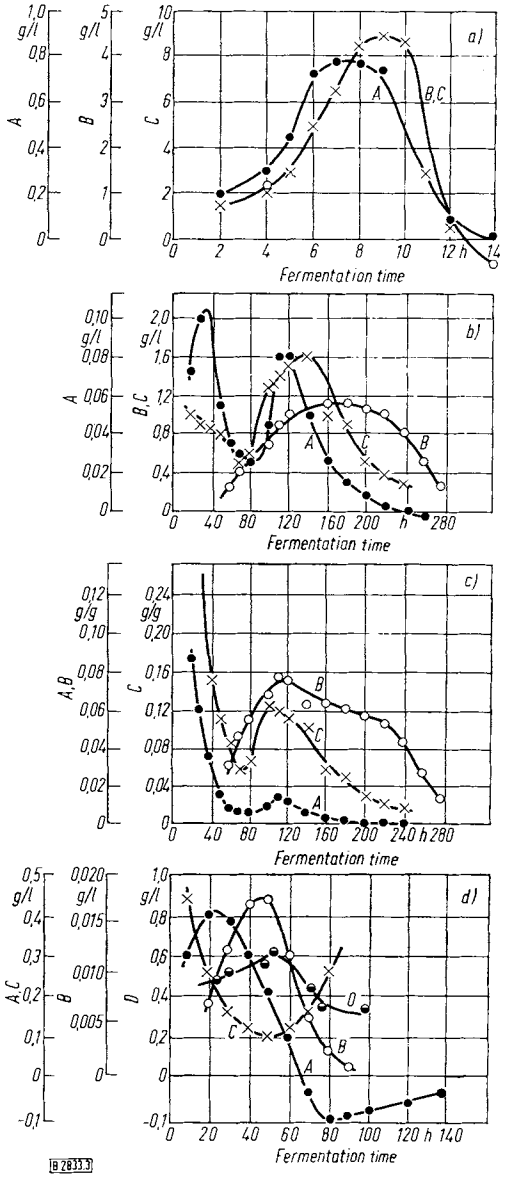


Fig. 3. Classification of fermentations according to *E. L. Gaden* and *F. H. Deindorfer* (cf. [4]).
a) Type I: Alcoholic fermentation. Volume growth rates; A, growth; B, alcohol synthesis; C, sugar consumption.
b) Type II: Citric acid formation. Volume growth rates; A, growth; B, citric acid formation; C, sugar consumption.
c) Type II: Citric acid formation. Specific growth rates; A, B, and C as in (b).
d) Type III: Penicillin formation. Volume growth rates; A, growth; B, penicillin formation; C, sugar consumption; D, oxygen absorption.

[4] *N. Blakebrough*: Biochemical and Biological Engineering Science, Vol. 1, Academic Press, London-New York 1967.

(Fig. 3c) shows that growth and sugar consumption are very closely related in the initial phase, whereas growth and product formation are closely related in the secondary phase.

Type III: This type of fermentation is found in all biosyntheses in which the main fermentation product is formed not from the energy metabolism, but relatively independently of it in the cell, *e.g.* in the formation of penicillin and streptomycin (Fig. 3d).

Thus, in Type I complex compounds are broken down into simpler compounds (catabolic processes), and in Type III complex molecules are formed from simple ones (biosyntheses, anabolic processes), while Type II lies between these.

4. Aeration of Microbiological Cultures

Aeration is one of the fundamental problems of aerobic microbiological fermentations. The oxygen requirement C of the cells varies widely, according to the nature of the microorganisms and the biochemical process taking place in the cells. The oxygen requirement per gram of newly formed dry cell substance [5] is:

$$C = A/Y - B$$

(A = theoretical quantity of oxygen necessary for the combustion of 1 g of substrate to CO_2, H_2O, and NH_3; B = theoretical quantity of oxygen necessary for the combustion of 1 g of dry cell substance to CO_2, H_2O, and NH_3; and Y = yield of dry cell substance per g of substrate consumed). The hourly consumption of oxygen per g of dry cell substance present Q_{O_2} is the product of the absolute oxygen requirement C and the growth rate k. For example, the hourly oxygen consumption for the formation of gluconic acid with *Pseudomonas ovalis* is 6.2 ml of O_2/100 ml h [6]. In the submerged formation of acetic acid by *Acetobacter suboxydans*, the oxygen consumption is 55 ml of O_2/100 ml h.

The rate of supply of oxygen is determined by the rate of transfer through the liquid film at the air bubble/nutrient solution interface. This transfer, and hence the entire oxygen supply, can be represented in the form of the general oxygen transfer equation (cf. [7,8]). The rate of oxygen transfer is thus the product of three factors:

1) The oxygen concentration gradient between the liquid film and the mass of the liquid (this concentration gradient is the driving force of the oxygen transfer).

2) The transfer area, which corresponds to the total surface area of all the gas bubbles present in the liquid.

3) A transfer coefficient, which is not a constant, but depends essentially on the thickness of the interfacial film and on the state of the interface.

The transfer rate is a maximum when the concentration of the oxygen dissolved in the liquid mass is zero, *i.e.* when the concentration gradient is greatest. However, the oxygen concentration must not fall to zero in cell cultures, but must always be greater than the critical oxygen concentration, at which the cell respiration starts to become affected. If the concentration of the dissolved oxygen is kept slightly above the critical value for the cells being grown, the rate of oxygen supply in cell cultures is optimal, and the capacity of an aeration system is fully utilized [9].

The development of oxygen-metering equipment has been greatly promoted by the fermentations. Many devices for the continuous determination of dissolved oxygen in fermentation cultures have been described in recent years. These make use of three principles:

1) paramagnetic measurements; 2) measurements based on the polarographic principle; and 3) measurements based on the galvanic principle.

Of the many aeration systems developed, the devices used for microbiological fermentations can be placed in the following basic groups (cf. *e.g.* [8]):

1) Bubble column fermenters. The air is finely distributed into individual bubbles at the base of the tank, and these ascend in the fermenter. The air is distributed in some cases by static (Fig. 4a) and in others by rotating (Fig. 4b) and oscillating (Fig. 4c) devices.

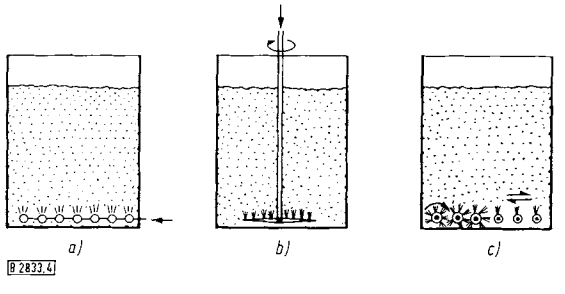


Fig. 4. Bubble column fermenters (from [8]).
a, aeration by jet pipes or sintered glass; b, rotational aeration; c, aeration by rotating or oscillating units.

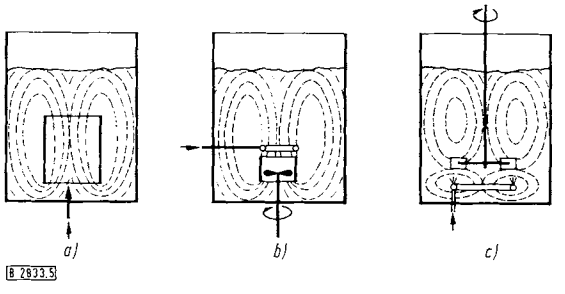


Fig. 5. Stirrer and air-jet fermenters (from [8]).
a, air distributor with guide cylinder; b, circulation of liquid under the aerator; c, circulation of liquid over the aerator (universal fermenter).

[5] *M. J. Johnson*, Chem. and Ind. *1964*, Sept. 5.

[6] *Sh. Aiba, M. Hara*, and *J. I. Someya*, J. gen. appl. Microbiol. (Tokyo) *9*, 163 (1963).

[7] *F. C. Webb*: Biochemical Engineering. D. van Norstrad, London 1964.

[8] *W. K. Bronn* in: Arbeitsmethoden und aktuelle Ergebnisse der technischen Mikrobiologie. Fischer Verlag, Stuttgart 1967, p. 45.

[9] *D. Hegner* and *H. Glossmann*, Z. Naturforsch. *20b*, 234 (1965).

2) Stirrer and air-jet fermenters. These have static fixed air distributors past which the liquid is pumped by built-in guide cylinders (principle of air lift pump) or stirrers (cf. Fig. 5).

3) Fermenter with rotating aerators. The air is distributed through hollow stirrers rotating at relatively high speed. Circular movement of the liquid is usually prevented by baffles on the walls of the container (cf. Fig. 6).

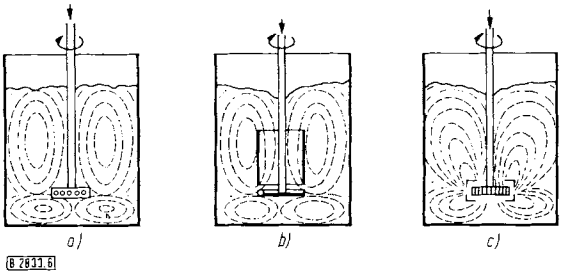


Fig. 6. Fermenters with rotating aerators.
a, hollow stirrer rotating freely; b, rotating aerator with guide cylinder; c, air sucked in by static inserts on the rotating aerator.

4) Shaking, rotating drum, vortex, and vibromix aeration. These types depend on movement of the culture liquid and absorption of oxygen from the air over the liquid (cf. Fig. 7).

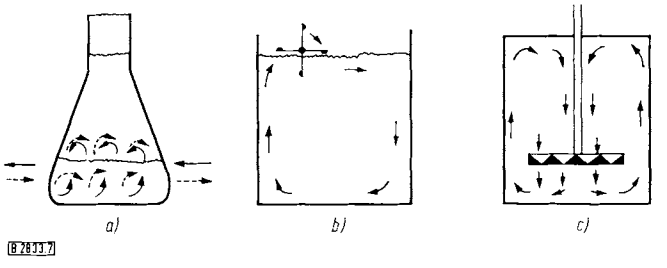


Fig. 7. Shaking, rotating drum, and vibro aeration (from [8]).
a, shaking flask; b, paddle aerator; c, vibromix aerator.

5) Surface aeration. In this case air is allowed to pass over the surface of the stationary culture solution (*e.g.* in the fermentation cup method) or is led past the solution by special devices (self-heating *e.g.* in the production of vinegar) (cf. Fig. 8).

It was only when a means of maintaining an adequate supply of oxygen to the microorganism cells in solutions had been found that it became possible to develop processes in which intensive biological oxidations could be carried out. Some examples are the sorbitol/sorbose oxidation with *Acetobacter* (including new biosyntheses for the production of vitamin C), the oxidation of ethanol to acetic acid, and many other oxidations with *Acetobacter* species, as well as steroid oxidations, particularly 11α-hydroxylations by microorganisms of various genera (*e.g.* for the production of cortisone/hydrocortisone or estrogen preparations), and finally oxidations of cardiac glycosides, antibiotics, and other substances.

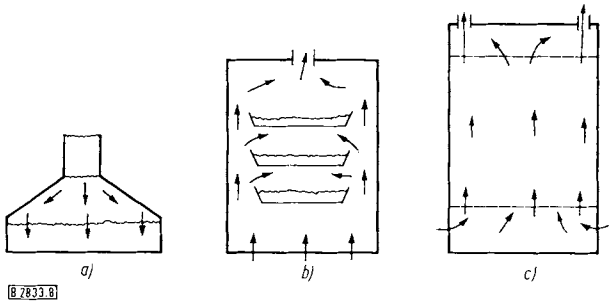


Fig. 8. Aeration of stationary surfaces.
a, stationary surface culture (Fernbach flask, penicillin flask); b, stationary surface culture (fermentation cups, enzyme production); c, filled tower.

5. Oxidations with High Oxygen Consumptions (Hydrocarbon Oxidations)

In the oxidation of steroids and of ethanol the microorganisms have a high oxygen consumption, but this can still just be satisfied by the aerators mentioned so far. Whereas only 33 moles of O_2 are consumed in the formation of 1 kg of cell material from 2.3 kg of glucose, about 75 moles of O_2 are necessary for the production of 1 kg of cell material from 1.1 kg of *n*-hexadecane [10]. This higher consumption is partly explained by the biochemistry of the oxidation of hydrocarbons. In this process a methyl group of a molecule that contains no oxygen is oxidized, first at one end and then possibly also at the other, to a carboxyl group, and ultimately, by continuous β or β and ω oxidation, to CO_2 and H_2O. If the degrading microorganisms are exposed to a reduced O_2 partial pressure, C_3, C_5, and C_7 fatty acids are formed in the substrate as intermediate products of incomplete degradation. For aromatic compounds we must first expect preoxidation, and then (as far as is known at present) three different types of ring cleavage, which can then lead by further oxidation to β-ketoadipic acid and finally also to CO_2 and H_2O.

The oxygen transfer in the four-phase system oil/water/microorganisms/air is a problem of primary importance. The more intensive the mixing of the air introduced with the substrate, the better is its utilization by the microorganisms. In many plants the air is finely emulsified in the substrate to provide the greatest possible surface and to allow optimum oxygen absorption for the oxidation of the hydrocarbons. Several types of fermenters have been developed for this purpose. In the multistage reactor of Chemap AG (Männedorf/Switzerland), for example, two-sided emulsifier wheels are fixed one above another on a central rotating shaft, and are surrounded by a multistage rotating tube with relatively fine outlet apertures (see Fig. 9). Midway between the wheels are large suction holes. At a speed of 2500 to 3000 rpm, the particle sizes of the insoluble phase are between 1 and 10 μm. The air supply can be increased to 5 v.v.m. [volumes of air/(volume of fermentation liquid × min)] in fermentations, so that oxidation

[10] *F. Wagner*, Lecture to Colloquium held at Botan. Inst. der Universität München 1969, unpublished.

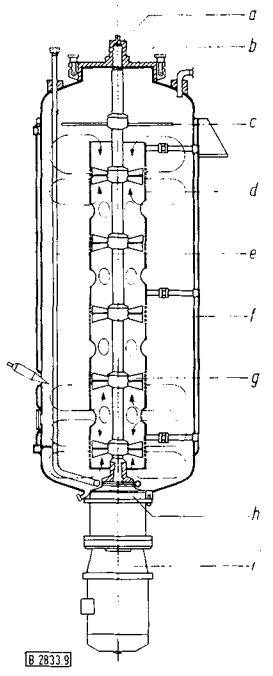


Fig. 9. Multistage reactor (Chemap AG).
a, top bearing; b, cover; c, defoamer; d, reaction tube with emulsifier and suction holes; e, gas feed tube; f, double jacket; g, multistage propeller shaft with double-sided wheels; h, lower bearing; i, motor.

rates of 350 mmole/l h can be obtained. Other less complicated types allow aeration rates of 1 to 2 v.v.m. and oxidation rates of 150 to 200 mmole/l h.

The removal of the large quantities of foam formed during the extremely intensive aeration and motion is particularly important in such processes. When the usual defoaming agents are used, however, there is a danger of oxidation by the microorganisms (*e.g.* in the case of fats and oils), or else the substances must be separated later, and are also very expensive (silicone oils). A design that has given good results is a mechanical foam separator (cf. Fig. 10) in which inverted conical plates are fitted to a rotating hollow shaft. The defoaming action is increased by radial

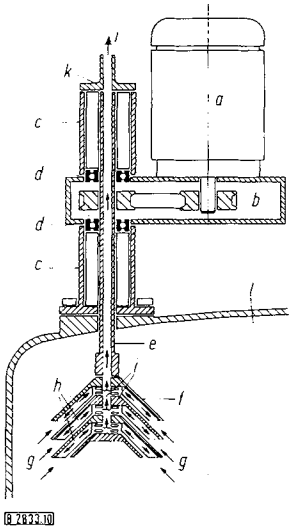


Fig. 10. Mechanical foam separator (Chemap AG).
a, motor; b, belt drive; c, slide ring seal, pressure equalizer; d, bearing; e, hollow shaft; f, rotating plate; g, foam inlet; h, liquid outlet; i, gas outlet; k, bearing housing with cooler; l, contents of tank.

baffles in the plates. The gas/liquid mixture passes upward in the fermenter into the rotating plate. Because of the speed of rotation, the liquid is thrown back into the fermenter vessel, while the lighter gas is forced through the hollow shaft and can escape.

Further problems are presented by the nature of the carbon source and the separation of the microorganisms from the oily substrate. Various industrial processes suitable for the oxidation of hydrocarbons can be derived from such biological fermentations with high oxidation rates, as is shown by the following examples:

1) One-step oxidation of pure paraffins. In these processes the paraffins have already been separated from other petroleum fractions. Such a process is currently being developed with yeast (species of *Candida* and *Torula*) by BP in Scotland.

2) One-step oxidation of paraffins without previous separation from the petroleum. The microorganisms in this case have the tasks of producing protein, *i.e.* cell material, on the one hand and freeing the petroleum from paraffins on the other. In a second stage the petroleum is processed further after separation of the microorganisms. BP are at present building a plant of this type in Southern France with a capacity of 16000 t/year, which is planned to start operation in 1970.

3) Multistage and complete microbial oxidation of petroleum. The long-chain paraffins are oxidized in the first stage, the cycloparaffins in the second, and the aromatic compounds in the third. Processes of this type are not very far advanced at present, and practical difficulties are being encountered because of the long times required for the oxidation of the aromatic compounds. One-step processes are also possible.

4) Production of metabolites (particularly secondary) from petroleum fractions. These processes are mostly one-step with respect to the carbon source. Paraffins that have already been separated from the petroleum are being used at present. The large-scale microbiological production of glutamic acid and 5'-nucleotides has already been in progress in Japan for several years. The industrial microbiological production of salicylic acid from naphthalene in the USA shows that there are also good prospects for the use of aromatic hydrocarbons as carbon sources for microorganisms.

These processes mark an entirely new development of microbiological fermentations. Many new secondary metabolites of microorganisms will soon be produced from hydrocarbons, and suitable processes for the various microorganisms and groups of substances will be devised.

6. Promotion of Certain Phases of Microorganism Growth

Once the various phases of microorganism growth in industrial fermentation plants had been established, the next problem was to prolong the phase in which

the desired metabolite is formed as much as possible or to intensify activity in this phase in order to optimize the yield of this product and to minimize the often expensive secondary cultivation of cell material. Semicontinuous and continuous culture processes were developed for this purpose.

6.1. Semicontinuous Culture

The submerged culture mentioned earlier is carried out in batches, *i.e.* a tank is filled with substrate and inoculated. After the fermentation, the entire contents of the tank are emptied out and the operation is started anew. If part of the fermented solution is held back for inoculation of the fresh nutrient solution, the first step has been taken toward continuous fermentation, since part of the microorganisms grows continuously, provided that the fermentation of the "inoculation liquid" retained has not been interrupted.

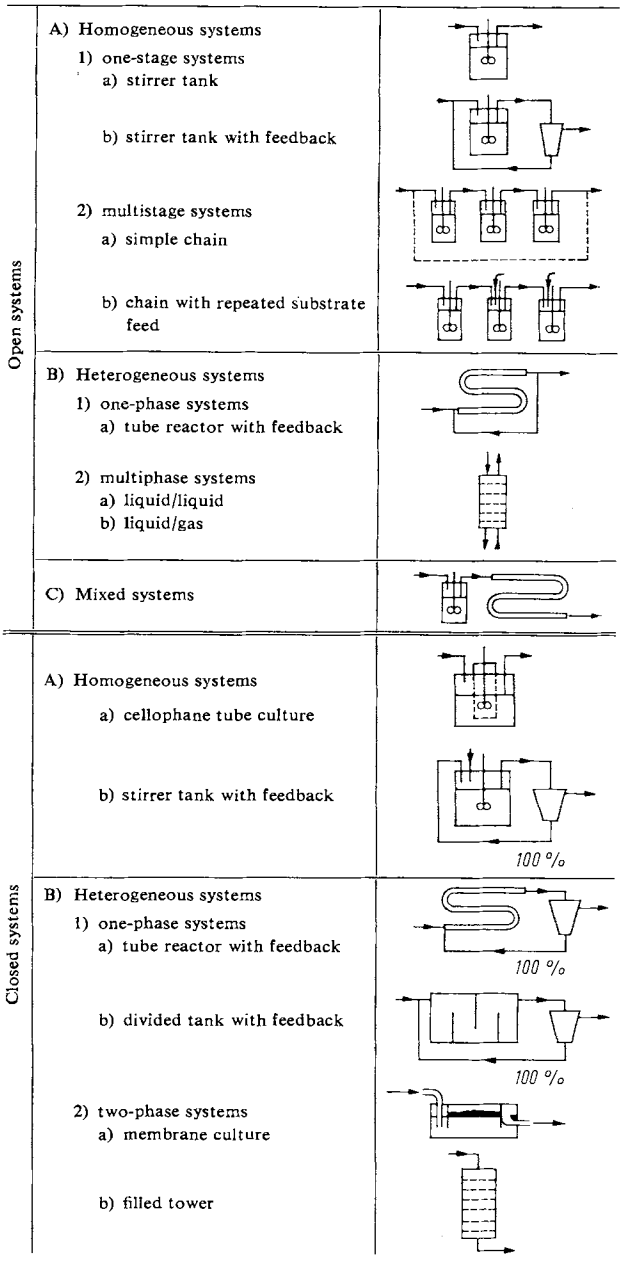
A "semicontinuous process" of this type has proved effective *e.g.* for the production of vinegar, and has led to a complete change in the microbiological methods commonly used for this purpose [11]. In this process, which was developed by Messrs. Heinrich Frings (Bonn/Germany) only about 60% of the contents of the tank are discharged after the fermentation (*i.e.* the oxidation of ethanol to acetic acid) is complete, and the remaining 40% are left in the tank with the microorganisms (*Acetobacter suboxydans*). The tank is then refilled with fresh nutrient solution. Since the microorganisms are extremely sensitive to ethanol and acetic acid if insufficient oxygen is present, aeration is necessary during the discharging and refilling operations. An oxygen utilization of 70 to 80% is achieved by intensive mixing of air with the liquid. Using this method, vinegar can be produced with an acetic acid content of 12%. The alcohol content in the acetator is determined with an Alcograph, and when it reaches a value of 0.1 to 0.3% an automatic discharge mechanism is started up. This causes part of the contents of the tank to be drawn off, and fresh nutrient is added to the remainder.

6.2. Continuous Culture

If the fresh nutrient solution is added continuously instead of in batches, fermented nutrient solution must be drawn off at the same rate.

In one-stage continuous fermentation only a stirring fermenter is used (cf. Table 1). In this fermenter the growth of the microorganisms begins as in a batch plant. At a suitable moment, *e.g.* almost at the end of the exponential growth phase, fresh nutrient solution is allowed to flow into the tank, and an equal quantity of fermentation product is simultaneously allowed

Table 1. Continuous fermentation systems (from [3]).



to flow out. These methods are suitable for processes in which the object is to obtain either large quantities of microorganism cells or substances that are formed in the exponential growth phase.

In multi-stage continuous fermentation, a set of tanks are connected in series with one another. A fermentation is started up in the first tank, and the introduction of fresh substrate is started at a suitable instant. The overflow is not collected for isolation of the product, but is allowed to continue its fermentation in the second tank, until this is also full. A third tank is then filled with the overflow, and so on. In a series of this type one stage can be specially promoted, or suitable precursors may be added in certain stages.

There are also other continuous systems, among which filled towers (Table 1) are important in the fast production of vinegar, and will undoubtedly be important in the future for the fermentation of gaseous

[11] *H. Ebner* in: Arbeitsmethoden und aktuelle Ergebnisse der technischen Mikrobiologie. Fischer Verlag, Stuttgart 1967, p. 65.

products. In this system the microorganisms are grown on a solid support inside the tower. The nutrient solution trickles down over the microorganisms, and a gas (*e.g.* oxygen or gaseous hydrocarbons) is brought into contact with the microorganisms in countercurrent from the bottom. Two gases may also be used, *e.g.* a heavy gas from the top and a light gas from the bottom; in most cases a liquid must also be allowed to trickle downward as the nutrient solution.

Cellophane cultures or cultures in dialysis vessels are still difficult to carry out continuously for industrial purposes. The microorganisms are grown in the dialysis vessel (Cellophane) which is immersed in a tank containing concentrated nutrient solution. The nutrient solution diffuses through the Cellophane membrane to the microorganism culture under the influence of the concentration gradient, while the metabolites diffuse out.

A new thin layer fermentation plant has been developed by *Gorbach* [12]. The microorganisms are grown on rollers in a pipe system, which dips into a nutrient solution on rotating (cf. Fig. 11). The thin layers of microorganisms can be intensively aerated in this process. Removal of the metabolism products and the introduction of nutrients are also very easy. The plant, which operates continuously, can be considerably increased in size by the use of a large number of tubes, and can also be automated.

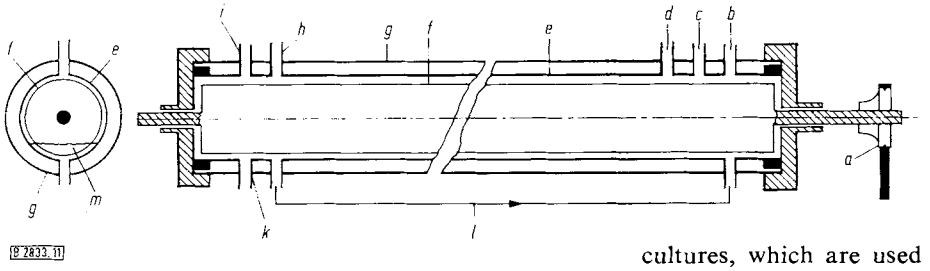


Fig. 11. Thin layer fermentation reactor (after [12]).
a, drive; b, nutrient solution inlet; c, air inlet; d, introduction of additional nutrient solution and pH control; e, fermentation tube; f, drum; g, heating and cooling jacket; h, air outlet; i, foam outlet; k, outlet for transformed nutrient solution and microorganisms; l, microorganism return; m, immersion of drum in nutrient solution.

The trend toward continuous fermentation has resulted in a number of industrial developments. Since the periods of uninterrupted operation must be as long as possible, the provisions for sterility in the fermentation plants must be better than in plants for batch operation. The nutrient feed and the growth of the microorganisms must also be carefully matched. This is ensured by external or internal control systems. With external control systems the rate of growth of the microorganisms is kept somewhat below the maximum by limiting the nutrient concentration ("chemostat"). With the internal control system, which is particularly suitable for high growth rates, the density of the population is measured and used as a basis for the control of the feed of nutrient solution ("turbidostat"). In view of the many parameters involved in the continuous system, it seemed feasible to use analog computers to control and optimize the fermentation. Experiments with this in view have already yielded promising results.

Continuous processes have long been established in practice for the cultivation of cell material (yeasts, algae, *etc.*). However, they have so far been used only in a few sectors for the production of primary and secondary metabolites, though *e.g.* dextran, antibiotics, fermentation products (including beer), oxidation products, amino acids, vitamins, and organic acids can be produced continuously. Nevertheless, once our knowledge in this field has been extended, continuous fermentation will probably be preferred in the future.

7. Cultivation of Very Sensitive Cells

Since microbiological methods are used in the cultivation of cells and tissues, this is generally regarded as belonging to the realm of microbiology. Despite the difficulty of maintaining the sterility of the equipment for the production of suitable substrates, it is already possible to grow a whole range of animal cells and very sensitive microorganisms, *e.g.* tetanus bacilli (for antitoxin production), by submerged culture in fermenters. The animal cells are used for the cultivation of viruses or for the production of cell cultures, which are used in turn for the testing of cancer-inhibiting substances.

Vibration systems are used instead of stirring systems for the cultures, since the conventional propellor

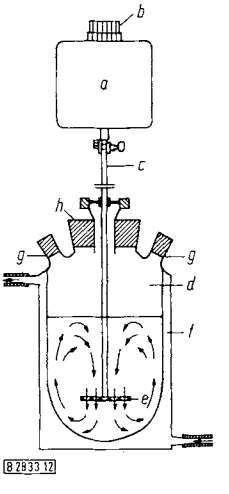


Fig. 12. Vibromix fermenter (Chemap AG).
a, motor; b, speed regulator; c, stirrer shaft; d, fermentation vessel; e, vibration plate; f, water jacket for cooling and heating; g, inoculation points (+ air inlet); h, opening for nutrient solution (↑ air inlet).

[12] *G. Gorbach*, Fette, Seife, Anstrichmittel *71*, 98 (1969).

stirrers would cause excessive damage to the cells. The action of the vibromixer shown in Figure 12 is based on the Bernoulli effect. Instead of a stirrer, the shaft inside the vessel is fitted with a plate having holes that taper in the downward direction. The plate is made to oscillate up and down, and so produces pressure differences in the holes, with the result that the liquid flows from the wide end to the narrow end of the holes. This ensures adequate movement of the cells and minimizes cell damage of the type caused by stirrers.

Since the metabolism products of growing cells are mostly the cause of cessation of growth of the cell cultures, *G. B. Gori*[13] developed a process for dialysis of the toxic metabolism products (see Fig. 13). A laboratory apparatus with an effective volume of 300 ml gives generation times of 40 to 50 h with high cell densities of up to 2.0 to 5.0 million cells/ml.

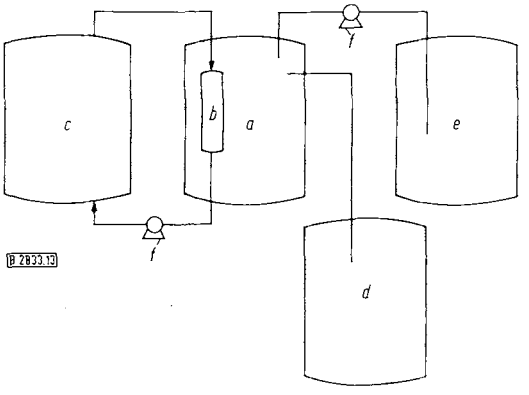


Fig. 13. Apparatus for continuous growth of animal cells in the submerged process with dialyzer (from [3]).

a, fermenter; b, dialysis membrane; c, reservoir for dialysis solution; d, reservoir for collected cells; e, reservoir for eluent; f, pumps.

The need for animal cells will undoubtedly increase greatly if it is desired to use apathogenically grown viruses which can only be cultured on animal cells, *e.g.* in aerosols for the mass immunization of whole population groups, as they are being used at present for the immunization of farm animals.

8. Continuous Culture of Hydrogen-Oxidizing Bacteria

Another group of microorganisms, known as hydrogen-oxidizing bacteria (species of *Hydrogenomonas*), can be used for the production of microorganism proteins. In a synthetic nutrient solution containing nitrogen, with CO_2 as the only carbon source and molecular hydrogen as the hydrogen donor, these bacteria produce organic substances, including proteins, as cell material under aerobic conditions. The oxidation proceeds with the aid of a hydrogenase in accordance with the following scheme:

$$\begin{array}{lll} 2\,H_2 + CO_2 & \rightarrow & (CH_2O) + H_2O \\ 4\,H_2 + 2\,O_2 & \rightarrow & 4\,H_2O \\ \hline H_2 + 2\,O_2 + CO_2 & \rightarrow & (CH_2O) + 5\,H_2O \end{array}$$

Thus the hydrogen-oxidizing reaction is carried out very slowly by the microorganisms. The resulting energy is used for the reduction of CO_2.

The introduction of the hydrogen-oxygen mixture into the bacterial culture in this fermentation is currently presenting a technical problem in large-scale plants. *Schlegel et al.*[14] have developed a continuously operating laboratory apparatus in which water is converted electrolytically into $H_2 + O_2$ in the nutrient solution itself, which contains no NaCl (cf. Fig. 14). Since some of the hydrogen is used for the reduction of CO_2, the corresponding part of the oxygen formed by electrolysis is available for other purposes. If CO_2 from the air were used in the plant, it could be developed as an air-regeneration system. Approximately 100 l of such a culture would be enough to regenerate the respiration air for one person. However, no suitable apparatus designs have been produced as yet.

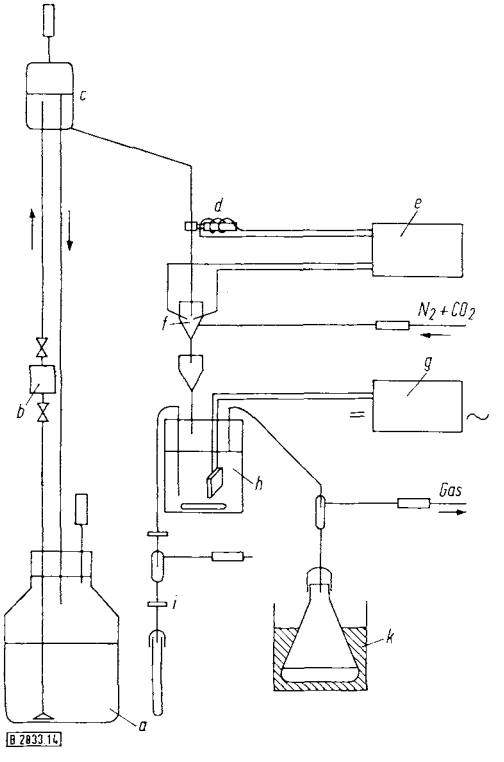


Fig. 14. Plant for continuous cultivation of hydrogen-oxidizing bacteria (after [4], taken from [3]).

a, storage vessel; b, pump; c, leveling vessel; d, magnetic valve; e, timer; f, contact; g, constant current source; h, H_2O electrolysis cell as fermenter; i, sampler; k, collecting vessel in cooling bath.

9. Production of Electrical Power by Microorganisms

Bacteria can change the redox potential of the nutrient substrate or its hydrogen-ion concentration, and can thus form a biological "half-cell" under certain

[13] *G. B. Gori*, Appl. Microbiol. *13*, 909 (1965).

[14] *H. G. Schlegel, F. Schuster*, and *Ch. König* in: Arbeitsmethoden und aktuelle Ergebnisse der technischen Mikrobiologie. Fischer Verlag, Stuttgart 1967, p. 73.

circumstances. A sterile medium can form another half-cell, which may be connected to the microorganism half-cell *e.g. via* a KCl/agar bridge to form an electric cell. The electric energy is produced by the metabolic activity of the microorganisms. Organic substances are oxidized, and the electrons ultimately flow to the oxygen.

Since the electron transport is not continuous but proceeds in steps, conditions must be provided such that a build-up of electrons is avoided, *i.e.* such that an electron flux occurs. A redox cell system with glucose as the substrate (combustion energy) and sea

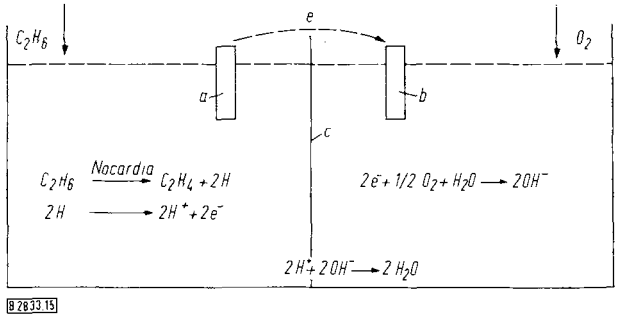


Fig. 15. Scheme of a cell for the biological production of energy (from [3]).

a, anode; b, cathode; c, semipermeable membrane.

water or other salt solutions as electrolytes may be regarded as a very simple form of half-cell (cf. Fig. 15). Gaseous hydrogen may be used instead of glucose as the fuel. Systems of this type have been tried with various microorganisms (*e.g. Escherichia coli, Desulfovibrio desulfuricans*, algae, and yeasts).

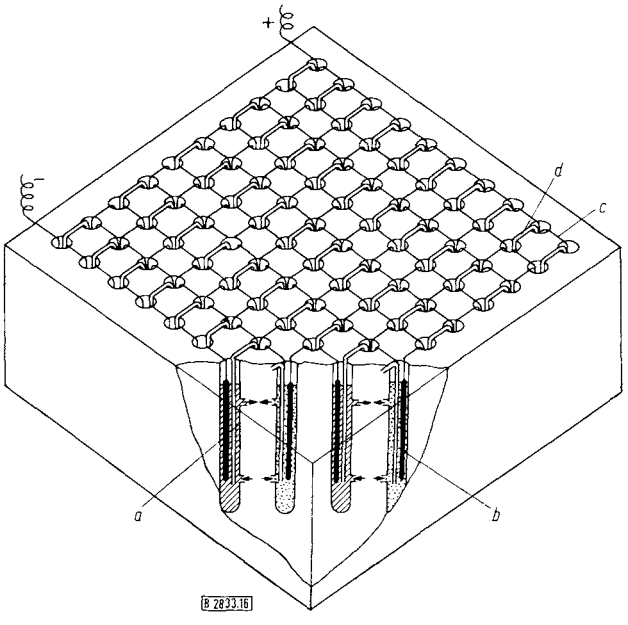


Fig. 16. System of biochemical-biological energy cells (from [3]).

a, tubes with reducing contents; b, tubes with oxidizing contents; e, wire; d, KCl/agar bridge.

Enzymes may be used instead of microorganisms. Thus a urease system by which NH_3 is formed from pure urea or from urine has proved suitable for this purpose. The anode consists *e.g.* of nickel, and the cathode is a glass cell with a fitted carbon stopper at the end, on which cathodic material such as aluminum is sprayed to produce an electrically active surface. An output of 20 W at 28 V has been obtained with a battery of 64 such cells (cf. *e.g.* Fig. 16). About 17 g of urea and 13.6 g of O_2/h were consumed over a working time of two weeks. Microbiological energy cells are still in the development stage at present, but they could be very important some day if naturally occurring reducing substances such as methane or ethane, or even effluent, could be used in this way for the direct production of electricity. This would present a totally new field of industrial microbiology.

10. Conclusions

In view of the quantity and diversity of the microbiological processes that are already being carried out, as well as those that seem promising or are still prospects for the "remote" future, it has only been possible to give a few examples in this review. Thus, no mention has been made of the mass growth of algae (which presents special technical problems), the submerged cultivation of mushrooms, attempts to obtain sulfur by industrial microbiological processes from water containing sulfate, sulfite, or hydrogen sulfide, and many other industrial microbiological processes. Many interesting metabolism products are being produced at present from and with the aid of microorganisms. However, there are also innumerable biochemical-microbiological reactions that could be utilized in practice, but which cannot be exploited at present. There are many reasons for this. One important reason is that most engineers who have the experience and know-how to develop an industrial microbiological process lack the necessary biochemical knowledge, while those who possess the biochemical knowledge do not know whether the development of these reactions might be of interest or which technical lines should be pursued. A future aim should therefore be to close the gaps by suitable training, to rise above classical fermentation technology, and to build up a modern science of biochemical-microbiological engineering.

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NMR Spectroscopy of Paramagnetic Complexes

By Karl E. Schwarzhans[*]

Serviceable NMR spectra can, with a few exceptions [1,6], be recorded for paramagnetic complexes in solution. These spectra provide information about the structure of the complexes and the distribution of the unpaired electrons, and hence also about reactive centers in the molecule. The elucidation of intermolecular and intramolecular exchange phenomena, e.g. the determination of ligand exchange rate constants, the determination of rotation barriers, and the detection of contact complexes in solution, or even of occupation equilibria of the electrons, is possible in this way. It can be seen, therefore, that NMR studies on paramagnetic complexes can be a rich source of information.

1. Introduction

The investigation of paramagnetic compounds with the aid of nuclear magnetic resonance was ignored during the first decade of the application of this spectroscopic method to chemical problems. It is now known that NMR spectra can be recorded for nearly all paramagnetic complexes [1]; exceptions are rare. In general, however, the spectra of paramagnetic metal complexes are not so well resolved as those of corresponding diamagnetic compounds; nucleus-nucleus coupling is rarely observed is such spectra [2, 3]. The half-widths of the NMR signals are between 1 Hz and several thousand Hz for dissolved paramagnetic species. Like the half-widths, the shifts of the signals also extend in part over a range that is several orders of magnitude greater than for the analogous diamagnetic compounds [4]. Roughly speaking, the shifts behave in the same manner as the susceptibilities of these compounds.

The first report of an investigation on the ^{1}H-NMR spectra of (dissolved) paramagnetic complexes was published in 1958 [5]. Since then, the number of publications on this subject has increased to about 400. The theoretical principles of the application of NMR spectroscopy to the study of paramagnetic substances have been described by various authors (cf. *e.g.* [6–10]).

Several mechanisms have been detected by which the nuclei examined by NMR spectroscopy in metal complexes can be influenced by unpaired electrons. The effects can be roughly divided into two groups, *i.e.* signal shifts due to Fermi contact interactions and those due to pseudo-contact interactions. Since it is only possible occasionally to distinguish between the contributions of the various mechanisms to the total shift of a given NMR signal, it has recently been suggested [3] that signal shifts in the NMR spectra of paramagnetic compounds should be referred to generally as "Knight shifts" [11]. This name has the advantage that it does not specify any mechanism that contributes to or is alone responsible for the shift, as is the case in the terms "contact shift" and "pseudo-contact shift". The Knight shift is thus defined as the difference in shift between the signals of the paramagnetic complex and the corresponding diamagnetic model compound. This definition naturally excludes any effect of ligand exchange on the shift of the signal.

The mechanisms of electron-nucleus interaction that may be regarded as established for paramagnetic metal complexes will be outlined below.

1.1. Fermi Contact Interaction

The Fermi contact interaction is defined as the interaction of the nucleus in question with the density of unpaired electrons on the nucleus.

If this Fermi contact interaction essentially causes shielding of the nucleus in question, and hence a shift of its signal, "unpaired electron density" (also known as spin density) could conceivably reach the position of the resonating nucleus, or could in general reach the ligands of a paramagnetic metal complex, in the following ways:

(a) Unpaired d electrons of the metal fill unoccupied antibonding orbitals of the ligands that have σ- or π character. This mechanism is involved in particular

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in the signal shifts in the NMR spectra of titanium(III) and vanadium(III) complexes[12]. Typical features pointing to an important contribution from this electron delocalization mechanism can also be found in the spectra of pyridine, pyridine *N*-oxide, and picoline adduct complexes of many 3d metals[13–15]. A particularly good example of the delocalization of spin density into the π system of the ligand is provided by the bis(2-amino-2,4,6-cycloheptatrieniminato)-nickel(II) complexes[16] (cf. Fig. 1).

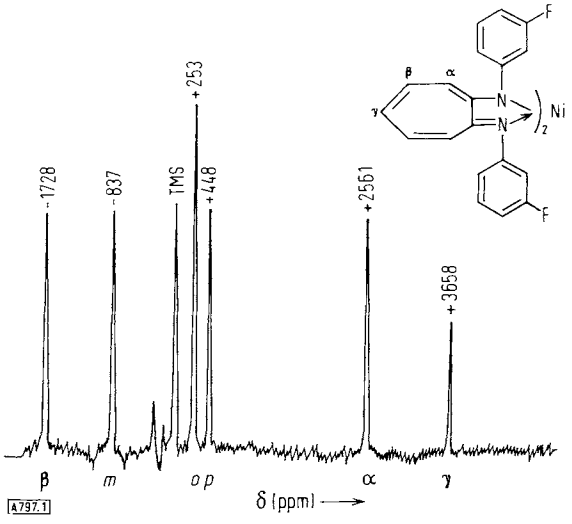


Fig. 1. ^{1}H-NMR spectrum of a bis(2-amino-2,4,6-cycloheptatrieniminato)nickel(II) complex in $CDCl_3$ (40 MHz).

These complexes are characterized by a very fast configuration change in solution between a square-planar diamagnetic form and a tetrahedral paramagnetic form. All the following mechanisms that can contribute to the Knight shift are averaged out by this process. The electrons of the C–H bonds are polarized by the free spin density[*] in the π system of the ligand in such a way that the spin density on the proton of the aromatic ligand is negative (shift to higher fields) for even numbers and alternately negative and positive (shift to lower fields) for odd numbers.

(b) Electrons in the highest occupied orbitals of the ligand or ligands are partly transferred into unoccupied or unfilled d orbitals of the metal. This transfer mechanism is possible in particular for the more highly charged ions of the 3d metals. A positive spin density also remains in the ligand orbitals, so that it is often practically impossible to distinguish between mechanisms (a) and (b).

(c) Partly occupied d orbitals of the metal overlap with occupied orbitals of ligand atoms having a sterically favorable arrangement, but which are not bonded directly (in the conventional sense of a chemical bond) to the metal atom or ion. This "direct interaction" is probably responsible *e.g.* for the strong negative shifts of the signals in the ^{1}H-NMR spectra of substituted and unsubstituted bis(cyclopentadienyl) complexes of vanadium(II) and chromium(II)[17]. In these compounds, positive spin density is transferred directly from the transition metal ion to the protons of the cyclopentadienyl rings, with the result that the signals of these protons are displaced by up to 360 ppm toward lower fields. Another very instructive example of the occurrence of a "direct interaction" is found in the ^{1}H-NMR spectra of iminodi(trimethyleniminomethyl-*o*-phenolato)-cobalt(II) (Fig. 2) and of the corresponding nickel(II) complex. Geminal protons in the alkyl chains of these compounds exhibit differences of up to 86 ppm in their shifts[18,19].

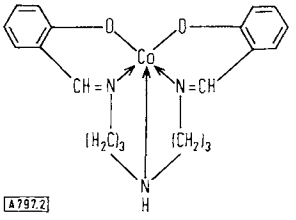


Fig. 2. Structural formula of iminodi(trimethyleniminomethyl-*o*-phenolato)cobalt(II).

Several reports dealing with the separation of the contributions of the types (a) to (c) to the Fermi contact shift for certain classes of complexes have been published during the past few years[12,20–26]. The clarification of this problem would enable information about the metal-ligand bond to be gained from the signal shifts of certain ligand nuclei.

1.2. Pseudo-Contact Interaction

The investigation of the NMR spectra of paramagnetic compounds is frequently made difficult by the fact that intramolecular (and also intermolecular in studies on solids) dipole-dipole interactions influence

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[*] The absolute probability of finding an unpaired electron at a given point is known in general as the "free spin density".

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the magnitude and sign of the shifts of the resonance signals in an extremely complicated manner that can only be determined in particularly simple cases. In complexes with extensive delocalization of electrons, the pseudo-contact contribution to the total shift of the resonance signals should be small, since the pseudo-contact model [27] is based on the assumption of a point charge localized on the central metal ion. It is not yet known, however, how much zero-field splitting, which is a property of all complexes with more than one unpaired electron, contributes to the pseudo-contact component of the shift. Information on this point should be obtainable from ESR experiments at very low temperatures [28].

2. Application and Results

Hetero-NMR measurements on paramagnetic complexes in solution have so far been confined to a few investigations on simple systems. For example, ^{17}O- and ^{14}N-NMR spectra of hexaaquo and hexaammine complexes respectively have been recorded for the determination of ligand exchange rates in these compounds [29, 30]. NMR experiments in which different types of atoms in a paramagnetic molecule are detected are therefore particularly interesting.

2.1. Investigations on Pyridine and Picoline Adducts of Bis(salicylaldehydato)iron(II), -cobalt(II), and -nickel(II)

Pyridine and simple methyl derivatives of pyridine form 2:1 adducts with paramagnetic bis(salicylaldehydato)metal(II) complexes, and these adducts are particularly suitable for NMR studies. They have a simple ligand system in a pseudo-octahedral arrangement, and are very readily soluble in organic solvents. The pyridine and picoline ligands readily undergo exchange with excess ligands, and this greatly facilitates the assignment of the resonance signals. Kinetic data for this exchange can also be determined from NMR studies.

2.1.1. ^1H-NMR Spectra

The data from the ^1H-NMR spectra of such adducts (Fig. 3) are presented in Tables 1 to 3. The assignment for the pyridine protons was possible on the basis of the signal intensities, by comparison of the spectra of the pyridine adducts with those of the β-picoline and γ-picoline adducts, and finally on the basis of the changes produced in the spectra by an exchange process on addition of small quantities of pyridine or picoline in excess. If the exchange frequency is very much greater than the difference in shift in Hz between the signals of the protons of the pyridine ligand in the paramagnetic complex and of free pyridine, an averaged signal appears in the NMR spectrum [31] at a position that depends on the ratio of the concentrations of the free ligand and of the complex. The ring protons of the salicylaldehyde ligands were assigned by comparison with the spectra of the derivatives with methyl substituents in position 3, 4, 5, or 6 of the ring [19]. The assumption that the symmetry of the complex changes only slightly on substitution appears to be confirmed by the invariance of the signal shifts of the pyridine and phenylene protons in the substituted and unsubstituted complexes.

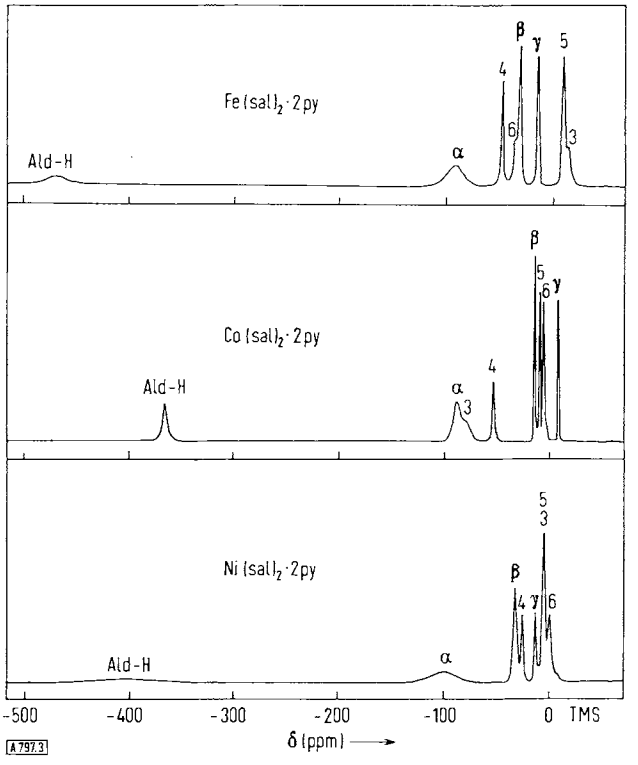


Fig. 3. ^1H-NMR spectra of bis(salicylaldehydato)bis(pyridine)metal(II) complexes in $CDCl_3$ (100 MHz).

The large shifts of the aldehydic protons, which change only slightly on substitution in the aromatic ring of the salicylaldehyde ligand are a characteristic feature of all the spectra.

Except in the case of complexes substituted in position 6 of the salicylaldehyde ligand (Fig. 4), the equivalent protons of the ligands generally give only one NMR signal. Methylation in position 6 evidently leads to moderate distortion of the complex. Separate resonance signals are found both for the two CH_3 groups and for the two aldehydic protons. A much greater distortion of the complex should be observed on replacement of the pyridine ligand by α-picoline.

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Table 1. ^{1}H-NMR data for paramagnetic pyridine and picoline adducts of bis(salicylaldehydato)iron(II) complexes. Shifts in Hz against internal TMS at 100 MHz. Saturated solutions in $CDCl_3$ at 32 °C.

	$Fe(sal)_2 \cdot 2$ py	$Fe(3\text{-sal})_2 \cdot 2$ py	$Fe(4\text{-sal})_2 \cdot 2$ py	$Fe(5\text{-sal})_2 \cdot 2$ py	$Fe(6\text{-sal})_2 \cdot 2$ py	$Fe(sal)_2 \cdot 2\,\beta$-pic	$Fe(sal)_2 \cdot 2\,\gamma$-pic
α	−9160	−9330	−8600	−8900	−9070	−7800	−7130
β	−3230	−3121	−3080	−3140	−3300	−3200	−3050
β-CH_3						−1130	
γ	−1460	−1920	−1458	−1340	−1602	−1750	
γ-CH_3							+50
C^3–H	+1300		+1300	+1290	+1100	+720	+720
C^3–CH_3		−1740					
C^4–H	−4810	−4460		−4950	−5646	−5440	−5390
C^4–CH_3			+1560				
C^5–H	+956	+986	+862		+750	+310	+350
C^5–CH_3				−2745			
C^6–H	−3270	−2860	−3241	−3360		−4010	−3950
C^6–CH_3					+340		
					+1430		
Ald-H	−46700	−43400	−45150	−47300	−48100	−46600	−48200
					−45300		

3-sal = 3-methylsalicylaldehydate, py = pyridine, pic = picoline.

Table 2. ^{1}H-NMR data for paramagnetic pyridine and picoline adducts of bis(salicylaldehydato)cobalt(II) complexes. Shifts in Hz against internal TMS at 100 MHz. Saturated solutions in $CDCl_3$ at 32 °C.

	$Co(sal)_2 \cdot 2$ py	$Co(3\text{-sal})_2 \cdot 2$ py	$Co(4\text{-sal})_2 \cdot 2$ py	$Co(5\text{-sal})_2 \cdot 2$ py	$Co(6\text{-sal})_2 \cdot 2$ py	$Co(sal)_2 \cdot 2\,\beta$-pic	$Co(sal)_2 \cdot 2\,\gamma$-pic
α	−8300	−11200	−8300	−8750	−9330	−7700	−8150
β	−1540	−1770	−1940	−1150	−1720	−1620	−1460
β-CH_3						+170	
γ	+474	+570	+384	+1060	+510	+464	
γ-CH_3							+1634
C^3–H	−8200		−8250	−8940	−8460	−7700	−8150
C^3–CH_3		−8360					
C^4–H	−5580	−6670		−5530	−6450	−5720	−5480
C^4–CH_3			−2050				
C^5–H	−1150	−1350	−1610		−1250	−1040	−1060
C^5–CH_3				−1520			
C^6–H	−790	−130	−895	−700		−704	−760
C^6–CH_3					−1720		
					−310		
Ald-H	−36520	−35700	−36200	−36900	−43100	−33800	−34120
					−40600		

Table 3. ^{1}H-NMR data for paramagnetic pyridine and picoline adducts of bis(salicylaldehydato)nickel(II) complexes. Shifts in Hz against internal TMS at 100 MHz. Saturated solutions in $CDCl_3$ at 32 °C. The absorptions marked ? could not be assigned because of excess line width or overlap.

	$Ni(sal)_2 \cdot 2$ py	$Ni(3\text{-sal})_2 \cdot 2$ py	$Ni(4\text{-sal})_2 \cdot 2$ py	$Ni(5\text{-sal})_2 \cdot 2$ py	$Ni(6\text{-sal})_2 \cdot 2$ py	$Ni(sal)_2 \cdot 2\,\beta$-pic	$Ni(sal)_2 \cdot 2\,\gamma$-pic
α	−8650	?	−9130	−10450	−9730	−9350	−10700
β	−3370	?	−3180	−3440	−3230	−3350	−3640
β-CH_3						−682	
γ	−1440	?	−1360	−1470	−1330	−1250	
γ-CH_3							+703
C^3–H	−647		−590	−650	−560	−632	−674
C^3–CH_3		−840					
C^4–H	−2630	−3080		−2610	−2760	−2460	−2700
C^4–CH_3			−50				
C^5–H	−805	?	−690		−690	−746	−810
C^5–CH_3				−100			
C^6–H	−97	?	−120	−180		−84	−81
C^6–CH_3					−360		
					0		
Ald-H	−41200	?	−36100	−46720	−39400	?	?

However, no 2:1 adduct of α-picoline with any of the bis(salicylaldehydato)metal(II) complexes has yet been obtained. Axial entry of the α-picoline is presumably impossible in these compounds on steric grounds. If, however, measurements are carried out on an exchange system with α-picoline in solution together with bis(salicylaldehydato)bis(pyridine)-cobalt(II), all the proton resonance signals of the salicylaldehyde ligands split into doublets. The two aldehyde ligands in the complex are thus no longer magnetically equivalent, *i.e.* the symmetry of the dissolved complex is reduced. NMR studies on paramagnetic compounds can thus also serve as a sensitive test for changes in the geometry of the arrangement of the ligands, since the Knight shifts of the resonance signals, as was mentioned earlier, are strongly dependent on the arrangement of the ligands with respect to the central metal ion.

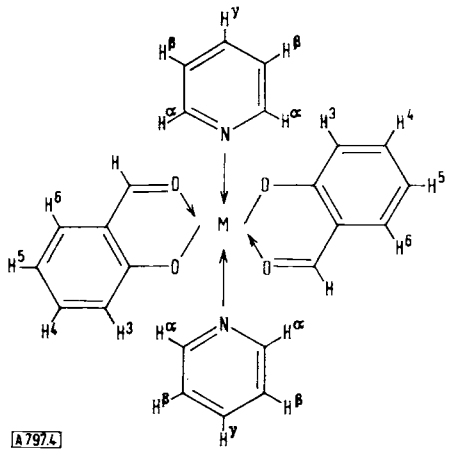


Fig. 4. Scheme of the structure of bis(salicylaldehydato)bis(pyridine) metal(II) complexes.

In a purely qualitative consideration of the ^{1}H-NMR shifts of this type of complex, the highest spin density is to be expected on the aldehyde grouping of the salicylaldehyde ligand. This position in the molecule should be particularly suitable for a free-radical reaction. The complexed salicylaldehyde is in fact oxidized by air to salicylic acid [32].

2.1.2. ^{14}N-NMR Spectra

The ^{14}N-NMR spectra of the bis(salicylaldehydato)-bis(pyridine)metal(II) complexes of iron, cobalt, and nickel could not be recorded with the pure compounds in solution. An important reason for this is the fact that the spectral sensitivity of the ^{14}N nucleus is lower by a factor of 10^3 than that of the proton. The complexes contain only a little nitrogen (about 6.1 %), so that even concentrated samples contain only a few ^{14}N nuclei. Moreover, because of the undoubtedly high spin density on the nitrogen atoms to be considered, the ^{14}N resonance signal is expected to be very broad [19]. It was possible to avoid both of these difficulties by measurements on the complex under the conditions of the exchange with excess pyridine. If the ^{14}N-NMR spectrum of pyridine is recorded with the addition of various quantities of the bis(salicylaldehydato)bis(pyridine)metal(II) complex, the shift of the ^{14}N signal varies linearly with the concentration of the complex in the case of the iron and cobalt compounds; for the analogous nickel compound, on the other hand, the ligand exchange rate constant must be much smaller. A Knight shift of −7800 ppm can be extrapolated for the Fe^{II} complex, and −5400 ppm for the Co^{II} complex, from the concentration dependence of the ^{14}N signals.

The ligand exchange rate constants found from these spectra, which merely indicate a lower limit for the exchange rate [33], differ only slightly for the two complexes ($k_{Fe^{II}} = 2.0 \times 10^5$, $k_{Co^{II}} = 1.8 \times 10^5$ Hz) [19]. The fall in rate constant from iron to nickel for exchange reactions on pseudo-octahedral complexes is a well-known phenomenon, and is associated with the ligand field stabilization energy in the trigonal-bipyramidal transition state [19, 34].

2.2. ^{1}H-NMR Studies on a Dimethylacetamide Adduct of Uranium Tetrabromide

Dimethylacetamide forms a 4:1 adduct with uranium tetrabromide. It was uncertain at first whether the bonding to the central metal ion occurs *via* the nitrogen or the oxygen atom of the ligand. Rotation about the C–N bond in free dimethylacetamide is hindered at room temperature; the two methyl groups on the nitrogen give different ^{1}H-NMR signals, showing that their chemical environments are different. If the spectrum is recorded at various temperatures the two signals of the $N-CH_3$ groups fuse at 49.8 °C, from which the height of the rotation barrier is found to be 12 ± 2 kcal [35].

Exactly the same behavior is found in the spectrum of the adduct. The two ^{1}H-NMR signals of the $N-CH_3$ groups, which are separated at lower temperatures, unite at 50 °C (Fig. 5). The height of the rotation barrier is therefore unchanged by the complex formation, and it follows that the dimethylacetamide cannot be bonded to the uranium ion *via* the nitrogen atom [36].

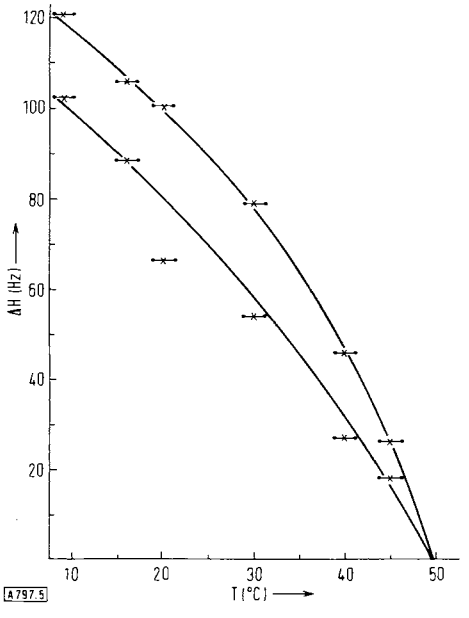


Fig. 5. Temperature dependence of the ^{1}H-NMR signal shifts of the $N-CH_3$ groups of dimethylacetamide in $(C_4H_9ON)_4UBr_4$ (dissolved in CH_2Br_2; 100 MHz).

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Because of the greater signal shifts in the ^{1}H-NMR spectra of the diamagnetic tetrabutylammonium and tetraphenylarsonium cations in solutions containing paramagnetic complex anions, such as hexacyanoferrate(III) or tetrachloroniccolate(II), a number of authors [37–42] postulated the presence of "ion pairs". The unusual signal shifts were attributed to pseudo-contact interaction, which depends on the *g*-factor anisotropy of the unpaired electrons and on the distance and the fixed steric relation between the ions [6].

However, there are three serious objections to such an interpretation of the ^{1}H-NMR spectra on the basis of ion associates of this nature:

(a) All the paramagnetic anions and diamagnetic cations investigated have approximately spherical symmetry. There is therefore no reason to insist on a preferred steric arrangement for the ions in solution over a long measuring period, which would be fundamentally necessary in order to be able to observe pseudo-contact shifts. Without a sufficiently long-lasting, definite relation between the paramagnetic ion and the nucleus that is interacting magnetically with it, the dipole-dipole contribution to the signal shift is averaged out. It is clear from the ^{1}H-NMR spectra of the ion associates, however, that a very much faster ion exchange takes place in the solution when the diamagnetic cation is present in excess.

(b) The octahedral and tetrahedral symmetries of the hexacyanoferrate(III), hexacyanochromate(III), and tetrachloroniccolate(II) anions [43] do not allow any anisotropy of the *g* factor, which is also an assumption for pseudo-contact interaction.

(c) In complexes with strong delocalization of electrons, as was mentioned in Section 1.2, the pseudo-contact contribution to the signal shift should be small or zero [27]. At least for the complex anions triiodotriphenylphosphanecobaltate(II) and triiodotriphenylphosphaneniccolate(II), however, the large shifts of the ^{1}H-NMR signals of the aromatic protons of the triphenylphosphane ligands point to strong delocalization of electrons in these compounds.

2.3.1. ^{1}H-, ^{14}N-, and ^{31}P–NMR Spectra

The ^{1}H-NMR spectra recorded for the diamagnetic cations of the ion associates (given in Table 4 for the tetrabutylammonium salt of triiodotriphenylphosphanecobaltate(II) at various concentrations) can be satisfactorily explained only if one postulates a direct transfer of spin density from the central metal ion of the anionic complex *e.g.* to the ammonium nitrogen atom.

Table 4. ^{1}H and ^{14}N Knight shifts (in ppm) of $(C_4H_9)_4N^+$ in $[(C_4H_9)_4N][CoI_3(C_6H_5)_3P]$ (dissolved in $CDCl_3$; 100 and 7.22 MHz).

c (mole/l)	H^α	H^β	H^γ	H^δ	^{14}N
1.07	4	1.4	1.4	0.4	−14.4
0.88	4	1.4	1.4	0.4	−13.5
0.71	4.2	1.4	1.4	0.5	−12.8
0.53	4.4	1.6	1.5	0.4	−13.0
0.26	5.0	2.0	1.7	0.5	−10.2
0.15	5.5	2.5	1.8	0.6	− 7.8
0.075	6.0	3.0	2.0	0.7	− 5.7
0.034	7.3	3.7	2.3	0.8	–
0.010	8.1	4.3	2.7	0.9	–
0.005	8.5	4.5	2.8	0.9	–
0.002	8.4	4.5	2.8	0.9	–
0.001	8.0	4.3	2.6	0.9	–

The monotonic decrease in the spin density transmitted along the σ bond skeleton of the carbon chain from the α- to the ω-C atom is typical of alkyl chains in paramagnetic transition metal complexes [44]. In $(C_4H_9)_4N^+$, the highest density of unpaired electrons should be localized on the nitrogen. On correct application of the pseudo-contact model [5, 27], a signal shift toward higher fields is to be expected for the nitrogen of the diamagnetic tetrabutylammonium ion [37]. In the case of a direct transfer of unpaired electrons from the central metal ion to the nitrogen atom, however, the ^{14}N resonance signal must be displaced to lower fields (negative sign) [42]. The positive spin density on the nitrogen atom would then pass over to the adjacent α-CH_2 group by configuration interaction [6].

Only shifts with negative signs were found for the ^{14}N and ^{31}P signals in the spectra of the ion associates with ammonium and phosphonium cations (Table 5).

Table 5. ^{14}N and ^{31}P Knight shifts of the diamagnetic cation in the ion associate (dissolved in $CDCl_3$; 7.22 and 40.5 MHz).

Compound	*c* (mole/l)	Shift (ppm) ^{14}N	Shift (ppm) ^{31}P
$[(C_4H_9)_4N]$ $[CoI_3(C_6H_5)_3P]$	0.53	−13	–
$[(C_4H_9)_4N]$ $[NiI_3(C_6H_5)_3P]$	0.52	− 7.1	–
$[(C_4H_9)_4P]$ $[CoI_3(C_6H_5)_3P]$	0.6	–	−3.5
$[(C_4H_9)_4P]$ $[NiI_3(C_6H_5)_3P]$	0.61	–	−5.1
$[(C_4H_9)_4N]_3$ $[Fe(CN)_6]$	0.7	−10.8	–

2.3.2. Discussion

The negative signal shifts that are always found in the ^{14}N- and ^{31}P-NMR spectra of the cations (Table 5) clearly show the transfer of positive spin density from the central metal ion of the anionic complex to the nitrogen or phosphorus atom. It can also be seen from Table 4 that the position of the ^{1}H-NMR signals of the cation is strongly dependent on the concentration, whereas the Knight shifts of the anion remain

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constant over the entire concentration range investigated. This is true of all the ion associates studied. In Figure 6, there are three easily recognizable regions at concentrations below 0.2 mole/l, in which the ratio of the change in shift to the change in concentration assumes different values.

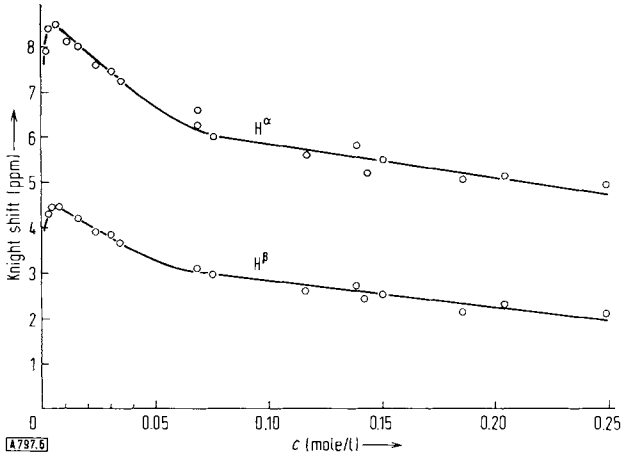


Fig. 6. Concentration dependence of the Knight shifts of the α and β protons of the tetrabutylammonium ion in $[C_4H_9)_4N][CoI_3(C_6H_5)_3P]$ (dissolved in $CDCl_3$).

This observation points to the presence of higher aggregates (associates), and is not compatible with the existence of "ion pairs" in solution. Such associates may be expected in solvents having low dielectric constants at relatively high salt concentrations [45]. There appear to be several definite aggregates, which evidently differ in their stability, and each of which is stable in a given concentration range.

2.4. ^{1}H-NMR Studies on the Occupation Equilibrium of the Electrons in Bis[4-(2-pyridyl)-2-(2-pyridylamino)-thiazolato]iron(II)

Complexes in which a temperature-dependent occupation equilibrium exists between the electronic ground state and nearby excited states are of interest in biochemistry. Examples of compounds belonging to this class are in the iron-porphyrin complexes, whose term diagrams show a change in the ground state with the nature of the other ligands as a result of crossover of two terms. The NMR-spectroscopic investigation of the anomalous magnetic behavior of such complexes is frequently found to be very difficult because of their extremely low solubility.

This anomalous magnetic behavior has been observed and studied by NMR spectroscopy for the electron configuration d^5 in dithiocarbamatoiron(III) complexes [46] and for the configuration d^7 in some chelate complexes of cobalt(II) iodide [47]. No example of such an anomaly is known as yet for the electron configuration d^4, while an iron(II) complex will be described here as a typical and confirmed example with the configuration d^6.

Though the anomalous magnetic properties of several bis(*o*-phenanthroline)iron(II) complexes [48] have been interpreted as a temperature-dependent quintet-singlet occupation equilibrium, the sudden change in the effective magnetic moment of these compounds at a certain temperature is definitely due to a phase change, *i.e.* to an intermolecular effect.

The complex bis[4-(2-pyridyl)-2-(2-pyridylamino)-thiazolato]iron(II) exhibits a characteristic decrease in its effective magnetic moment with falling temperature [49]. μ_{eff} is 4.96 μ_B at room temperature and 1.55 μ_B at −170 °C, and decreases steadily in the intervening range. If this behavior is due to an intramolecular effect, it can only be explained by the existence of a singlet-quintet occupation equilibrium, naturally with participation of interjacent triplet states in accordance with their energy levels. On the basis of the IR spectra recorded at various temperatures, it was possible to show that the magnetic anomalies of bis-[4-(2-pyridyl)-2-(2-pyridylamino)thiazolato]iron(II) are not due to any intermolecular effect [50]. Where a temperature-dependent occupation equilibrium exists between the singlet ground state and the lowest quintet state, the NMR spectra of the compound must show characteristic changes with temperature. The Knight shifts of the resonance signals of a paramagnetic compound are directly proportional to the density of the unpaired electrons on the nucleus in question, and inversely proportional to the absolute temperature [6–10]. Thus the signal shifts in the NMR spectra of paramagnetic substances normally increase with falling temperature. In our example, the effective magnetic moment decreases slowly with falling temperature, *i.e.* the singlet state becomes more highly populated and the free spin density in the molecule as a whole decreases. Two opposing effects are therefore operative in the spectrum of such a complex. In bis[4-(2-pyridyl)-2-(2-pyridylamino)-thiazolato]iron(II) at room temperature, the quintet state is predominantly populated (μ_{eff} = 4.96 μ_B). The Knight shifts of the resonance signals will therefore initially become larger with falling temperature, as is to be expected for any magnetically normal paramagnetic complex. Ultimately, however, the occupation of the singlet ground state becomes so high that the direction of the signal shift in the NMR spectrum is reversed; the Knight shifts thus pass through a maximum on cooling. The shifts then decrease rapidly with further population of the singlet ground state. This effect is shown in Table 6 for seven ^{1}H-NMR signals of the complex in question in the temperature range between +30 and −60 °C.

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Table 6. Shifts of the ^{1}H-NMR signals 1 to 7 of bis[4-(2-pyridyl)-2-(2-pyridylamino)thiazolato]iron(II) in relation to TMS (internal) toward lower fields with falling temperature (100 MHz).

T (°C)	Knight shift (Hz)					
	1	2	3	4	5/6	7
30	4630	4410	2810	2580	2210	865
20	4980	4700	2930	2695	2280	860
10	5120	4800	3020	2740	2380	915
0	5150	4850	3040	2780	2405	915
−10	5220	4880	3050	2820	2450	(960?)
−20	5245	4900	3050	2840	2450	915
−30	5120	4815	3000	2790	2410	905
−40	4970	4700	2920	2780	2405	875
−50	4600	4300	2645	2565	2210	750
−60	4200	4200	2350	2350	2020	660

The signal shifts of the protons, which are not assigned, are measured in Hz. All the resonance signals pass through a maximum at −20 °C. The variation of the shifts (measured in solution) with falling temperature is directly parallel to the molar susceptibility (measured in the solid state [49]). These experimentally observed anomalies of bis[4-(2-pyridyl)-2-(2-pyridylamino)thiazolato]iron(II) are thus not due to an intermolecular effect, but they can be plausibly explained by a temperature-dependent occupation equilibrium of the electrons between the $^1A_1$ ground state and the energetically nearby excited $^5T_2$ state, *i.e.* by an intramolecular effect.

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COMMUNICATIONS

Photoelectron Spectrum of Cyclobutane[1]

By *Peter Bischof, Edwin Haselbach,* and *Edgar Heilbronner*[*]

The vertical ionization potentials I_v of cyclobutane C_4H_8, as determined from the photoelectron spectrum[2], are listed in Table 1. An assignment to orbitals of particular symmetry can be performed, assuming the validity of Koopmans' theorem[3], on the basis of the orbital energies $\varepsilon = -I_v$ obtained for cyclobutane by a SCF *ab initio* technique[4], by the MINDO/2 method[5], or by the extended Hückel theory (EHT)[6] (see Table 1).

The *ab initio* and EHT results, which were made available to us by *L. Salem* and *J. S. Wright* (cf. ref. [7]), are based on the following structural parameters: Symmetry D_{4h}; C–C = 1.556 Å; C–H = 1.095 Å, ∢ HCH = 116 °[8]. In the MINDO/2 method the total energy of the cyclobutane molecule was minimized without any restriction of the topography except for C–H = 1.093 Å and HCH = 120 °. In this case, the calculation yields a D_{4h} structure with C–C = 1.534 Å within the convergence criteria of the minimization process. It should be noted that a D_{2d} structure is found experimentally for cyclobutane[9]. For this reason the classification of the orbitals according to D_{2d} symmetry is also included in Table 1.

Table 1. Vertical ionization potentials and orbital energies of cyclobutane.

Orbital		I_v (eV) ±0.1 eV	Calculated orbital energies (eV)			Orbital character
D_{4h}	D_{2d}		*ab initio* [a]	MINDO/2	EHT [a]	
$3e_u$	4e	10.7 [b]; 11.3 (JT) [c]	−10.50	− 9.88	−12.83	mixed; Walsh type
$1b_{1u}$	$4a_1$	11.7	−11.82	−10.35	−13.92	CH_2 (π)
$1b_{1g}$	$1b_1$	12.5	−12.47	−11.93	−14.09	CC (σ)
$1e_g$	3e	13.4; 13.6 (JT) [c]	−14.38	−13.17	−15.36	CH_2 (π)
$3a_{1g}$	$3a_1$	15.9	−16.05	−15.23	−15.68	$CH_2(\sigma)+CC(\sigma)$
$3a_{2u}$	$3b_2$	18.2	−17.53	−17.94	−16.81	CH_2 (π)

[a] See ref. [4]. [b] Electron impact value: 10.58 eV, cf. [13]. [c] Jahn-Teller splitting.

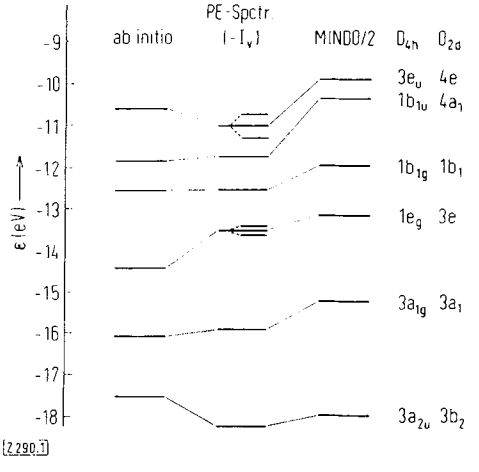


Fig. 1. Comparison of the calculated SCF orbital energies ε with the vertical ionization potential $I_v = -\varepsilon$ of cyclobutane.

As shown by the correlation diagram (Fig. 1), the experimental values are in excellent agreement with the calculated *ab initio* and MINDO/2 data. The reasonable results obtained from the EHT model are probably due to the high degree of symmetry of the molecule. As predicted, the first band in the PE spectrum (at 11 eV) is split into two partial bands separated by about 0.6 eV. Since the photoelectron vacates a degenerate orbital ($3e_u$ or 4e), the radical cation $C_4H_8^+$ must be subject to a Jahn-Teller distortion in its electronic ground state, which leads to the observed splitting. (Compare the analogous behavior of cyclopropane[10].) Similarly, the form of the band at 13.5 eV seems to indicate a small splitting of 0.2 eV, which would agree with the theoretical prediction that in this case the photoelectron is ejected from the $1e_g$ (or 3e) orbital. It should be noted that the PE spectroscopic findings confirm the prediction[7] that, by analogy to the situation prevailing in cyclopropane[10, 11], the highest occupied orbital in cyclobutane is also degenerate and can consequently be regarded as a kind of Walsh orbital.

The structure of the radical cation $C_4H_8^+$ (in the electronic ground state) has been studied in the course of an investi-

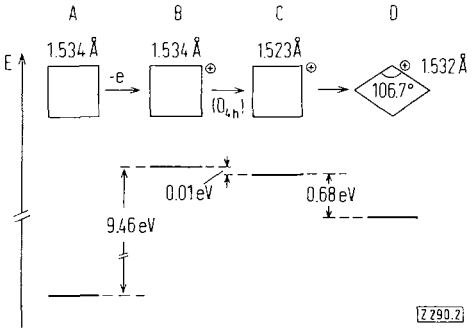


Fig. 2. Jahn-Teller distortion of the cyclobutane radical cation.

gation into the nature and extent of the Jahn-Teller distortion in the radical cations of cyclopropane and allene [12].

The results are summarized in Fig. 2. If the total energy of $C_4H_8^+$ (B) is calculated by MINDO/2 with the equilibrium distances found for C_4H_8 (A), the difference in the heats of formation yield a vertical ionization potential of 9.46 eV, *i.e.* 0.4 eV smaller than the value found from the orbital energies of A using Koopmans' theorem (see Table 1). If the total energy of $C_4H_8^+$ is minimized under the restrictive condition that the D_{4h} symmetry, the C—H distances, and the HCH angles are conserved, then the C—C distance is reduced to 1.523 Å and the system becomes more stable by 0.01 eV: B→C. Minimization without restricting the system to D_{4h} symmetry leads to a considerable gain in energy of 0.68 eV and the molecule distorts to a D_{2h} conformation (C→D in Fig. 2). If the structural parameters thus obtained are applied to a neutral cyclobutane molecule (*i.e.* a cyclobutane having a structure which corresponds to that of the radical cation D), the degeneracy of the $3e_u$ orbital of A is lifted and a Jahn-Teller splitting of 2.6 eV is predicted (regarding the discrepancy between this theoretical value and the experimental Jahn-Teller splitting of 0.6 eV (Table 1) cf. ref. [12]).

To conclude it should be noted that the theory predicts a shortening of the C—C bond as a consequence of ionization. It appears that in the cyclobutane radical cation ionization leads to a weakening of those repulsive interactions between diagonally opposed C centers which are considered responsible for the abnormally long C—C bonds in neutral cyclobutane [14].

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[1] Applications of photoelectron spectroscopy, Part 19. This work represents part of Project No. SR 2.120.69 of the Schweizerischer Nationalfonds. – Part 18: *E. Heilbronner, A. K. Muszkat,* and *J. Schäublin,* Helv. Chim. Acta, in press.

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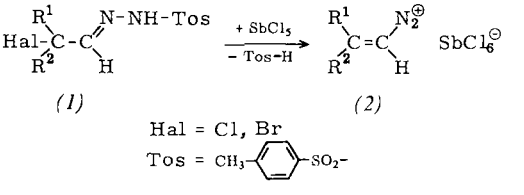
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Substituted Ethylenediazonium Salts

By *Kaspar Bott* [*]

In contrast to the large number of known aromatic diazonium compounds, only 2,2-diethoxyethylenediazonium hexachloroantimonate [1] and the diazonium chelates derived from β-diketones [2, 3] have been described in the aliphatic series. By the action of antimony pentachloride on the *p*-toluenesulfonylhydrazones *(1)* of α-halo aldehydes we have found a simple and efficient synthesis (75—90% yields) of ethylenediazonium hexachloroantimonates *(2)*; their stabilities depend considerably on the nature of the residues R^1 and R^2.



Antimony pentafluoride, aluminum chloride, or tin tetrachloride may be used instead of antimony pentachloride, though the resulting salts do not crystallize so well as the hexachloroantimonates *(2)* [4]. As a variant of the scheme given above, the 2,2-(2,2'-biphenylylene)ethylenediazonium salt *(2d)* can also be synthesized from the halogen-free 9-fluorenecarbaldehyde toluenesulfonylhydrazone, the antimony pentachloride then acting both as oxidant and as complexing agent.

	R^1	R^2	Decomp. pt. (°C)	Color	IR: asym. $-N\equiv N$ (cm^{-1})
(2a)	Cl	Cl	above 116	colorless	2241 [a]
(2b) [b]	Br	Br	58	pale yellow	2238 [c]
(2c) [d]	Cl	$(CH_3)_3C$	86—87	colorless	2240 [e]
(2d)	2,2'-biphenylylene		95—96	deep green	2218 [f]
(2e) [d]	Cl	*p*-$CH_3O-C_6H_4$	112	yellowish-brown	2200 [f]

[a] In methylene dichloride.

[b] According to elemental analysis the anion consists of $SbCl_6$ (70%) and $SbCl_5Br$ (30%).

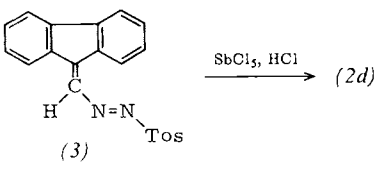
[c] In 1,2-dichloroethane.

[d] The NMR spectrum indicates the existence of only one isomer.

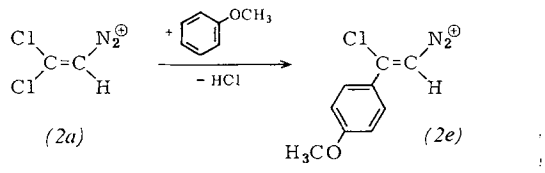
[e] Solid in Nujol.

[f] In nitrobenzene.

Formation of the compounds *(2a)* to *(2c)* probably occurs analogously to the *Chattaway* reaction [5] *via* an azo sulfone intermediate, the toluenesulfinate group being split off later. Further variants of this reaction sequence, leading to acetylenes, have been described by other authors [6–8]. The sulfonylhydrazone *(1d)*, Hal = Br, of 9-bromo-9-fluorenecarbaldehyde loses hydrogen bromide even during its preparation in ethanol, and the sulfonylazofulvene *(3)*, m.p. 125—126 °C, that can be isolated is converted by the Lewis acid and hydrogen chloride almost quantitatively into *(2d)*.



According to its strikingly short-wavelength N—N absorption band, the substance *(2a)*, which is the most stable of the series, has the greatest reactivity towards "basic" compounds[9]. Even below room temperature *(2a)* reacts with



anisole to give a 61% yield of the 2-chloro-2-(*p*-methoxyphenyl)ethylenediazonium compound *(2e)*; in reactions of the diazonium ion of *(2a)* "azo coupling" is apparently suppressed in favor of attack on the β-carbon atom.

2-tert-Butyl-2-chloroethylenediazonium hexachloroantimonate (2c)

A solution of 2,2-dichloro-3,3-dimethylbutyraldehyde *p*-toluenesulfonylhydrazone, m.p. 91 °C, (6.74 g) in methylene dichloride (30 ml) is added dropwise to a mixture of antimony pentachloride (13.5 g), methylene dichloride (30 ml), and carbon tetrachloride (60 ml) at 20 °C. After the mixture has been kept for 18 h at 0 °C, crude *(2c)* (93%) is filtered off; it is purified by dissolution in 1,2-dichloroethane (200 ml) and by precipitation with carbon tetrachloride (250 ml).

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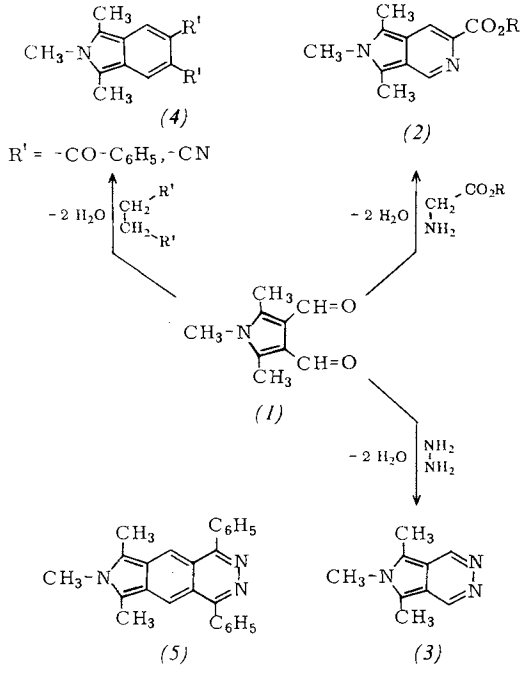
Cyclizing Condensation of 3,4-Pyrroledicarbaldehydes with Compounds Containing Acidic CH and NH Groups[1,2]

By *Richard Kreher* and *Günther Vogt*[*]

Bicyclic systems containing 3,4-fused pyrrole rings[1,4] have been synthesized by cyclizing condensation of 3,4-pyrroledicarbaldehydes with 1,3-bifunctional compounds containing acidic CH groups[3]. Building on this, we have now condensed 1,2,5-trimethyl-3,4-pyrroledicarbaldehyde *(1)* with components containing 1,2-bifunctional acidic NH and CH groups[5].

Thus the hitherto unknown 2*H*-pyrrolo[3,4-*c*]pyridines *(2)* could be prepared simply and in satisfactory yields from *(1)* and alkyl α-aminoacetates in presence of diethylamine as base. The condensation began with formation of an azomethine, from which water was liberated in an intramolecular reaction.

Use of hydrazine provided entry into the 6*H*-pyrrolo[3,4-*d*]-pyridazine series *(3)*, which has astonishing thermal stability. The nitrogen atoms at positions 5 and 6 confer on this system a basic character that is proved by monoalkylation by trialkyloxonium tetrafluoroborates and by solubility in 2N-hydrochloric acid. The reactivity with dienophiles is appreciably less than that of 2-alkylisoindoles[6]; thus, neither compounds of type *(3)* nor those of type *(2)* undergo Diels-Alder addition with *N*-phenylmaleimide at room temperature.



Reaction of *(1)* with 1,2-dicyano- or 1,2-dibenzoyl-ethane occurs with double removal of water, giving substituted isoindole derivatives *(4)*. The 5,6-dibenzoylisoindole derivative *(4)*, R' = C_6H_5CO-, can be converted by hydrazine into the intensely red tricyclic system *(5)*, which has very great thermal stability and absorbs at 535—537 nm.

Experimental:

For preparation of *(2)*, R = C_2H_5, *(1)* is allowed to react with an equivalent amount of glycine ethyl ester in ethanol in presence of diethylamine for 14 hours under reflux, and the product is purified by recrystallization from ethyl acetate. M.p. 168—172 °C; yield 48%; λ_{max} (in methanol) (log ε): 251 nm (4.57), 318 nm (3.92), 386 nm (3.47). — NMR: τ = 1.13—1.16 (1 H doublet), τ = 1.81—1.84 (1 H doublet), τ = 5.37—5.69 (2 H quartet), τ = 6.30 (3 H singlet), τ = 7.43 (3 H singlet), τ = 7.50 (3 H singlet), τ = 8.43—8.67 (3 H triplet)[7].

For preparation of *(3)*, *(1)* is heated with a 12-fold excess of hydrazine hydrate for 1 hour in ethanolic solution; purification is by recrystallization from acetonitrile. M.p. 184 to 190 °C; yield 82%; λ_{max} (in methanol) (log ε): 231 nm (4.28), 285 nm (3.57), 359 nm (3.33). — NMR: τ = 1.00 (2 H singlet), τ = 6.25 (3 H singlet), τ = 7.50 (6 H singlet).

For preparation of *(4)*, R' = CN, *(1)* is treated with an equimolar amount of 1,2-dicyanoethane in the presence of 2 equivalents of potassium *tert*-butoxide in *tert*-butyl alcohol. After 30 min the yellowish-green crystals are filtered off, purified by chromatography, and recrystallized from chloroform. M.p. 272–275 °C (dec.); yield 17%; λ_{max} (in

methanol) (log ε): 210 nm (4.13); 228 nm (4.13); 270 nm (4.80); 337 nm (2.79); 401—402 (3.30). — NMR: τ = 2.13 (2 H singlet); τ = 6.20 (3 H singlet); τ = 7.43 (6 H singlet).

For preparation of *(4)*, R' = C_6H_5CO-, *(1)* is refluxed for 2 hours with an equimolar amount of 1,2-dibenzoylethane in ethanolic potassium hydroxide solution. The yellowish-green crystals are filtered off and recrystallized from ethyl acetate/dimethylformamide (3:1). M.p. 217 °C (dec.); yield 50%; λ_{max} (in methanol) (log ε). 250 nm (4.57); 288 nm (4.37); 293 nm (4.86). — NMR: τ = 2.18—2.78 (12 H multiplet); τ = 6.25 (3 H singlet); τ = 7.49 (6 H singlet).

For conversion of *(4)*, R' = C_6H_5CO-, into *(5)* it is refluxed for 2 hours with a 25-fold excess of hydrazine hydrate in ethanol for 2 hours. The reddish-violet crystals are purified by recrystallization from 2-propanol. M.p. 210 °C (dec.); yield 26%; λ_{max} (in methanol) (log ε): 230 nm (4.48), 278 nm (4.50), 372 nm (3.76), 536 nm (3.35). — NMR: τ = 1.87 (2 H singlet), τ = 2.23 (10 H singlet), τ = 6.09 (3 H singlet), τ = 7.38 (6 H singlet).

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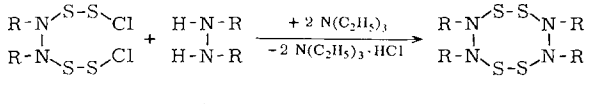
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Preparation of Sulfur-Nitrogen Rings Containing Nitrogen-Nitrogen Bonds[**][1]

By *Herbert Lingmann* and *Karl-Heinz Linke*[*]

Sulfur-nitrogen compounds that can be considered as sulfane derivatives of hydrazine have not hitherto been described. The reaction of hydrazine with sulfur affords only nitrogen and hydrogen sulfide[2].

Treatment of diethyl 1,2-hydrazinedicarboxylate *(1)*, which is very resistant to oxidation, with dichlorodisulfane by the dilution technique in the presence of triethylamine as HCl-acceptor affords, besides polymeric substances, the two cyclic compounds tetraethyl 1,2,5,6,3,4,7,8-tetrathiatetraazacyclooctane-3,4,7,8-tetracarboxylate *(2)* and diethyl 1,2,3,4,5,6,7,8-hexathiadiazacyclooctane-7,8-dicarboxylate *(3)*.



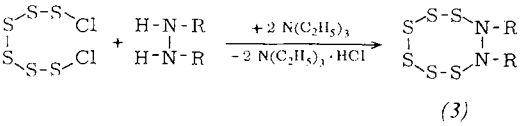
(4) *(1)* *(2)*

R = $CO_2C_2H_5$

Preparation of *(2)* was effected in 22% yield by interaction of diethyl 1,2-bis(chlorodisulfanyl)-1,2-hydrazinedicarboxylate *(4)* with *(1)* and triethylamine:

Compound *(4)* is formed when *(1)* and the requisite amount of triethylamine in dioxane solution is added dropwise to a large excess of dichlorodisulfane; on filtration of the solution and removal of the dioxane and dichlorodisulfane it remains as an oily orange-colored residue.

The heterocyclic compound *(3)* is formed in 19% yield on reaction of dichlorohexasulfane[3] with *(1)* in the presence of triethylamine:



(3)

R = $CO_2C_2H_5$

The products *(2)* and *(3)* are isolated by preparative thin-layer chromatography in dichloromethane on silica gel H[4] (R_F values 0.23 and 0.62, respectively). Each of them is obtained from hexane as colorless crystals: *(2)* m.p. 110 °C; *(3)* m.p. 80 °C. They were characterized by elemental analyses, IR spectra, and mass spectra. The IR spectra of *(2)* and *(3)* show that neither molecule contains an NH group. The S—S bond absorbs at 475 cm^{-1}. A band at 1010 cm^{-1} can be assigned to the N—N bond.

The mass spectrum of *(2)* shows, alongside the molecular peak, important fragments that have the composition $(NCO_2C_2H_5)_2S_4N_2H$ and $(NCO_2C_2H_5)_2S_4H$. The first steps in the degradation of *(3)* in the mass spectrometer occur according to the same principles, the largest fragments having the composition S_6N_2H and S_6H.

The survival of the N—N bond, which can be recognized from the mass spectra by loss of two N atoms at a time, can also be proved by chemical degradations: the compound *(1)* is formed on desulfuration of *(2)* or *(3)* with Raney nickel.

General experimental technique:

Compound *(1)* (0.02 mole) and triethylamine (0.04 mole) are dissolved together in anhydrous dioxane and made up to a fixed volume (200 ml). An equimolar amount (0.02 mole) of S_nCl_2 (n = 2 or 6) or *(4)* (titration as described by *Böhme* and *Schneider*[5]) is diluted with ether (to 200 ml). These two solutions are simultaneously added dropwise over 4 hours to vigorously stirred anhydrous ether (1.5 liters). After reaction, the solution is filtered and the solvent is removed. A small amount of *(1)* can be filtered off after the residue has been taken up in a little dichloromethane. The product is worked up by chromatography.

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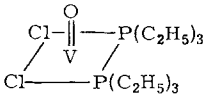
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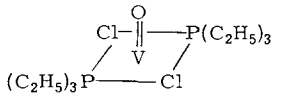
ESR Studies on Vanadyl-Phosphorus Complexes[1]

By *Gisela Henrici-Olivé* and *Salvador Olivé*[*]

Vanadyl chloride, which is insoluble in toluene, can be made to dissolve in the presence of an excess of triethylphosphine ($P/V \geq 4$). The solution exhibits the ESR spectrum shown in Fig. 1a. The intensity of the signal corresponds to essentially all the vanadium present in the solution. The signal is characteristic of the interaction of the unpaired electron of V(IV) with the ^{51}V nucleus (nuclear spin $I = 7/2$) and with two equivalent ^{31}P nuclei ($I = 1/2$), the latter interaction being responsible for the triplet splitting (1 : 2 : 1) of the eight vanadium lines. The ESR data, which are shown in Table 1, line 1, are consistent with structure *(1)* or *(2)*.

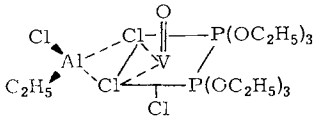


(1)



(2)

When the phosphine is replaced by triethyl phosphite, $VOCl_2$ again dissolves but the ESR spectrum of the solution consists mainly of the $VOCl_2$ signal (eight lines showing no splitting) overlapped by a low-intensity doublet signal (one phosphorus nucleus, $a_P \approx 110$ MHz). Addition of ethylaluminum dichloride ($Al/V \geq 6$), however, immediately gives a triplet signal (Fig. 1b and line 2 of Table 1). The Lewis-acid character of $VOCl_2$ is probably too low for a comparable EDA interaction to occur with the weaker base $(C_2H_5O)_3P$. However, complex formation between $VOCl_2$ and the alkylaluminum lowers the electron density on the vanadium and thereby permits an ESR-active interaction between V and P. A possible formulation which takes account of the equivalence of the two P nuclei is shown in *(3)*.



(3)

No ESR signal indicative of phosphorus nucleus interactions is obtained on treatment of vanadyl acetylacetonate $[VO(acac)_2]$ with phosphine or with phosphite. Instead, the unchanged eight-line signal of $VO(acac)_2$ is observed. On addition of $(C_2H_5)AlCl_2$, however, triplet spectra appear almost immediately which are in good experimental agreement with Fig. 1a (for ethylphosphine) and 1b (for ethyl phosphite) — see Table 1. These complexes are decomposed

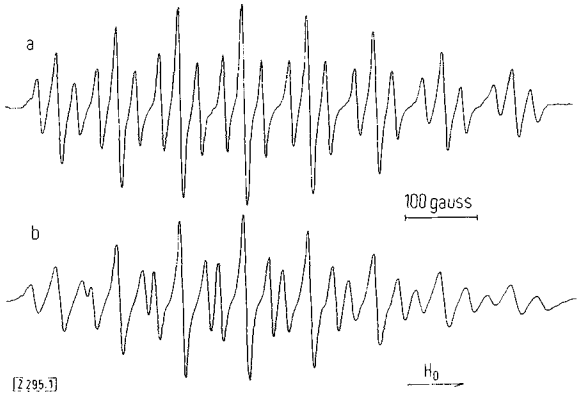


Fig. 1. ESR signals of vanadyl-phosphorus complexes in toluene $T = 20$ °C, $[VOCl_2] = 7 \times 10^{-3}$ mole/liter.
a) $[(C_2H_5)_3P] = 4 \times 10^{-2}$ mole/liter;
b) $[(C_2H_5O)_3P] = 4 \times 10^{-2}$ mole/liter;
$[(C_2H_5)AlCl_2] = 7 \times 10^{-2}$ mole/liter.

Table 1. ESR data of the complexes investigated (corrected for second-order effects). Solvent: toluene.

No.	System	g value	a_V (MHz)	a_P (MHz)
1	$VOCl_2/(C_2H_5)_3P$	1.981 ± 0.001	250 ± 2	71 ± 1
2	$VOCl_2/(C_2H_5O)_3P/(C_2H_5)AlCl_2$	1.980 ± 0.001	254 ± 2	100 ± 1
3	$VO(acac)_2/(C_2H_5)_3P/(C_2H_5)AlCl_2$	1.981 ± 0.001	250 ± 2	71 ± 1
4	$VO(acac)_2/(C_2H_5O)_3P/(C_2H_5)AlCl_2$	1.981 ± 0.001	252 ± 2	101 ± 1
5	$VOCl_2$ [a]	1.968 ± 0.001	300 ± 2	—
6	$VO(acac)_2$ [a]	1.970 ± 0.001	287 ± 2	—
7	System 4 + THF	1.965 ± 0.001	300 ± 2	—

[a] Measured in tetrahydrofuran for comparison with No. 7.

by tetrahydrofuran. The vanadyl signal then observed is no longer that of $VO(acac)_2$ but rather resembles that of $VOCl_2$ (line 7 in Table 1). We tentatively interpret this observation in terms of replacement of the (acac) ligands by Cl ligands and formation of the above-mentioned bridged complex in order to reduce the electron density at the vanadium to the required value. The processes appear to be very rapid.

Comparison of the a_P values in Table 1 shows that in the phosphite complexes the unpaired electron has a higher probability of being found at the phosphorus nucleus. Phosphites are better π acceptors and poorer σ donors than the corresponding phosphines. The electrons that effect π and σ bonding between transition metal and phosphorus compound are shifted more toward the phosphorus atom in the phosphite than in the phosphine. The highest occupied molecular orbital of the complex, the frontier orbital, which contains the unpaired electron, seems to reflect the general donor-acceptor properties of the ligands. Similar observations have already been made with other complexes[2].

In all those cases in which alkylaluminum is present in the reaction solution, a reduction V(IV) → V(III) is observed which is first order in V(IV). (Magnitudes measured: magnetic susceptibility and intensity of ESR signals.) Reduction is very slow with the phosphine complex ($t_{1/2} \approx 200$ h), significantly faster with the phosphite complex ($t_{1/2} \approx 50$ h), and faster by powers of ten when diethylaluminum chloride is used in place of ethylaluminum dichloride ($t_{1/2} \approx 10$ min for the phosphite complex of $VO(acac)_2$). Reduction presumably proceeds by the same route as that of similar titanium complexes[3], *i.e. via* alkylation of the transition metal and cleavage of the unstable V—C bond, the rate-determining step probably being that of alkylation. The higher electron density on vanadium in the phosphine complexes opposes alkylation.

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Fluorine-Bridged Heteroadducts of Organometallic Lanthanoid and Actinoid Complexes[**]

By *Basil Kanellakopulos*, *Ernst Dornberger*, *Reinhard von Ammon*, and *Rainer Dieter Fischer*[*]

The *self*-association[1] of the complex[2] $(C_5H_5)_3UF$ *(1)* indicates that in monomeric *(1)* neither the central U(IV) ion nor its F(−I) ligand would be completely coordinately saturated. ^1H-NMR studies[1] have shown that *(1)* behaves

as a Lewis *acid* towards bases such as pyridine and tetrahydrofuran (THF). We have now been able to prepare two novel and remarkably stable *hetero*adducts of the type

$$\{(C_5H_5)_3UF \cdot M(C_5H_5)_3\} \qquad (M = Yb,\ U)$$

and have thus obtained independent evidence for the exceptionally high *basicity* of the fluorine compound *(1)*.

When equimolar solutions of *(1)* and the Lewis acid[3] $(C_5H_5)_3Yb(III)$ *(2)* are mixed and stirred at room temperature, a fine yellowish green crystalline precipitate is formed almost immediately; after the precipitate has been washed with pentane and dried under high vacuum it is found to have the composition of the 1:1 adduct

$$(C_5H_5)_3UF \cdot Yb(C_5H_5)_3 \qquad (3)$$

In a very similar reaction, the THF-ligand of $(C_5H_5)_3U(III) \cdot THF$ *(4)*[4] is substituted by *(1)* to give the bronze-colored complex *(5)*, which can be extracted with benzene without decomposition.

$$\frac{1}{n}[(C_5H_5)_3UF]_n + (C_5H_5)_3Yb \xrightarrow{\text{benzene, 25 °C}} \{(C_5H_5)_3UF \cdot Yb(C_5H_5)_3\}\downarrow$$

$$\frac{1}{n}[(C_5H_5)_3UF]_n + (C_5H_5)_3U \cdot THF \xrightarrow{\text{benzene, 25 °C}} \{(C_5H_5)_3UF \cdot U(C_5H_5)_3\}\downarrow + THF \qquad (5)$$

Surprisingly, no adduct of comparable stability is formed from *(1)* and $(C_5H_5)_3Tm(III)$ *(6)*[5]; the reaction of $(C_5H_5)_3U(IV)Cl$ *(7)* with *(2)* or *(3)* seems to proceed beyond the hypothetical Cl-bridged adduct[6].

Unlike their components, the adducts *(3)* and *(5)* are pyrophoric in air and are neither substantially soluble in C_6H_6 or THF nor sublimable in high vacuum. Whereas *(1)*, *(2)*, and *(4)* give rise to excellent mass spectra[7] below 200 °C[4,8], even the strongest signals of *(3)* and *(5)* are only detectable above 350 and 400 °C, respectively. The appearance of fragments of composition $(C_5H_5)_xUMF$ ($x = 0$ to 6; relative intensities: 0.5 to 7.0 based on $I(C_5H_5UF^+) = 100$) could indicate at least some volatility of the binary heteroadducts *(3)* and *(5)*.

Differences in fragmentation behavior suggest that the bond strength of the U · · · F · · · M bridge decreases along the series *(5)* ≥ *(3)* ≫ *(1)*.

The IR spectra of *(3)* and *(5)* are almost identical between 600 and 3000 cm^{-1} and compatible with the assumption of centrally coordinated C_5H_5 ligands. The absorption bands highly characteristic for the U · · · F · · · M group at 432 *(3)* and 423 cm^{-1} *(5)*, respectively, (see Fig. 1) show remarkable long-wave shifts compared with the relevant absorption bands of other M · · · F · · · M′ systems[9], including *(1)*[11]. Although in the case of *(5)*, in contrast to *(3)*, a molecular structure with a strictly symmetrical U · · · F · · · U bridge is conceivable, no support for such an assumption comes from the rather numerous absorption bands between about 100 and 350 cm^{-1} (range of metal-ring skeletal vibrations, see Fig. 1). Instead, similarities between the solid-state electronic spectra of the adducts and their components, as well as the results of magnetic susceptibility measurements between 4.2 and 300 °K, suggest rather the conservation of the original electronic configurations of U(IV), Yb(III), and U(III) (*i.e.* $5f^2$, $4f^{13}$, and $5f^3$). Unlike polycrystalline *(1)*, compounds *(3)* and *(5)* give no evidence for U · · · M spin exchange, even at low temperatures.

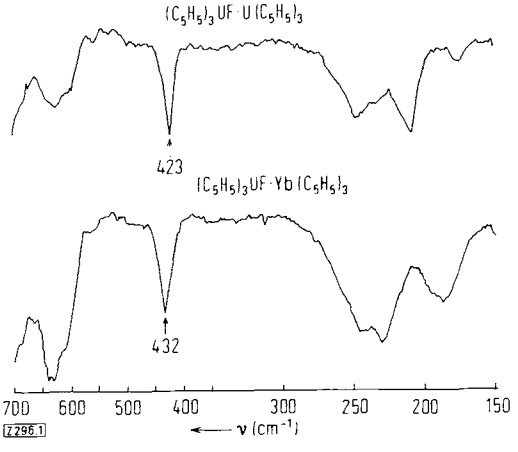


Fig. 1. FIR spectra of the adducts *(3)* and *(5)*. (Nujol mulls; Beckman Model IR 11 instrument).

Apart from a non-linear fluorine bridge (which could be stabilized by a C_5H_5 ligand with partial bridging character[10]) the possibility of an unsymmetrical linear[11] U · · · F · · · M arrangement is also open to discussion.

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[1] *R. D. Fischer, R. v. Ammon*, and *B. Kanellakopulos*, J. Organometal. Chem., in press; according to recent studies, crystalline $(C_5H_5)_3Th(IV)F$ also exists in an associated form similar to that of *(1)*.

[2] *P. G. Laubereau*, Dissertation, Technische Hochschule München, 1966.

[3] *E. O. Fischer* and *H. Fischer*, J. Organometal. Chem. *3*, 181 (1965).

[4] *B. Kanellakopulos, E. O. Fischer, E. Dornberger*, and *F. Baumgärtner*, J. Organometal. Chem. *24*, 507 (1970).

[5] In solution, *(6)* and *(1)* undergo only weak interactions similar to those between *(1)* and THF [1].

[6] Results of ^1H-NMR studies suggest the equilibrium $(C_5H_5)_3UCl + Yb(C_5H_5)_3 \rightleftarrows (C_5H_5)_4U + 1/2\,[(C_5H_5)_2YbCl]_2$.

[7] Varian Mat-CH5 with an internal sampling system (70 eV).

[8] *B. Papadopulos, L. Stieglitz, W. Roth*, and *B. Kanellakopulos*, unpublished.

[9] *I. R. Beattie, K. M. S. Livingston, G. A. Ozin*, and *D. J. Reynolds*, J. chem. Soc. A *1969*, 959.

[10] For X-ray studies suggesting formation of C_5H_5 ligands with partial bridging character, see *C.-H. Wong* and *J.-Y. Lee*, Acta Crystallogr. B *25*, 2580 (1969).

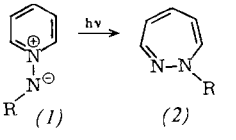
[11] Cf. *H. Schmidbaur* and *H. F. Klein*, Angew. Chem. *78*, 750 (1966); Angew. Chem. internat. Edit. *5*, 726 (1966).

Structure of a Tricarbonyl-1-isopropoxycarbonyl-1,2-diazepineiron Complex

By *Rudolf Allmann*[*]

Substituted 1 *H*-1,2-diazepines *(2)* have been prepared from pyridinium imidates *(1)* by photochemically induced ring expansion[1].

In order to gain information about the conformation of the 1,2-diazepine ring and particularly about the existence of



an isolated imine bond —N=C— in the ring, an attempt was made to elucidate the structure of 1-isopropoxycarbonyl-1,2-diazepines *(2)*, R = $CO_2C_3H_7$. However, X-irradiation (CuK_α) decomposes this substance within 8 to 12 h.

Therefore the tricarbonyliron complex of this compound was studied: $C_{12}H_{12}N_2O_5Fe$, M = 320.1, m.p. 104 to 105 °C, yellow crystals, space group $P2_1/n$, a = 12.277 ± 3 Å, b = 17.241 ± 5 Å, c = 6.639 ± 2 Å, β = 101.60 ± 0.05 °, Z = 4, D_m = 1.53 ± 2, $D_{X\text{-ray}}$ = 1.545 g cm^{-3}. Out of 2112 independent reflections, 1800 could be measured (CuK_α, ϑ_{max} = 60 °). The iron atoms were found at x = 0.4446, y = 0.1958, z = 0.6276 by a Patterson map. The remaining atoms could be localized by two subsequent Fourier syntheses using the heavy atom method. After several least-squares cycles with anisotropic temperature factors the R ndex fell to 4.5 % for the observed reflections (4.7 % if the 26 unobserved reflections with $F_c > F_{min}$ are included). The anomalous scattering of the iron atoms was taken into account.

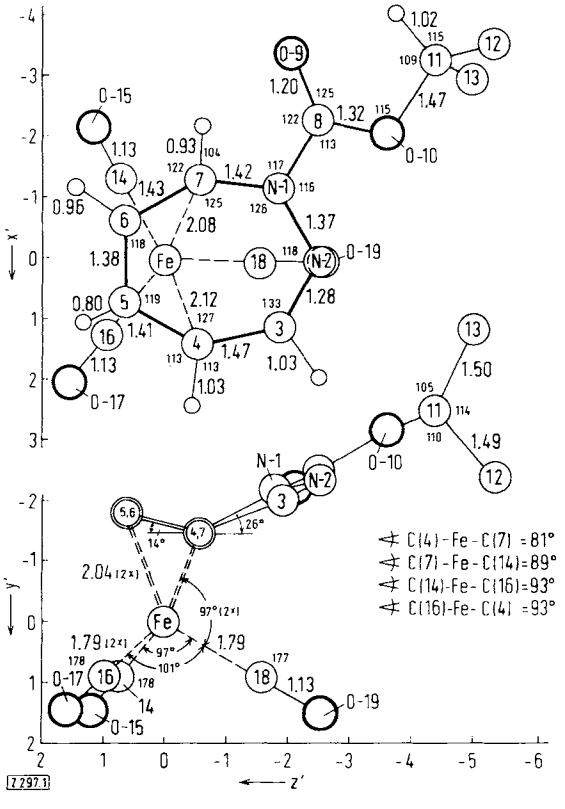


Fig. 1. Bond lengths (Å) and angles (degrees, small figures) in the tricarbonyliron complex of 1-isopropoxycarbonyl-1,2-diazepine.

Upper part: Projection onto the plane through C(14), C(16), C(18) of the carbonyl groups. The protons of the methyl groups C(12) and C(13) have been omitted.

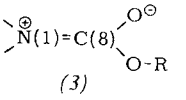
Lower part: Projection along C(4)—C(7) perpendicular to the above projection. All protons have been omitted.

The standard deviations are 0.01 Å except for C—H (0.1 Å). Scale in Å.

The resulting distances and angles are shown in Fig. 1. The tricarbonyliron group is attached not to the imine bond N(2)—C(3) but to the butadiene group of the ring [C(4) to C(7)] in such a manner that C(4) and C(7) have partial sp^3 character. As a result, H(4) and H(7) are displaced by 0.5 Å out of the planes C(3)—C(4)—C(5) and C(6)—C(7)—N(1), respectively, and away from the iron atom.

Apart from 5 and 6, the atoms 1 to 11 are almost coplanar. The diazepine ring is bent by 40 ° along the line C(4) to C(7). The iron atom is five-coordinated (tetragonal pyramid); it is shifted by 0.25 Å out of the C(4)—C(7)—C(14)—C(16) plane toward the apex of the pyramid C(18). In spite of the short distance of 2.04 Å, C(5) and C(6) appear only weakly bound to the iron atom. The imine bond N(2)—C(3) (1.28 Å) is very short, thus indicating an isolated double bond.

Compared with the bonding in similar ester groups, O(10) should be 0.03 Å closer to C(11), since C(8)—O(10) is too short (1.32 Å) and O(10)—C(11) is too long (1.47 Å), both



(3)

by *ca.* 0.03 Å. The bond N(1)—C(8) (1.40 Å) corresponds to a single bond, *i.e.* the resonance form *(3)* participates to only a limited extent in the bonding state.

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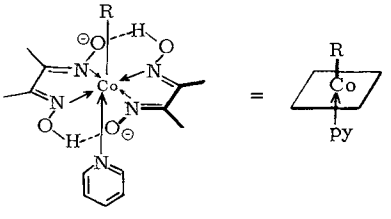
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[1] *J. Streith* and *J. M. Cassal*, Angew. Chem. *80*, 117 (1968); Angew. Chem. internat. Edit. *7*, 129 (1968); Tetrahedron Lett. *43*, 4541 (1968); Bull. Soc. Chim. Fr. *1969*, 2175.

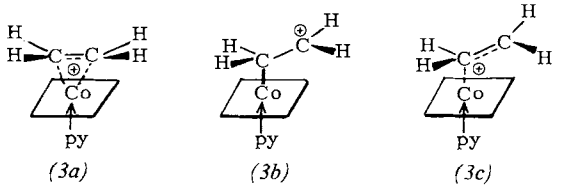
Solvolysis of σ-2-Acetoxyalkylbis(biacetyldioximato)pyridinecobalt: Evidence for a Novel Intermediate Olefinic Complex[**]

By *B. T. Golding*, *H. L. Holland*, *U. Horn*, and *S. Sakrikar*[*]

Schrauzer and *Windgassen*[1] observed that bis(biacetyldioximato)-σ-2-hydroxyethylpyridinecobalt *(1a)* undergoes a rapid decomposition in aqueous hydrochloric acid, producing ethylene and the chloro compound *(2a)*.



(1a), R = CH_2CH_2OH
(1b), R = $CH_2CH_2OCOCH_3$
(1c), R = $CH_2CH(OCOCH_3)CH_3$
(1d), R = $CH_2CH_2OCH_3$
(1e), R = $CH_2CH_2OCH_2CH_3$
(1f), R = $CH_2CH(OCH_2CH_3)CH_3$
(1g), R = $CH_2CH(OH)CH_3$
(2a), R = Cl
(2b), R = OH



(3a) *(3b)* *(3c)*

We have considered the possibility that the symmetrical π-complex *(3a)* or the unsymmetrical species *(3b)* or *(3c)* could be intermediate(s) in this reaction[2,3] and that there might exist a solvolytic chemistry of other derivatives of *(1)* *via (3)*[5] as intermediate, akin to the known[6] rapid solvolyses which occur within certain ligands bound to transition metals.

We have found that σ-2-acetoxyethyl- *(1b)* [7,8] and σ-2-acetoxypropylbis(biacetyldioximato)pyridinecobalt *(1c)* [7,8] are compounds of extraordinary solvolytic reactivity. Their hydrolysis, methanolysis, and ethanolysis occur at 25 °C with half-lives of a few hours. High yields of products from these reactions have been isolated and identified as alcohols [*e.g. (1a)* from *(1b)*] from hydrolysis and *significantly* ethers from alcoholysis. Thus, methanolysis of *(1b)* gave the methyl ether *(1d)* [8]. Ethanolysis of *(1b)* gave *(1e)*, which was identified by comparison with a sample prepared by independent synthesis [1].

Good first-order kinetics [9] were observed for the solvolysis of *(1b)* in absolute ethanol at 25 °C [$k = 4.37 \pm 0.06 \times 10^{-6}$ s^{-1}, $E_a = 19.9 \pm 1.2$ kcal · $mole^{-1}$, $\Delta S^{\neq} = -18.2 \pm 4.2$ cal · deg^{-1} $mole^{-1}$]. Ethanolysis of *(1c)* gave *(1f)* [8] at a rate 20 times faster at 25 °C than the rate for *(1b)*. These values should be compared with data for other solvolytically reactive acetates [10]: *(1b)* and *(1c)* are of comparable reactivity to trityl acetate! Furthermore, ethanolysis of *(1b)* in ethanol saturated with propene and of *(1c)* in ethanol saturated with ethylene gave no crossed products [*e.g. (1e)* from *(1c)*], thereby eliminating a fragmentation-recombination mechanism from consideration. The σ-vinyl compound is not an intermediate, because alcoholysis of *(1b)* in [D_4]-methanol gave *(1d)* containing deuterium only in the methoxy group of the side-chain.

These results are in accord with a mechanism in which ionization of *(1b)* to *(3)* and of *(1c)* to methyl-substituted *(3)* is rate-determining followed by capture of these intermediates by solvent. A small amount of leakage occurs to give dealkylated products [*e.g. (2b)* in hydrolysis] presumably by loss of ethylene from *(3)* giving coordinatively unsaturated Co^{III} which reacts with solvent. A similar mechanism applies to the decomposition of *(1a)* in the presence of acid, except that the reaction is now equilibrium-controlled and leads to products of type *(2)* exclusively. The appreciable negative entropy of activation observed for ethanolysis of *(1b)* suggests that in *(3)* there is restriction of rotation about the C–C bond of the CH_2—CH_2 unit, which would be expected of any of the suggested structures for *(3)*.

Further evidence for the intermediacy of methyl-substituted *(3)* was obtained by carrying out hydrolysis of *(1c)* in dioxane / water (1 : 1) in the presence of $NaBH_4$ (3 eqvts. / *ca.* 5 °C / 90 min). In addition to the alcohol *(1g)* and products derived from reductive cleavage of the Co—C bond, 10% of the σ-propyl derivative was formed (identified by comparison with a sample prepared in the standard way [11]).

The acid-promoted decomposition of *(1a)* [1] resembles the acid-catalyzed deoxymercuration of 2-hydroxyalkylmercury(II) derivatives [12], whilst the solvolyses of *(1b)* and *(1c)* bear similarity to the neutral solvolytic chemistry of 2-acetoxyethylmercuric iodide [13]. The reactions of the mercuric derivatives have long been thought to proceed *via* a π-complex of Hg^{II} with alkene (mercurinium ion) [12], although the precise role and nature of this species is still uncertain [4c, 14]. *(3a)* corresponds to a symmetrical mercurinium ion. However, the present system differs clearly from deoxymercuration in that the loss of ethylene from *(3)* is kinetically slower than its capture by solvent, whereas in deoxymercuration, the contrary kinetic situation probably obtains.

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[1] *G. N. Schrauzer* and *R. J. Windgassen*, J. Amer. Chem. Soc. *89*, 143 (1967); *G. N. Schrauzer*, Accounts Chem. Res. *1*, 97 (1968).

[2] The possible existence of alkene-cobalamin complexes has been discussed by *M. L. H. Green* in *G. E. Coates*, *M. L. H. Green*, and *K. Wade*: Organometallic Compounds, Methuen, London, 1968, Vol. 2, p. 249, in the context of the analogous acid-induced decomposition of 2-hydroxyethylcobalamin.

[3] *(3a)*, *(3b)*, and *(3c)* would be new types of olefinic complex having an alkene bound to a metal (Co^{III}) within a ligand system assumed to remain approximately planar. The bonding between alkene and cobalt in *(3a)* can be visualized through the Chatt-Duncanson model [4a]. *(3b)* is represented as a primary carbonium ion, but is expected to be stabilized by overlap with neighboring orbitals (*i.e.* filled d_{xz} and d_{yz} of Co and/or bonding π-levels of biacetyldioxime). *(3c)* is based on the concept of σ–π hyperconjugation [4b, c] *i.e.* the carbonium ion center is stabilized only by overlap with the Co–C_1 σ-bond and there is no displacement of Co towards the electron deficient carbon atom as in *(3a)* and possibly *(3b)*.

[4] a) *E. O. Fischer* and *H. Werner*: Metal π-Complexes. Elsevier, Amsterdam 1966, Vol. 1, Chapter III; b) *T. G. Traylor* and *J. C. Ware*, J. Amer. Chem. Soc. *89*, 2304 (1967); c) *W. Hanstein*, *H. J. Berwin*, and *T. G. Traylor*, *ibid. 92*, 829 (1970).

[5] Hereinafter, *(3)* will refer to the intermediate whose actual structure may be *(3a)*, *(3b)*, or *(3c)*.

[6] *G. Gokel*, *P. Hoffmann*, *H. Klusacek*, *D. Marquarding*, *E. Ruch*, and *I. Ugi*, Angew. Chem. *82*, 77 (1970); Angew. Chem. internat. Edit. *9*, 64 (1970), and references cited therein; *R. S. Bly* and *R. L. Veazey*, J. Amer. Chem. Soc. *91*, 4221 (1969), and references therein.

[7] *(1b)* and *(1c)* were prepared by acetylation (acetic anhydride/pyridine/room temperature/36 h) of *(1a)* and *(1g)* respectively.

[8] New compounds gave satisfactory combustion analyses for C, H, and N and spectroscopic data (IR, UV, and NMR) consistent with their assigned structures.

[9] Reactions were sealed and thermostated in darkness. Their extent was assayed by NMR spectroscopy of aliquots.

[10] Cf. *E. A. Hill* and *J. H. Richards*, J. Amer. Chem. Soc. *83*, 3840 (1961).

[11] *G. N. Schrauzer* and *R. J. Windgassen*, J. Amer. Chem. Soc. *89*, 1999 (1967).

[12] *W. Kitching*, Organomet. Chem. Rev. *3*, 61 (1968) and references cited therein.

[13] *M. M. Kreevoy* and *G. B. Bodem*, J. Org. Chem. *27*, 4539 (1962).

[14] *J. Halpern* and *H. B. Tinker*, J. Amer. Chem. Soc. *89*, 6427 (1967).

Anionic 3 + 2 Cycloaddition of 2-Azaallyllithium Compounds to CN and NN Double Bonds [1] [**]

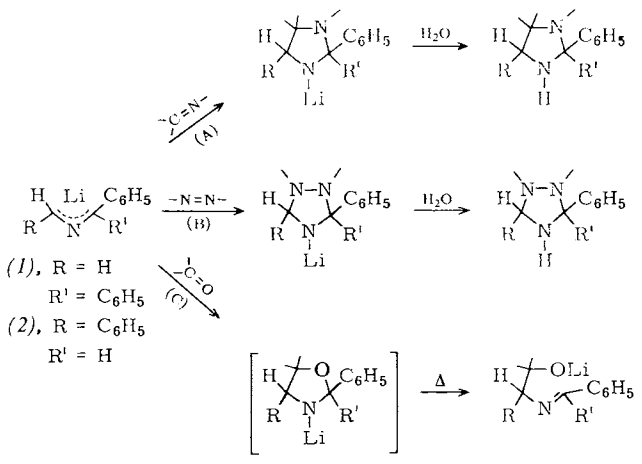
By *Thomas Kauffmann*, *Heike Berg*, *Elisabeth Ludorff*, and *Annegret Woltermann* [*]

2-Azaallyllithium compounds were recently reported [2] to react with olefinic CC double bonds to give anionic cycloadducts that afford pyrrolidines on hydrolysis with water.

We have now observed analogous anionic 3 + 2 cycloadditions [3] with azomethines and azo compounds. These reactions, designated (A) and (B) in the reaction scheme, take place when a solution of the 2-azaallyllithium compounds *(1)* and *(2)* [2] in THF/ether (9 : 1) is treated at −60 °C under nitrogen with an equimolar amount of one of the azomethines or azo compounds listed in the Table and then warmed. After hydrolysis of the reaction mixture with water the respective imidazolidine or 1,2,3-triazolidine could be isolated. The constitution of these apparently hitherto undescribed compounds follows from analyses, molecular-weight determinations, and the NMR, IR, and mass spectra.

These reactions represent the first application of a new synthetic method for the little-studied class of imidazolidines [4] and 1,2,3-triazolidines [5].

The reactions of 1,3-diphenyl-2-azaallyllithium *(2)* with azomethines or azobenzene, with should theoretically yield



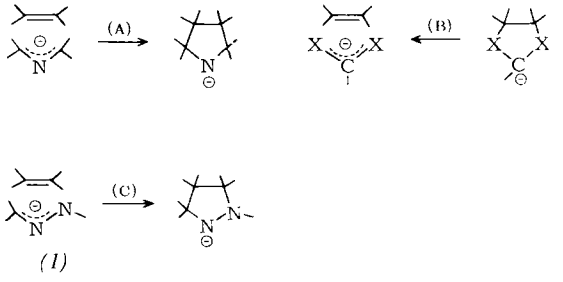
(1), R = H, R' = C_6H_5
(2), R = C_6H_5, R' = H

Anionic 3 + 2 Cycloaddition of a 1,2-Diazaallyllithium Compound[1][**]

By *Thomas Kauffmann, Dieter Berger, Björn Scheerer,* and *Annegret Woltermann*[*]

The energy barrier to be overcome in anionic 3 + 2 cycloadditions according to (A)[2] and the corresponding cycloeliminations according to (B) (X = O, S)[3] should be low since the symmetry of the π orbitals is conserved[4,5]. The direction of reaction is dictated by the arrangement of the electronegative hetero atoms: The reaction that occurs is that in which the negative charge is transferred from the carbon to more electronegative atoms.

It therefore appeared questionable whether 1,2-diazaallyl anions *(1)* can add to olefinic double bonds as shown in (C) since this would involve only slight transfer of negative charge from a carbon to a nitrogen atom because of extensive localization of the negative charge on the peripheral nitrogen atom in *(1)*.



(1)

We have now found that benzeneazomethane *(1a)* undergoes extensive (> 88%) metalation to the hitherto unknown orange-red compound benzeneazomethyllithium *(2)* on treatment with 1.1 mol. equiv. of *n*-butyllithium in THF/*n*-hexane (*ca.* 9:1) at −70 °C[6]; moreover, the anion of *(2)*, 1,2-diazaallyl anion, is able to add to the angle-strained olefinic double bond of acenaphthylene (according to (C)). Addition of water to the reaction mixture yielded the hydrolysis product *(5)*[7] of the cycloadduct *(4)*; treatment with ethyl bromide instead of water gave the dehydrogenation product *(6)* (for reaction conditions and yields, see Table).

A corresponding cycloaddition did not occur with the 1,2-bisazaallyllithium compound *(3)*, which is obtained almost quantitatively as an orange-red solution (THF/*n*-hexane, *ca.* 5:1) on reaction of benzaldehyde phenylhydrazone and one mol. equiv. of *n*-butyllithium at −70 °C. This finding, together with the fact that neither *(2)* nor *(3)* could be induced to add to styrene, *trans*-stilbene, or tolan, confirms the prediction that 1,2-diazaallyllithium compounds are less prone to 3 + 2 cycloaddition than 2-azaallyllithium compounds[2].

Addition of benzeneazomethyllithium to carbonyl compounds (see Table) leads — possibly *via* an unstable

2-Azaallyl cpd.	Azomethine or azo cpd.	Temp. (°C) [a]	Product	Yield (%) [b]	M.p. (°C)
(1)	Benzylideneaniline	20	2,2,3,4-Tetraphenylimidazolidine	43	121–122
(2)	Benzylideneaniline	20	2,3,4,5-Tetraphenylimidazolidine	52	111–113
(1)	2-Pyridinecarbaldehydeanil	20	2,2,3-Triphenyl-4-(2-pyridyl)imidazolidine	41	164
(2)	2-Pyridinecarbaldehydeanil	20	2,3,5-Triphenyl-4-(2-pyridyl)imidazolidine	54	153–155
(1)	Azobenzene	20	1,2,3,3-Tetraphenyl-1,2,4-triazolidine	43	139
(2)	Azobenzene	20	1,2,3,5-Tetraphenyl-1,2,4-triazolidine	50	190–191
(1)	*p,p'*-Azotoluene	65	3,3-Diphenyl-1,2-di-*p*-tolyl-1,2,4-triazolidine	58	139–140
(1)	3,3'-Azopyridine	65	3,3-Diphenyl-1,2-di(3-pyridyl)-1,2,4-triazolidine	10	184–186

[a] After addition of the azomethine or the azo compound to a solution of the lithium compound at −60 °C the reaction mixture was slowly warmed to the temperature given. [b] Yield not optimized.

four racemic imidazolidines or give one meso and one racemic 1,2,4-triazolidine, were found to give only one imidazolidine or triazolidine. The apparent stereospecificity strongly suggests that the cycloaddition of *(2)* to CN and NN double bonds is a concerted process, as predicted by the Woodward-Hoffmann rules[6].

It would also appear likely, from the close similarity between the CN and the CO double bond, that the reactions of 2-azaallyllithium compounds with carbonyl compounds, which leads to open-chain hydroxy azomethines[7], are also initiated by a concerted 4π + 2π cycloaddition and therefore proceed *via* a 1,3-oxazolidine-lithium compound.

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] Organo-lithium and -aluminum Compounds, Part 4. – Part 3: [2].

[2] *Th. Kauffmann, H. Berg,* and *E. Köppelmann,* Angew. Chem. *82*, 396 (1970); Angew. Chem. internat. Edit. *9*, 380 (1970).

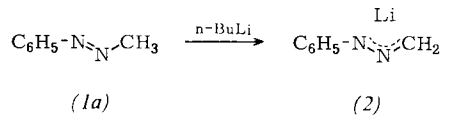
[3] The extremely reactive extra bond of dehydrobenzene is able to add allylmetal compounds in a kind of 3 + 2 cycloaddition: cf. *G. Wittig* and *E. Knauss,* Chem. Ber. *91*, 895 (1958); *C. F. Huebner* and *E. M. Donoghue,* J. Org. Chem. *33*, 1678 (1968); *W. T. Ford, R. Radue,* and *J. A. Walker,* Chem. Commun. *1970*, 966.

[4] Imidazolidines: cf. *R. J. Ferm* and *J. L. Riebsomer,* Chem. Rev. *54*, 606 (1954).

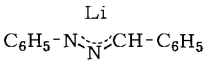
[5] 1,2,4-Triazolidines: cf. *J. Strating, W. E. Weening,* and *B. Zwanenburg,* Recl. Trav. Chim. Pays-Bas *83*, 387 (1964); *84*, 408 (1965).

[6] *R. B. Woodward* and *R. Hoffmann,* Angew. Chem. *81*, 797 (1969); Angew. Chem. internat. Edit. *8*, 781 (1969).

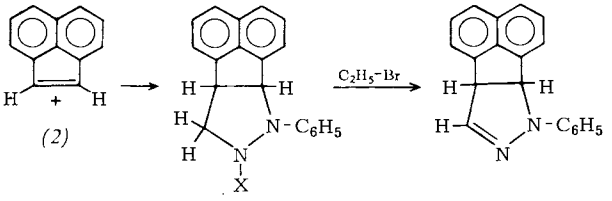
[7] *Th. Kauffmann, E. Köppelmann,* and *H. Berg,* Angew. Chem. *82*, 138 (1970); Angew. Chem. internat. Edit. *9*, 163 (1970).



(1a) (2)

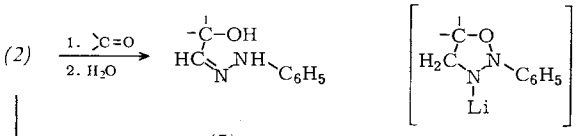


(3)

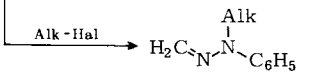


(2) (4), X = Li (5), X = H (6)

cyclic intermediate (8) — after subsequent hydrolysis with water to phenylhydrazones (7) of α-hydroxy aldehydes.



(2) (7) (8)



(9)

Reactions with alkyl halides designed to determine the content of benzeneazomethyllithium (see Table) surprisingly led exclusively to the *N*-alkylation products, *i.e.* formaldehyde (*N*-alkyl-*N*-phenyl)hydrazones (9).

Table. Reactions with benzeneazomethyllithium (2) in THF/*n*-hexane (*ca.* 9:1) at −60 °C [a].

Reactant(s) [b]	Product	Yield (%)	M.p. or refractive index
Acenaphthylene	7-Phenyl-6b,8,9,9a-tetrahydro-7*H*-acenaphtho[1,2-*c*]pyrazole	32	154 °C
Acenaphthylene ethyl bromide	7-Phenyl-6b,9a-dihydro-7*H*-acenaphtho[1,2-*c*]pyrazole	27	171 °C
n-Butanal	α-Hydroxyvaleraldehyde phenylhydrazone	47	59 °C
Cyclopentanone	(1-Hydroxycyclopentyl)formaldehyde phenylhydrazone	77	95 °C
Cyclohexanone	(1-Hydroxycyclohexyl)formaldehyde phenylhydrazone	65	105 °C
Benzophenone	Diphenylglycolaldehyde phenylhydrazone	40	132 °C
Methyl iodide	Formaldehyde (*N*-methyl-*N*-phenyl)hydrazone [c]	87	oil; $n_D^{20} = 1.6042$
Ethyl bromide	Formaldehyde (*N*-ethyl-*N*-phenyl)hydrazone	88	oil; $n_D^{20} = 1.5908$

[a] Before hydrolysis the reaction mixture was warmed to 65 °C (alkyl halides), otherwise only to +20 °C.

[b] Equimolar amounts relative to benzeneazomethane.

[c] Described by *H. H. Stroh*, Chem. Ber. *91*, 2660 (1958).

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[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

[1] Organo-lithium and -aluminum Compounds, Part 5. — Part 4: *Th. Kauffmann, H. Berg, E. Ludorff*, and *A. Woltermann*, Angew. Chem. *82*, 986 (1970); Angew. Chem. internat. Edit. *9*, 960 (1970).

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[6] The instability of formaldehyde phenylhydrazone prohibits any preparation of (2) from this compound.

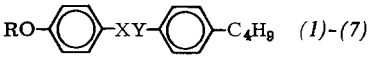
[7] The constitution of the reaction products, which, with one exception (see Table), apparently have not been described previously, follows from analyses, molecular-weight determinations, and NMR, IR, and mass spectra.

Liquid Crystalline Phases Having Particularly Low Freezing Points

By *Hans Kelker, Bruno Scheurle, Rolf Hatz*, and *Werner Bartsch* [*]

In continuation of earlier work [1,2] on the synthesis of low-melting nematogenic substances such as (1) and (2) we have prepared new azo and azoxy compounds (see Table).

For optical and electro-optical experiments, we chose azo compounds in order to obtain substances having a low



(1)-(7)

Compound	R	X Y	M.p. (°C)	Transition point (°C), behavior
(1)	CH_3	CH=N	22	47—48 (nemat.) [a] [2]
(2)	C_2H_5	CH=N	37	80 (nemat.) [2]
(3)	CH_3	N=N	32	42 (nemat.)
(4)	C_2H_5	N=N	48	81 (nemat.)
(5)	CH_3	N(O)=N	43	≥71 (nemat.) [b]
(6)	CH_3	N=N(O)	41	≥69 (nemat.) [b]
(7)	H	N=N	82	— (isotrop.)

[a] This value is valid for extremely pure (1), *e.g.* after purification by electrodialysis [3]. The value given in [2] is to be corrected.

[b] The melting and clearing points of (5) and (6) were obtained with chromatographically isolated substances (*ca.* 30 mg in each case). Since the mixed clearing point of these fractions was determined as 69—70 °C and the mixture of pure isomers before separation showed an even higher clearing point (75—76 °C), it can be assumed that the clearing points the pure components on working up larger quantities of substances of could also reach a value of 75—76 °C.

melting point and no central dipole, and azoxy compounds so as to have available compounds with a relatively high permanent moment. The new azo and azoxy compounds *(3)* - - *(6)* listed in the Table form nematic phases.

Compounds *(3)* and *(4)* were prepared by coupling of diazotized *p-n*-butylaniline with phenol; compound *(7)* is formed first and this is reacted either with diazomethane or — better — with dimethyl sulfate to give the methyl ether *(3)* or with ethyl iodide/sodium ethoxide to give the ethyl ether *(4)*. The reaction with dimethyl sulfate affords very pure *(3)* after two recrystallizations from petroleum ether.

Compounds *(5)* and *(6)* were obtained by the known[4] method of oxidation of *(3)* with 30% hydrogen peroxide in acetic acid; a mixture of isomers is formed (m.p. 19 °C, N/I transition point 75—76 °C) that can be separated chromatographically[**].

Remarkably, uniaxially oriented layers exhibit clearly defined dichroism in the IR spectra of substances *(1)*, *(3)*, *(5)*, and *(6)*. Thus, for example, in the case of *(3)* the extinction coefficient ε(isotropic) for the wave numbers 1292 and 1178 cm^{-1} is considerably higher than that of the uniaxially oriented phase $\varepsilon\perp$. The order of the ε-values is reversed at 1100 cm^{-1}, *i.e.* $\varepsilon\perp >$ ε(isotropic). Similar effects occur in the case of the other substances. Investigations on this anisotropic effect are still in progress.

The position of the O atoms in *(5)* and *(6)* was determined by mass spectrometry. Whereas in the oxidation mixture the fragmentation masses 137 $(CH_3O—C_6H_4—NO)^+$ and 163 $(C_4H_9—C_6H_4—NO)^+$ occur in the ratio of about 3:1, the component more strongly absorbed on silica gel (later eluted with methylene chloride) [*(5)*] showed the mass 137 but not $M = 163$, the other isomer [*(6)*] showed mass 163, while $M = 137$ was absent. Since each isomer forms its own nematic phase it follows that the *trans* compound is involved in each case. The ratio of the isomers occurring in the oxidation is *ca.* 60% *(5)* and 40% *(6)*.

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[**] A good separation was obtained on an SIF thin-layer chromatography plate (Riedel-de Haën) after a previous two hours' activation of the plate at 150 °C or — better — in a column under the following conditions: 25 cm V4A tube; $\varnothing_i$: 9 mm; stationary phase: silica gel Camag D—O, air-classified fraction 5—10 μm, dried at 150 °C and packed dry in the column; elution medium: methylene cloride dried over silica gel; apparatus: Siemens chromatograph S 200 with PM—IV UV detector at 350 nm; initial pressure: 9 at, flow rate: 2 ml/min. The relative retention was 1.4 with complete separation of both components.

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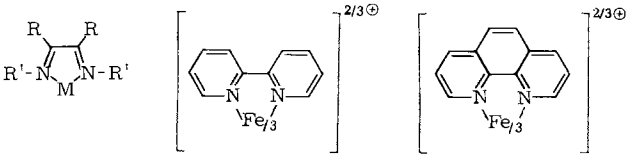
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α-Diimine-Metal Chelates: Cyclic Delocalization of π-Electrons and ^{13}C Chemical Shifts[***]

By *Christian Tänzer*, *Roger Price*, *Eberhard Breitmaier*, *Günther Jung*, and *Wolfgang Voelter*[*]

IR spectroscopic determination of the MO π-bonding order[1], as well as ^1H-NMR studies[2], indicate cyclic delocalization of π-electrons in α-diimine-metal chelates *(1)—(3)*. Since ^{13}C chemical shifts depend characteristically on the π-electron density at each C atom[3], a comparison of the chemical shifts of ^{13}C-NMR signals of some non-benzenoid aromatic compounds of known π-electron distribution with the corresponding shifts for some α-diimine-metal chelates should provide further evidence about the so-called aromaticity[1,4] of these chelates.



(1) *(2)* *(3)*

The ^{13}C signals in NMR spectra are shifted upfield by 29.9 and 46.6 ppm when, respectively, cyclopentadiene and cyclooctatetraene are converted into the aromatic cyclopentadienyl and cyclooctatetraenyl anions[3]: the opposite effect is, however, observed on conversion of cycloheptatriene into the cycloheptatrienyl cation, namely, a downfield shift of the three olefinic ^{13}C signals by 24.7, 28.9, and 35.2 ppm[3].

Comparison of the Fourier transform ^{13}C-NMR spectra of some α-diimine-metal chelates with those of the free di-

Table 1. ^{13}C shifts δ of diimines and α-diimine chelates (TMS as external standard).

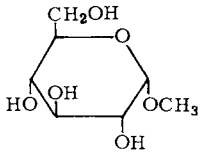
Type	Diimine / α-Diimine chelate	δ (ppm) C_α	C_β	C_γ	$\delta_{Diimine} - \delta_{Chelate}$ C_α	C_β	C_γ	Solvent
(1)	$H_2NN=CH—CH=NNH_2$	−147.75			−3.05			D_2O
	$[H_2NN=CH—CH=NNH_2]_3FeCl_2$	−150.8						
(1)	$H_2NN=C(CH_3)—C(CH_3)=NNH_2$	−150.55	− 10.6		−8.95	−6.4		$(CD_3)_2SO$
	$[H_2NN=C(CH_3)—C(CH_3)=NNH_2]FeCl_2$	−159.5	− 17.0					
(1)	$(CH_3)_3CN=CH—CH=NC(CH_3)_3$	−162.4	− 60.5	− 31.9	+3.3	+0.8	+0.75	CH_3I [a]
	$[(CH_3)_3CN=CH—CH=NC(CH_3)_3]_3Mo(CO)_4$	−159.1	− 59.7	− 31.15				
	α,α'-Bipyridyl [b]	−160.6 −154.05	−128.2 −124.75	−141.6	−3.1 −4.35	−3.75 −3.75	−1.7	$(CD_3)_2SO$
(2)	[α,α'-Bipyridyl]$_3FeCl_2$ [b]	−163.7 −158.4	−131.95 −128.4	−143.3				
	o-Phenanthroline [b]	−155.2 −150.75	−131.3 −128.0	−141.1 −133.2	−5.9 −3.35	−1.45 −2.85	−1.2 −1.15	$(CD_3)_2SO$
(3)	[*o*-Phenathroline]$_3FeCl_2$ [b]	−161.1 −154.1	−132.75 −130.85	−142.3 −134.35				

[a] TMS as internal standard.
[b] The entries in the Table refer to the signals of the magnetically nonequivalent ring carbon atoms in the α,β, or γ positions relative to the nitrogen.

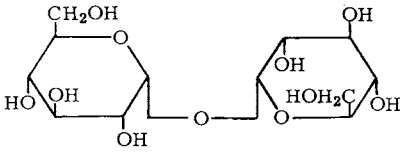
imines shows that the coordinative bonding of the metal ion to the chelating agent causes a downfield shift of all the ^{13}C signals of the ligands. The shifts increase with decreasing distance between the metal ion and the C atom responsible for the ^{13}C signal in question: the magnetic shielding of the C atom of a chelating agent is thus weakened by incorporation of a metal ion into the structure. This corresponds to a decrease in the π-electron density at each sp^2-hybridized C atom on transition of a chelating agent into a chelate, an effect that can also be interpreted as cyclic delocalization of the π-electrons in the α-diimine-metal chelate ring. The downfield shift of the ^{13}C signals on transition from chelating agent to chelate must be weakened or reversed if the metal cation in the chelate ring is replaced by a zerovalent metal, as in tetracarbonyl-α-diiminemolybdenum[2,5]. Experimentally, the ^{13}C signal of the sp^2-hybridized carbon is shifted by 3.3 ppm to higher field on conversion of *N,N'*-di-*tert*-butylethanediimine into tetracarbonyl-(*N,N'*-di-*tert*-butylethane-1,2-diimine)-molybdenum (Tabelle 1).

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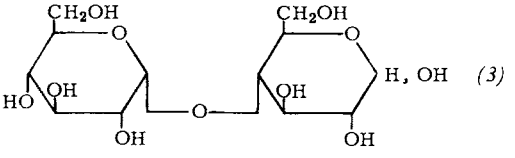
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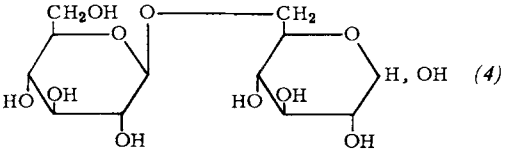
(1)



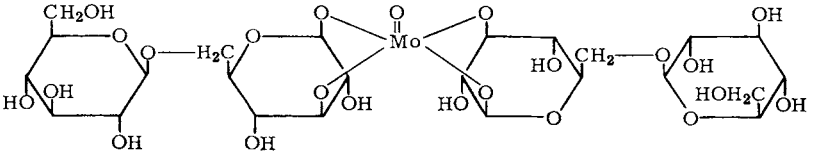
(2)



(3)



(4)



[**] *W. Voelter* thanks the Deutsche Forschungsgemeinschaft for a Habilitation grant.

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Determination of the Type of Linkage in Disaccharides by Measurement of Circular Dichroism[**]

By *Wolfgang Voelter, Gisela Kuhfittig*, and *Ernst Bayer*[*]

A problem most frequently met with in the structure elucidation of naturally occurring disaccharides is the differentiation between 6-*O*-pyranosyl and 4-*O*-pyranosyl sugars. By classical methods this entails a great deal of experimental effort: by our new method relevant information for such a differentiation can be obtained rapidly and easily. The circular dichroism spectra (CD spectra) of molybdate complexes of monosaccharides can be correlated with the configuration on C-1 to C-3 of the pyranose ring[1–3]. The results of CD investigations on disaccharide-molybdate complexes can be summarized as follows:

a) Non-reducing disaccharides, *e.g.* α,α-trehalose *(2)*, like methylglycosides[1–3], *e.g.* methyl α-D-glucopyranoside *(1)*, do not react with molybdate; consequently, molybdate-containing solutions of these sugars do not exhibit a Cotton effect at wavelengths >200 nm. Sugars of the trehalose type again demonstrate that only carbohydrates possessing free glycosidic hydroxyl groups yield molybdate complexes under the conditions given.

b) No molybdate complexes are formed in the case of 2-, 3-, and 4-*O*-pyranosyl sugars such as, *e.g.*, maltose *(3)*. Since the three hydroxyl groups necessary for complex formation with molybdate are present on C-1 to C-3 of the pyranose residue in 4-*O*-pyranosylpyranoses the reaction must, in this instance, be hindered energetically or sterically[4].

c) Molybdate-containing aqueous solutions of 6-*O*-pyranosyl-pyranoses, *e.g.* gentiobiose *(4)*, on the other hand, exhibit Cotton effect bands above 200 nm; hence, such disaccharides form molybdate complexes. Thus, a

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[4] Only pyranosyl sugars of Group I were considered (cf. [3]).

negative Cotton effect is observed at 242 nm ([Θ] = —7100) and a positive Cotton effect at 275 nm ([Θ] = 2500) in the CD spectrum of the gentiobiose molybdate complex (0.02 mole/l gentiobiose +0.04 mole/l sodium molybdate in water, adjusted to pH = 5.19 with hydrochloric acid).

The spectrum thus resembles that of D-glucose[1–3]; the glucose residue functions as the complexing agent. Furthermore, the complexing ratio, which was determined according to *Job*'s method, is also in agreement with that found for the glucose-molybdate complex (gentiobiose: molybdate = 2:1).

The CD spectrum of a disaccharide-molybdate solution thus permits the following conclusions to be drawn:

1. If a Cotton effect appears at wavelengths > 200 nm then a 6-*O*-pyranosyl sugar type is present[4].

2. If the solutions do not exhibit a Cotton effect then either a linkage of the type mentioned above in a) (trehalose type) or in b) is present. Sugars of the trehalose type can be differentiated quite easily from 2-, 3-, and 4-*O*-pyranosyl sugars by their non-reducing properties.

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CONFERENCE REPORTS

Transition between Metallic and Ionic Bonding in the Silicides of the Alkali and Alkaline Earth Metals

By *Herbert Schäfer*[*]

Intermetallic compounds of the alkali and alkaline earth metals with silicon can be classified into three groups according to structure.

a) The majority of these silicides fit into the scheme proposed by *Klemm* and *Busmann*. In the formal ionic formulation according to this concept the base metal donates electrons to the more noble partner of the alloy, the "anion former". In the phases treated here, the silicon is the electron acceptor. If N is the number of outer electrons of the Si "anion", then as many bonds participate in the anionic part of the lattice as correspond to the $8N$-rule. In those compounds in which the silicon carries a fractional charge the concept is preserved by charge sharing — according to stoichiometry — between the nearest whole number values (see Table 1).

b) The compounds most rich in alkali or alkaline earth metal form metallic lattices. $Li_{10}Si_3$ and $Li_{22}Si_5$ correspond, according to structure type (cubic, "γ-brass" type) and concentration of valence electrons (VEC) (21 : 12.4, 21 : 13.5), to Hume-Rothery phases. Cubic close-packing of the alkaline earth metal atoms occurs in Ca_7Si, Sr_7Si, and Ba_7Si.

c) The silicon atoms in K_8Si_{46}, Na_8Si_{46}, and $Na_{11}Si_{136}$ are tetrahedrally surrounded by neighbors of the same kind as in the element itself. A three-dimensional network is formed which corresponds to that found in the gas hydrates $8X \cdot 46\,H_2O$ or $11X \cdot 136\,H_2O$. The silicon atoms take up the positions of the water molecules. The alkali metal atoms are distributed in cage-like holes (pentagonal dodecahedral holes, fourteen-sided holes, sixteen-sided holes).

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Table 1. Silicides of alkali and alkaline earth metals that can be formulated ionically according to their structure.

	Formal charge on Si atom according to stoichiometry	Corresponding to an element of	Structure of silicon part of lattice	
NaSi, KSi, RbSi, CsSi, $BaSi_2$	Si^{1-}	Group V	Si_4 tetrahedron ≙ P_4 tetrahedron in white P	
$CaSi_2$ $Ca_{0.9}Sr_{0.1}Si_2$ $Ca_{0.5}Sr_{0.5}Si_2$	Si^{1-}	Group V	puckered hexagonal layer ≙ gray As	
$SrSi_2$	Si^{1-}	Group V	three-dimensional network of triple bonded Si atoms	
CaSi, SrSi, BaSi	Si^{2-}	Group VI	zig-zag chains of infinite length ≙ Se	
Li_2Si	Si^{2-}	Group VI	Si_2 dumbbells ≙ O_2	
Mg_2Si	Si^{4-}	Group VIII	anti-CaF_2 type	isolated Si atoms
Ca_2Si, CaMgSi SrMgSi	Si^{4-}	Group VIII	anti-$PbCl_2$ type	isolated Si atoms
BaMgSi	Si^{4-}	Group VIII	anti-PbFCl type	isolated Si atoms
Li_2BaSi	Si^{4-}	Group VIII	own structure type	isolated Si atoms
Li_7Si_2 ($2\,Li_4Si + Li_6Si_2$)	$Si^{3.5-}$ ($2\,Si^{4-} + Si_2^{6-}$)	Groups VII and VIII	"isolated" Si atoms and Si_2 dumbbells (≙ Cl_2 dumbbells)	
Ba_5Si_3, Sr_5Si_3, Ca_5Si_3 ($A_2Si + A_3Si_2$)	$Si^{3.33-}$ ($Si^{4-} + Si_2^{6-}$)	Groups VII and VIII	"isolated" Si atoms and Si_2 dumbbells (≙ Cl_2 dumbbells)	
Ba_3Si_4 ($BaSi_2 + 2\,BaSi$)	$Si^{1.5-}$ ($Si^{1-} + Si^{2-}$)	Groups V and VI	isolated Si_4 units of two-bonded and three-bonded Si atoms	
$Ca_{0.5}Sr_{2.5}Si_4$ [(Sr, Ca)Si_2 + (Sr, Ca)Si]	$Si^{1.5-}$ ($Si^{1-} + Si^{2-}$)	Groups V and VI	double chains (two-bonded and three-bonded Si atoms)	
Sr_4Si_7 ($3\,SrSi_2 + SrSi$)	$Si^{1.14-}$ ($6\,Si^{1-} + Si^{2-}$)	Groups V and VI	three dimensional network of two-bonded and three-bonded Si atoms	

Transfer Paths in Heterogeneous Catalysis

By *John Happel*[*]

Atomic transfer rates furnish a useful method for characterizing the structure of heterogeneous catalytic reactions. Such transfer rates may be measured by means of isotopes of appropriate elements. Reaction rate expressions may be developed from such information more effectively than by means of the usual techniques based on net reaction rates of molecular species.

Transfer of atomic species proceeds through a number of paths, each consisting of a single unbroken series of mechanistics steps whereby a given atomic species can move from a chosen reactant to a chosen product or the reverse. If we assume a steady state is attained, it is possible to make simple material balances to determine how overall transport rates are related to the velocities of individual mechanistic steps.

This concept has been applied to studies of the kinetics and mechanism of several heterogeneous catalytic reactions of industrial importance.

Studies using a differential flow type reactor were conducted in which iso- and *n*-butane were dehydrogenated over a chromia-alumina catalyst. Radioactive ^{14}C was used to trace the unidirectional rate of atomic carbon transfer. In both cases it was found possible to express the rate in the form

$$v = v_+ \left[1 - \frac{p_{H_2}\, p_{ENE}}{p_{ANE}\, K}\right]$$

where v_+ is the forward rate in terms of carbon transfer; p_{H_2}, p_{ENE}, p_{ANE} are partial pressures; K is the equilibrium constant. In the case of isobutane dehydrogenation v_+ can be expressed as a simple one term function of the Langmuir-Hinshelwood type. However, a more complicated expression is necessary for v_+ in the case of *n*-butane. A mechanistic interpretation of the data indicates that the rate controlling step or steps occur in the reaction steps involving the carbon skeleton of the species involved.

Oxidation of SO_2 was also studied in a recirculating type reactor over a vanadium pentoxide catalyst using radioactive ^{35}S as a tracer. It was not possible to express the result in the form of equation used for butanes above in which a potential factor can be separated. It appears that at low concentrations of SO_2 reactions involving sulfur are rate determining but that at higher concentrations adsorption of oxygen becomes increasingly important.

The technique should be useful in planning exploratory research for catalyst development as well as for modeling reaction kinetics.

Lecture at Stuttgart on July 9, 1970 [VB 256 IE]
German version: Angew. Chem. *82*, 959 (1970)

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Accurate MO Calculations of Chemical Reactivity

By *Michael J. S. Dewar*[*]

While the structures of molecules can be determined experimentally, there is no way of observing directly the intermediate phases in a chemical reaction. If therefore these could be calculated theoretically, the resulting treatment would serve as a practical chemical tool in the study of reaction mechanisms and chemical reactivity.

To be of practical value, such calculations must be both accurate and reliable. Since only approximate quantum mechanical treatments are available, these must first be checked against experiment for systems (*i.e.* normal molecules) where experimental data are available. Unless these properties are reproduced with "chemical" accuracy (order of magnitude of errors in dissociation energies, ±1 kcal/mole; in bond lengths, ±0.01 Å; in bond angles, ±1 °; in valence force constants, ±10 %), corresponding calculations of potential surfaces, and so of reaction paths, are meaningless. It is also necessary that the calculations should be feasible for systems large enough to be of chemical interest. Since it is necessary in such cases to calculate several thousand points on the potential surface to define the reaction path, it is essential that each calculation take seconds rather than hours, or even minutes; for otherwise the cost of the calculation is too great in relation to its chemical value.

Until recently, available procedures (*ab initio* SCF, CNDO/2, extended Hückel) failed completely to meet these requirements, the errors in dissociation energies in particular being of the order of 1000 kcal/mole. The time required for *ab initio* calculations is also utterly prohibitive; calculations of this kind have for this reason usually been carried out with assumed geometries, an unacceptable simplification which leads to gross errors.

We have now developed a semiempirical SCF MO treatment (MINDO/2) which comes reasonably close to meeting the required specifications and which has given encouraging results for a number of simple chemical reactions; *e.g.* rotational barriers in ethylene and the cumulenes, valence tautomerism in cyclobutadiene and diphenylcyclobutadiene, tub →tub inversion and bond exchange in cyclooctatetraene, chair →boat isomerization of cyclohexane, hydrogen abstraction from methane by methyl radicals, and insertion of carbon atoms into olefins to give allenes. In the latter case, our calculations account for the fact that excited (^1S) carbon atoms seem to be needed, and for the failure of the intermediate cyclopropyl carbene to rearrange if generated by other means.

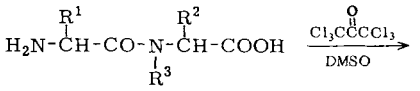
The most elaborate application so far has been to the Cope rearrangement of biallyl where we correctly predict the "chair" transition state to be more stable than the "boat" and by the right amount (calc. 6.6; obs. 5.7 kcal/mole). We also correctly predict the difference (calc. 2.0; obs. 1.5 kcal/mole) between conformers of the chair transition state with an equatorial or axial methyl substituent. Furthermore, we have established that the difference in energy between the chair and boat transition states arises entirely from an antibonding 2,5 interaction in the latter. This calculation not only reproduced the results of two extensive experimental studies but also established additional details concerning the mechanism, at much less cost (1 man month + 5 hours CDC 6600 computer time, *i.e.* <20 000 DM).

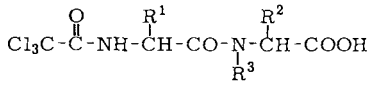
While our present procedure is far from perfect, it is also far from fully developed. This type of approach therefore seems much the most promising at present available and likely to soon become an important practical chemical tool.

Lecture at Freiburg on June 12, 1970 [VB 255 IE]
German version: Angew. Chem. *82* 960 (1970)

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The University of Texas at Austin
Austin, Texas 78712 (USA)

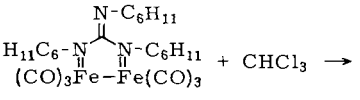
The trichloroacetylation of peptides with hexachloroacetone in almost neutral solution at room temperature has been described by *C. A. Panetta* and *T. G. Casanova*. Dimethyl



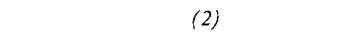


sulfoxide is used as solvent; chloroform is eliminated. *N*-Trichloroacetyldipeptides were hitherto unknown. / J. Org. Chem. *35*, 2423 (1970) / —Ee. [Rd 248 IE]

A new dichlorocarbene generator has been discovered by *N. J. Bremer*, *A. B. Cutcliffe*, and *M. F. Farona*. On refluxing dicyclohexylcarbodiimide with $Fe(CO)_6$ in heptane the authors obtained the complex *(1)* in the form of red diamagnetic crystals. The structure was proved by spectroscopic data (mass, NMR, and IR spectra) and by acid hydrolysis to $C(NHC_6H_{11})_3^{\oplus}Cl^{\ominus}$. In the presence of *(1)*,



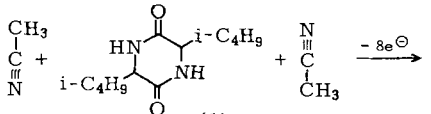
(1)



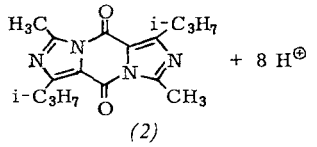
(2)

$CHCl_3$ containing 0.75% of ethanol evolves dichlorocarbene; the complex *(1)* is converted into the salt *(2)* in the reaction. The carbene can be trapped with olefins. Thus it reacts with cyclohexene to give dichloronorcarane along with isomeric products formed by insertion into the C—H bonds of C-2 and C-3. Conventionally generated $:CCl_2$ reacts differently. / Chem. Commun. *1970*, 932 / —Ee. [Rd 251 IE]

Anodically induced 1,3-cycloaddition of acetonitrile to 3,6-diisobutylpiperazine-2,5-dione *(1)* is reported by *L. A. Simonson* and *C. K. Mann*. In a particular experiment [in 0.5 M $NaClO_4/CH_3CN$, divided cell, anode potential + 2.2 V relative to $Ag/AgNO_3$(0.5 M)—CH_3CN] the only result expected was C—N cleavage, by analogy with the behavior of other amides. In fact the cycloadduct *(2)* is formed in 5 and 50% yield (relative to the amount of *(1)* used and the amount that undergoes electrochemical reaction, respectively). No monoadducts were found. / Tetrahedron Lett. *1970*, 3303 / —Ee. [Rd 252 IE]



(1)

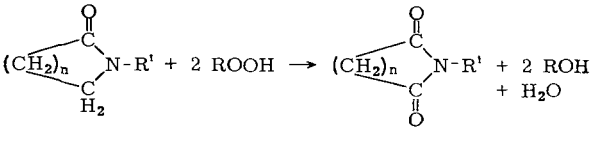


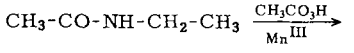
(2)

The conversion of bromo into chloro compounds with silver chlorodifluoroacetate is the subject of report by *J. A. Vida*. A mixture of the bromo compound and reagent in stoichiometric quantities is heated in a suitable solvent. Silver bromide precipitates out; the chloro compound can be isolated in good yields. For example: 1-chloroadamantane (85% yield); 1-chloro-1-phenylethane (95%); *N*-(2-chloroethyl)phthalimide (92%). / Tetrahedron Lett. *1970*, 3447 / —Kr. [Rd 254 IE]

The chlorine difluoride radical has been obtained by *G. Mamantov*, *D. G. Vickroy*, *E. J. Vasini*, *T. Maekawa*, and *M. C. Moulton* by photolysis (2800—4200 Å) of mixtures of $ClF/F_2/Ar$ or $ClF/F_2/N_2$ (molecular ratios of 1:10:100 or 1:5:300) on a CsI window cooled to 15 °K. Formation of the angular radical ClF_2 is recognized by bands at 575 cm^{-1} (N_2 matrix) and at 535 and 242 cm^{-1} in the IR spectrum which disappear completely on warming to ≈ 50 °K. The radicals either react with fluorine atoms to give ClF_3 or disproportionate to give ClF and ClF_3. / Inorg. Nucl. Chem. Lett. *6*, 701 (1970) / —Kr. [Rd 255 IE]

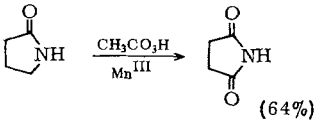
A new method for the synthesis of imides has been described by *A. R. Doumaux jr.* and *D. J. Trecker*. Hydroperoxides or peroxy acids in combination with catalytic amounts of a Mn(II) or Mn(III) salt oxidize lactams or *N*-alkylamides under very mild conditions (0 °C to room temperature, ethyl acetate) to imides (yields up to 84%). Cyclic amides and compounds bearing two substituents on the neighboring atom to the nitrogen do not react. Examples:





$CH_3-CO-NH-CO-CH_3 + CH_3CONH_2$

(58%)



(64%)

/ J. Org. Chem. *35*, 2121 (1970) / —Ma. [Rd 258 IE]

Grundlagen der analytischen Chemie (Principles of Analytical Chemistry). By *F. Seel.* Verlag Chemie, Weinheim/Bergstr. 1970. 5th Edit., 387 pp., 53 tables, plastic DM 36.—.

This is the fifth improved edition of the well-known textbook which first appeared in 1955 and which caters in particular for those chemistry students whose introductory laboratory work consists essentially of analytical inorganic chemistry, which is still the case at most universities. The author provides the reader with a detailed introduction to the principles of classical analytical chemistry, the methods of which are based on equilibria. Practical instructions are intentionally omitted. Other analytical methods like instrument techniques, which are becoming more and more important, are also purposely left out.

In the introductory chapters elementary concepts are explained and defined, and detailed treatment is given to the law of mass action. Finally, the principles of chemical reaction types are discussed in the following order with reference to the most important analytical methods: dissolution and precipitation, complex formation, acid-base reactions, and redox processes. Appropriate space has been allocated to the combination of these four types of reaction. Furthermore, special chapters have been included on the colloidal state and adsorption, ion exchangers, reactions in molten salts, potentiometric titration, electrolytic precipitation and, an important improvement on the last edition, the thermodynamic principles of analytical chemistry in aqueous solvents.

This book gives a very good introduction to the systematic treatment of the chemistry of aqueous systems.

Gerhard Geier [NB 911 IE]

Methodensammlung zur Rückstandsanalytik von Pflanzenschutzmitteln (Methods for the Analysis of Residues of Crop Protection Products). Ed. by the Abt. "Analytik" der Kommission für Pflanzenschutz-, Pflanzenbehandlungs- und Vorratsschutzmittel der Dtsch. Forschungsgemeinschaft, Bad Godesberg. Verlag Chemie, Weinheim/Bergstr. 1969. 1st Edit., 376 pp., loose-leaf DM 48.—.

This collection, which was compiled by a specialist commission of the Deutsche Forschungsgemeinschaft (German Research Association), is the first of its kind to be published in German. The methods discussed for determining residues of crop protection products in foods relate to agents selected on the basis of whether they are of "practical interest" in the Federal Republic of Germany.

An enormous number of analytical procedures for the determination of the residues of many important crop protection products have been described in the relevant literature in the last 20 years, which only goes to show that really "good" methods are rare. It should therefore be realized that the most important objective in selecting the material for the present collection was not to produce a complete survey of the literature but only to include those methods that are based on "experience gained in relevant university laboratories and in relevant Federal and industrial research institutes". Another advantage of the book is that it gives the source for each method so that in cases of doubt the author can be consulted or informed of improvements.

This highly commendable approach naturally also has disadvantages, particularly in cases where analytical techniques have undergone further development before the collection appeared. This was inevitable particularly in the case of gas chromatography which, with the development of new types of detectors, rapidly gained importance in the field of residue analysis. It is to be hoped that this collection, which is in loose-leaf form, will be suitably expanded (the first supplement is at present in preparation). Future supplements will in particular have to devote more attention, in the interests of public analysts' laboratories, to the simultaneous determination of several different residues, *i.e.* to group or "multi-residue" methods.

Particularly praise-worthy is the exemplary uniform, schematic presentation of the methods by the editors. Structural formulas and general physical data are also given for each active ingredient. The compounds are designated by their common names; trade names do not appear. In its present form the collection already provides a wealth of highly useful information, at a reasonable price, for all laboratories working on the problems of residues.

Helmut Frehse [NB 912 IE]

Handbuch der experimentellen Pharmakologie (Manual of Experimental Pharmacology). Edited by *H. Herken.* Vol. XXIV: Diuretics. Springer Verlag, Berlin-Heidelberg-New York 1969. 1st Edit., xix, 764 pp., 124 figures, bound, DM 248.—.

The editor of this volume has drawn on the services of ten prominent colleagues in the field of renal physiology and pharmacology, so that it should attract not only pharmacologists, physiologists, internists, chemists, and pharmacists but also students of medicine and the natural sciences. The fundamentals of renal physiology and diuretics are given detailed treatment in twelve chapters.

In the section "Fundamentals of Renal Physiology" the ultra-structure of the kidney is discussed lucidly with the aid of schematic diagrams and clear electron micrographs. Open questions are left open, as befits a manual of this type. The clear tables in the chemistry section of the chapter entitled "Mercurial Diuretics" have a pleasing and striking layout. Commercially available products are cited by their trivial, chemical, and trade names. [It might have been better, however, to take "Organic Chemical Drugs and their Synonyms" (*Negwer*, Berlin 1967) as a recent source book for trivial names, since it is more easily available here than *Marler* (1961); also not the possibility of confusing Diucardin and Diucardyn.] The fact that basic pharmacological investigations have been included is an asset for a handbook of experimental pharmacology.

The era of modern sulfonamide diuretics begins with the chapter "Renal Carbonic Anhydrase and the Pharmacology of Sulfonamide Inhibitors". The comprehensive data on the importance of carboanhydrase are reproduced completely, concisely, and clearly. Finally, the other diuretics having sulfonamide structures (sulfamoyl substitution) — "Thiazide Diuretics and Related Drugs" — are discussed. The table and the description of the relationships between structure and effect are very creditable. A few printing errorsi n the text and tables and in the references should be corrected.

The difference between "potency" and "efficacy" is justifiably emphasized. Perhaps it was these technical terms that induced the authors to submit their contributions in English since it is impossible to reproduce these concepts exactly in German without resorting to circumlocutions.

Furosemide and ethacrynic acid have been treated separately as diuretics with different modes of action. In the reviewer's opinion there is no justification for speaking of an ethacrynic acid type of saluretic action in both compounds, since it is well known that ethacrynic acid does not have the same effect on all animal species and it might lead to misunderstandings. The concepts of diuretic and natriuretic should, in my opinion, be supplemented by the concept of salidiuretic for diuretics with the action of furosemide or ethacrynic acid. The introductory sentences of the chapters

on furosemide and ethacrynic acid do not, on the basis of my own experience, entirely fit the real facts (for instance. notice the use of "accidentally"). The chapters on furosemide and ethacrynic acid are laid out in the same way and in clear manner. The references contain nothing later than 1967.

The mode of action and the clinical application of aldosterone antagonists (spironolactone) are explained lucidly and reference is made to the experimental procedure for the investigation of these substances. The pseudoantialdosterones which reduce K^+ elimination or retention by the kidneys are described with particular reference to the two main representatives of this group, triamterene and amiloride, whose clinical applicability has not yet been fully demonstrated (bibliography up to 1968). The diuretic uses of the glucocorticoids and the inhibitors of corticosteroid biosynthesis are described by *G. Senft* (deceased). Finally, the book deals with the use of cation exchangers as diuretics. The reviewer agrees with the editor on the important historical contribution of the chapter "Xanthine Derivatives as Diuretics".

The pleasing appearance of the printing is somewhat marred by the fact that art paper has been used only where histological illustrations are reproduced (production costs?). The editor and his colleagues have succeeded in producing a coherent and didactically well constructed book which, in addition to its uses as a handbook, will be of great value to both the student and the teacher of natural sciences.

Roman Muschaweck [NB 906 IE]

Organic Geochemistry. Methods and Results. Ed. by *G. Eglinton* and *M. T. J. Murphy*. Springer-Verlag, Berlin-Heidelberg-New York 1970. 1st Edit., xxiv, 828 pp., 246 figures, bound DM 178.—.

While biogeochemistry deals with the relation of sediments and minerals to plant and animal life, organic geochemistry concerns the characterization of organic substances as they occur in sediments and other natural environments.

The present book attempts for the first time to give comprehensive coverage to one of the youngest and most heterogeneous fields of knowledge on the fringes of organic chemistry, biology, and geology: 37 authors write about their own special fields in 31 chapters.

Chapters 2—6 present the organic chemist's approach and discuss the analytical possibilities for isolating and characterizing organic compounds: general methods, gas chromatography, mass spectrometry, isolation of kerogen and related substances from sediments and fossils.

Chapters 7—12 stress the biological and geological aspects: evolution, fossilization, sedimentology, organic substances in sediments, microbiological decomposition, and the biochemistry of the stable carbon isotopes. Chapters 13—19 give an account of the geological frequency of the classes of organic compounds most commonly occurring in sediments, hydrocarbons, fatty acids and alcohols, fossil carbohydrates, terpenoids, carotenoids, proteins, peptides and amino acids, and porphyrins.

Chapters 20—30 deal with the occurrence of certain compounds in specific geological situations: conchiolin in fossils and mussel shells, organic substances in gas occlusions in minerals, chemistry of the humic acids and related pigments, soil lipids, earth waxes, peat, Montan wax, fossil and recent kauri resins; kerogen from the Green River formation, crude oil, petroleum formation, carbon, importance of pre-paleozoic sediments in organic geochemistry.

Chapter 31 deals with the organic derivatives of clay minerals, zeolites, and related minerals.

In spite of the diverse nature of the material and the large number of authors this book provides a first survey of our knowledge of a field which in future will play an increasingly important role not only in science but also in practice.

German Muller [NB 914 IE]

Elektronenspinresonanz (Electron Spin Resonance). By *K. Scheffler* and *H. B. Stegmann*. Vol. 12 in the series Organic Chemistry Monographs. Ed. by *H. Bredereck, K. Hafner*, and *E. Müller*. Springer Verlag, Berlin-Heidelberg-New York 1970. 1st Edit., viii, 506 pp., 145 figures, bound, DM 120.—.

Electron spin resonance (ESR) spectroscopy has in recent years gained increasing importance as a physicochemical method of studying the paramagnetic properties of radicals. A monograph dealing with the use of this technique from the standpoint of the organic chemist is now available. ESR spectroscopy can be used to obtain information on the spin density distribution and the structure, as well as the dynamic behavior of radical molecules, *e.g.* in various solvents. However, the method has been used successfully for the detection of short-lived radical intermediates generated chemically or by electro-, photo-, or radiation-chemical processes.

The subdivision of the present book into two main sections is based on the realization that an introduction to the principles of ESR spectroscopy that is to be readily understandable whilst at the same time taking into account all the important recent developments in the technique should be separated from the detailed treatment of the most interesting classes of organic radicals. In adopting this subdivision it is of course necessary to reconcile oneself to repetition, since the theoretical treatment in the first part is elucidated by reference to numerous experimental results, which then appear again in the systematic section. In this way it may be possible to guide someone with limited experience, who turns to the book for the solution of practical problems, to the principles underlying the observed effects.

The chapters on dynamic effects and on electron-nucleus interactions are especially pleasing. As, indeed, in the rest of the book, extraordinary care has been taken here in citing the original literature. On the other hand, at many points opportunities have been missed for helping the reader who wishes to delve further into the subject, and who would have welcomed advice on more advanced textbooks and monographs.

The systematic section contains a chapter on organic radicals in solution, the relevant data appearing in valuable tables. Aids are given to the identification and interpretation of ESR spectra, as well as instructions for the preparation of standard radicals.

The book is well and clearly written and the general presentation is attractive. It will prove to be an essential tool not just to organic chemists but also to many others.

Klaus Eiben [NB 905 IE]

Physikalische Chemie. Teil I: Einführung in die Gastheorie, Quantentheorie, Thermodynamik (Physical Chemistry. Part I: Introduction to the Theory of Gases, Quantum Theory, Thermodynamics). By *G. M. Barrow*. Friedr. Vieweg u. Sohn, Braunschweig 1969. 1st Edit. 257 pp, 67 figures, 35 tables, paperback DM 19.80.

Gordon M. Barrow's textbook "Physical Chemistry" which is widely used in English-speaking countries, is to be published in German in three volumes. The first part, which was translated by *G. W. Herzog*, is now available. It contains an introduction to the theory of gases, the quantum theory, and thermodynamics.

The first half of the book (Chapters 1 to 4) presents an insight and an introduction into the actual principles of physical chemistry and its concepts. Some general properties and concepts are first presented with the empirical gas laws. This is followed by a discussion of the kinetic theory of gases and an introduction (confined to the barest essentials) to the constitution of matter and quantum mechanics and to classical and quantum statistics. The partition function is dealt with in rather more detail. However, it has been necessary here to

anticipate laws that are derived only in the volumes to be published later.

The second half of the book deals with thermodynamics. Though the layout differs only little from that of most textbooks on physical chemistry (first law, thermochemistry, second and third laws, equilibria), the preceding introduction to statistics is helpful, since the discussion of a thermodynamic quantity can be followed immediately by its statistical calculation.

The presentation of individual items of knowledge is deliberately avoided, and greater weight is placed instead on a detailed discussion of the laws of physical chemistry and the properties of the quantities described. This aim is reinforced by numerous examples of calculations in the text and in problems for practice at the end of each section.

The presentation and type are clear, and the illustrations are good. The book should make it easier for students to understand the thinking of physical chemistry.

Gerd Wedler [NB 899 IE]

Toxic Properties of Inorganic Fluorine Compounds. By *R. Y. Eagers*. Elsevier Publishing Company, Amsterdam-London-New York 1969. 1st Edit. x, 152 pp., bound, Dfl. 24.—.

This book differs fundamentally from the familiar Elsevier Monographs on Industrial Toxic Agents edited by *Ethel Browning* (e.g. *Pattison*: Toxic Aliphatic Fluorine Compounds, 1959). The difference is to be found not only in the external format of 6 × 9 in. as against the earlier 5 × 7½ in., but also in the approach to the subject. *Eagers* confines his attention essentially to cases of acute poisoning with inorganic fluorine compounds described in the literature, mass poisoning due to confusion between baking powder, *etc.* and fluorine compounds apparently being a subject of special preoccupation with him. An interest in history is evidenced in reports of cases of poisoning from the last century and the first half of the present one. Practically the only industrial poisonings described are those involving hydrogen fluoride. When dealing with their prevention and treatment the author also refers to more recent work. Regrettably, substances of such different toxicities as sulfur hexafluoride (MAC 1000 ppm) and sulfur pentafluoride (MAC 0.025 ppm) are referred to with merely the bare statement of these figures, whereas in the case of the latter a description should surely have been given of the fatal accidents that had occurred. Even the highly toxic boron trifluoride is no more than touched upon. Chronic and endemic fluorine poisoning (affecting the bones and teeth) is disposed of in 23 pages, and the effects on animals, insects, plants, enzymes, and bacteria in 28 pages, mainly in the form of tables. The book does have a bibliography with 730 entries (476 of them concerned with effects on animals, plants, enzymes, and bacteria!), but the authors are not arranged alphabetically and the titles of the works cited are not given. The Definition of Terms given on pages 2 and 3, which includes explanations of such items as acute, chronic, endemic, local, and systemic poisoning, makes one think that the book is intended primarily for laboratory workers, although the latter are hardly likely to be interested in the historical aspects. The industrial toxicologist will be disappointed, especially if, like the reviewer, he was expecting a continuation of the excellent Elsevier Monographs.

Heinz Oettel [NB 903 IE]

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